A Small (nano) Dose of Nanotoxicology

An Introduction to the Effects of Nanomaterials – Nanoparticles - Small Size - Big Problems?

CHE-WA Children’s Environmental Health Working Group
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www.asmalldoseof.org
www.toxipedia.org

A Cobalt nanoparticle coated with layers of graphene
A Small Dose of Toxicology 2nd Edition

Free e-book
Healthy World Press

PowerPoint slides for each chapter
Nanotox

See: www.asmalldoseof.org -- smdose
Nanomaterials

- Very Small
- Very disruptive
  (electricity, telephone, birth control …)
- Huge benefits
- Potential for huge harm
Nanotechnology

Latin from Greek *nanos* ‘dwarf’

“Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications.” http://www.nano.gov/

Multiple disciplines, including science, engineering, technology, toxicology, biomedical, government, *materials science* (manufacture / characterization)
Nano in History

4th C: The Lycurgus Cup (Rome) - dichroic glass; colloidal gold and silver in the glass allow it to look opaque green when lit from outside but translucent red when light shines through the inside.

http://www.nano.gov/timeline
13th-18th C: “Damascus” saber blades contained carbon nanotubes and cementite nanowires—an ultrahigh-carbon steel formulation that gave them strength, resilience, the ability to hold a keen edge

http://www.nano.gov/timeline
1857: Michael Faraday discovered colloidal “ruby” gold, demonstrating that nanostructured gold under certain lighting conditions produces different-colored solutions.

http://www.nano.gov/timeline
Nano in History

1936: Erwin Müller, working at Siemens Research Laboratory, invented the field emission microscope, allowing near-atomic-resolution images of materials.

http://www.nano.gov/timeline
1981: Russia’s Alexei Ekimov discovered nanocrystalline, semiconducting quantum dots in a glass matrix and conducted pioneering studies of their electronic and optical properties.

1985: Rice University researchers Harold Kroto, Sean O’Brien, Robert Curl, and Richard Smalley discovered the Buckminsterfullerene (C60), more commonly known as the buckyball, which is a molecule resembling a soccerball in shape and composed entirely of carbon, as are graphite and diamond.

http://www.nano.gov/timeline
1991: Sumio Iijima of NEC is credited with discovering the carbon nanotube (CNT). Iijima shared the Kavli Prize in Nanoscience in 2008 for this advance and other advances in the field.

http://www.nano.gov/timeline
1999–early 2000’s: Consumer products making use of nanotechnology began appearing in the marketplace

http://www.nano.gov/timeline
Nano in History

2004: Britain’s Royal Society and the Royal Academy of Engineering published Nanoscience and Nanotechnologies: Opportunities and Uncertainties advocating the need to address potential health, environmental, social, ethical, and regulatory issues associated with nanotechnology.

2011: The NSET Subcommittee updated both the NNI Strategic Plan and the NNI Environmental, Health, and Safety Research Strategy, drawing on extensive input from public workshops and online dialog with stakeholders from Government, academia, NGOs, and the public, and others.

http://www.nano.gov/timeline
Promises of Nanotechnology

**Clean Energy**
Clean, secure affordable energy
Solar panels more efficient.
Fuel cell development

**Clean Water**
Nanomaterials - detection of impurities (pollutants, microbes, etc), as well as removal of them, catalysts reduce waste water
How big is a nanometer (nm)?

- Sheet of paper is about 100,000 nm thick.
- A strand of human DNA is 2.5 nanometers in diameter.
- A human hair is approximately 80,000-100,000 nanometers wide.
- There are 25,400,000 nm in an inch.
- A single gold atom is about a third of a nanometer in diameter.
- A nanometer is a millionth of a millimeter (10^-9).
Common engineered nanomaterials

- Amorphous silica
- Carbon nanotubes
- Nanosilver
- TiO2 (nanotubes)
- Nanogold
Nanomaterials can exhibit different fundamental physical, biological, and chemical properties than their larger counterparts.

Consequences?
Classes of nanomaterials

- **Engineered nanomaterials**: Manufactured materials with engineered structure between 1 - 100 nm.

- **Incidental nanomaterials**: Materials with a structure between 1 - 100 nm produced as a by-product of a process. Examples: welding fume and diesel emission particulates.

- **Natural nanomaterials**: Materials with a structure between 1 - 100 nm that are a result of natural processes. Example: volcanic emissions, sea spray, and atmospheric gas-to-particle conversion.

- **Mimic of natural nanomaterials**: - create engineered nanomaterials. Example: Metallic Organic Frameworks (MOFs) similar structure and characteristics of volcanic ash.
Nanomaterial New Properties?

- Unusual physical, chemical, and biological characteristics at nano-scale
- Individual nanoparticles have different properties than bulk solutions
- Greater surface area/volume-potentially more reactive
- Ability to manipulate individual particles
- Surface chemicals

Consequences?
Nano Products Growing

March 2011, consumer products inventory contains 1317 products or product lines

http://www.nanotechproject.org/inventories/consumer/analysis_draft/
goods based on nanotechnology is predicted to grow from $147 billion in 2007 to $3.1 trillion in 2015
Seattle NanoMetro Map

WA 35 companies / universities working with nano

http://www.nanotechproject.org/inventories/map/
Examples

• **Hummingbird Scientific**
  Analytical instruments
  http://www.hummingbirdscientific.com/home/
  Lacey, WA 98516

• **Nordstrom**
  3LAB 'Super h' Age-Defying Serum
  An advanced treatment serum that contains Nano-Claire GY™—the world’s first cosmetic grade synthetic growth hormone $320
  http://shop.nordstrom.com/sr?keyword=nanotechnology&origin=keywordsearch

• **APEX NANOTECH, LLC**
  Gasoline additive (secret technology)
  http://www.apexnanotech.com/
  http://www.nanotechproject.org/inventories/map/
Take Precautions

Prey -- novel by Michael Crichton
Known Nano Products

- Baby Bear - With the additive of Silver Nanoparticles, our product has been **clinically proven** to fight against harmful bacteria, molds and mites.

- Baby Blanket - The fabric is made using so-called ‘nano technology’ and allows the naturally occurring metal silver to be incorporated into the material.

http://www.nanotechproject.org/inventories/consumer/browse/categories/goods_for_children/
Known Nano Products

- **Antibacterial Silver Athletic and Lounging Socks: Sharper Image® PRODUCT** “Cushioned, fitted, quarter-length sports socks knitted with a cotton material containing millions of invisible silver nanoparticles. Innovative socks are naturally antibacterial and antifungal.”

- **3XDRY® ESSEX SHIRT: Simms Fishing Products** -- “UPF 30 offers all day sun protection Fabric features a special silver-based nanotechnology -

http://www.nanotechproject.org/inventories/consumer/browse/categories/health_fitness/clothing/
Known Nano Products

- **Antibacterial Kitchenware: Nano Care Technology, Ltd.** -- Our Antibacterial tableware with nano silver coating could kill the attached bacteria and microbial in ten minutes and the effect can last for a long time even permanently and keep the surface always clean.

- **Nano-in Natural Environmental Cleaning Agent: Nano-Infinity Nanotech Co., Ltd.** -- “this Nano micelle product containing natural glycerin can completely remove any pesticide residues on fruits/vegetable, and all the oil/dirt on cutlery. Its efficient and safe cleaning power is a must for your healthy life.”

http://www.nanotechproject.org/inventories/consumer/browse/categories/food_beverage/cooking/
Known Nano Products

- **Behr® PREMIUM PLUS® Exterior Paint**: Behr® Process Corporation -- “…Nanophase’s proprietary nanoparticles are now being used in Behr’s Premium Plus Ultra paint. Nanophase’s nanoparticles not only lend the paint improved adhesion and anti-mildew properties.”

- **Samsonite® Silhouette® 11 Collection**: Samsonite – “Tricore Nylon with DuPont Nano Technology fabric protection

http://www.nanotechproject.org/inventories/consumer/browse/categories/food_beverage/cooking/
Case Study – Titanium dioxide (TiO2)

- white pigment
- Many uses - paints, coatings, plastics, papers, inks, foods, medicines, toothpastes
- cosmetic and skin care products
- strong UV light absorbing capabilities
- coated with silica or alumina
- NANO – clear instead of white
Case Study – Titanium dioxide (TiO2)

- titanium dioxide (TiO2) and zinc oxide (ZnO) rub on clear instead of white.

- “The U.S. Food and Drug Administration’s newly released sunscreen rules fail to meaningfully consider the risks posed by nanoscale ingredients, according to public interest groups including Friends of the Earth, The International Center for Technology Assessment and Consumers Union.” June 23, 2011

History –

- Hippocrates, noted beneficial healing and antidisease properties
- Silver coins in milk (1900s)
- Regulatory approval as an antimicrobial agent
- Use declined in 1940s with antibiotics

- Silver sulfadiazine – antibacterial – wound treatment – burns, external infections
- Colloidal silver as an alternative medicine treatment – no data, claims unsupported
Case Study – Silver Nanoparticles

- Silver nanoparticles of between 1-100 nm in size
- Uses - catalysis, optics, electronics, medical, water treatment, textiles, consumer products
- Silver nanoparticles are now replacing silver sulfadiazine – wound dressing

Case Study – Silver Nanoparticles

- More than 200 products -- including odor-resistant socks, baby bottles and clothes-washing machines -- are laced with specks of nanosilver

- Harms aquatic organisms
- Regulate the chemical as a pesticide
- Harms bacteria in wastewater treatment plants

- Health – allergic reaction, accumulation in liver, brain?, Argyria and staining
Nanosilver
Weighing the Risks and Benefits

Silver nanoparticles are added to a variety of textiles and home goods as an antimicrobial. Although silver has been used safely for centuries, some question whether the rapid expansion of new exposure sources to nanosilver could have adverse consequences. © Jim Filipe/Getty Images
Case Study - Quantum Dots

- Semiconductor Nanocrystals
  - Ranging in size from approximately 2 - 150 nm
  - Metalloid crystalline core
    - Zinc (Zn)
    - Cadmium (Cd)
  - Cap or shell covering core
    - Selenium (Se)
    - Tellurium (Te)
- Coating
  - Biocompatible coating
  - Functional groups
- Green Dots (no heavy metals)
  - Functional groups
- Market size $7.5 billion - 2022
Case Study - Quantum Dots

Quantum Dots and You

- **Medical imaging**
  - Cancer
  - Diagnostics
  - Therapeutics

- **Biological imaging agent**
  - “Tag” proteins
  - Monitor cellular uptake

Figure 7. Sensitivity and multicolor capability of QD imaging in live animals. Approximately 12 million QD-beads in green, yellow, and red were injected sub-cutaneously at three adjacent locations on a host animal.
Key Words

Dose / Response

Hazard \times Exposure = Risk

Individual Sensitivity
Nanotoxicology Issues

- Occupational Health
  - Workers
- Human Health
  - Consumers
  - Vulnerable – kids / elderly
- Environmental Health
  - Eco-system --- Aquatic life, Terrestrial life, Plant, Wildlife
Nanotoxicology Practical Issues

- How to properly take field (environment / work place) samples, detect, characterize, quantify
- Standard testing procedures, protocols
- Incorporating into laws, regulations
- Air quality and sediments standards as examples?
Environmental, Health, and Safety research

Who is responsible?

- National Institute for Standards and Technology (NIST)
  - Instrumentation, metrology, and analytical methods
- National Institutes of Health (NIH)
  - Nanomaterials and human health
- Environmental Protection Agency (EPA)
  - Nanomaterials and the environment
- National Institutes of Occupational Safety and Health (NIOSH)
  - Human and environmental exposure assessment
- Food and Drug Administration (FDA)
  - Risk management (also EPA)
- Consumer Product Safety Commission (CPSC)
  - xx?
Evaluation of Consumer Products
The potential safety and health risks of nanomaterials, as with other compounds that are incorporated into consumer products, can be assessed under existing CPSC statutes, regulations and guidelines. Neither the Consumer Product Safety Act (CPSA) nor the Federal Hazardous Substances Act (FHSA) requires the pre-market registration or approval of products. Thus, it is usually not until a product has been distributed in commerce that the CPSC would evaluate a product’s potential risk to the public.

“The people that research, develop, manufacture, package, handle, transport, use and dispose of nanomaterials will be those most exposed and therefore most likely to suffer any potential human health harms. As such, worker protection should be paramount within any nanomaterial oversight regime.”

WHO -- http://www.who.int/occupational_health/background_review_1.6.12.pdf
Is PPE adequate?
Individual sensitivity / vulnerability
Are MSDS sheets informative? EU and Canadian MSDS yes, not US
Transparency about use?
Regulation adequate?
High concern – inhalation – carbon nano tubes, nano-silver
Human Health

- **Products**
  - Expanding products
  - Absorption (sun screens)
  - How much of what? Right to know?
  - Weak regulation – CPSC
  - Who regulates socks / washing machines?

- **Medical**
  - Expanding products
  - FDA regulating medical uses more of a precautionary approach
  - Supplements not regulated (silver is natural)
The physical and chemical characteristics of nanomaterials that give promise, also have the potential for peril.

Effects are not well characterized.

Ultrafine particles (UFPs) generally cause more toxicity in lung models.

Reactivity of some particles increases as surface area-volume ratio increases.

Surface coatings?

Represents a very important need for research.
Environmental Health

- Persistence
- Bioaccumulation
- Release to environment
- Water / Air
- Coating
- Surface area (not weight)
Carbon Nanotubes / Asbestos

Carbon Nanotubes aligned  Carbon Nanotubes powder  Asbestos fibers

A Small Dose of Toxicology
Nanomaterial challenges

Nanomaterials synthesis

- the control of physical properties
- obtaining uniform particle size distribution
- identical shape
- morphology
- chemical composition
- crystal structure.
Cradle to Grave challenges

- Manufacture – many methods chemical coatings
- Use – consumer to industry human / environmental exposure
- Disposal / Reuse / Recycle
One of The Problems

Thousands of nanoparticle types, each having unique chemical and physical characteristics, and potentially, unique biological reactivity.
Methodological Needs

- developing methods to measure
  - nanosilver concentration
  - size
  - shape
  - surface charge
  - crystal structure
  - surface chemistry
  - surface transformations

Range of tools
Solutions

Hummingbird Scientific
http://www.hummingbirdscientific.com/home/
Analytical equipment - Lacey, WA 9851

Center for Nanotechnology at UW
The NanoTech User Facility (NTUF) established in 1998 to provide the nanotechnology community with access to advanced characterization and nanofabrication equipment
https://depts.washington.edu/ntuf

Pacific Northwest National Laboratory
Materials sciences -- http://www.pnnl.gov/

The draft foods guidance
The draft cosmetics guidance

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm300914.htm?source=govdelivery
The draft foods guidance

- Affects the identity of the food substance;
- Affects the safety of the use of the food substance;
- Affects the regulatory status of the use of the food substance;
- Warrants a regulatory submission to FDA.

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm300914.htm?source=govdelivery
The draft cosmetics guidance
safety assessment of nanomaterials when used in cosmetic products.

- Cosmetics are not subject to premarket approval; however, they must be safe for consumers under labeled or customary conditions use, and they must be properly labeled.
- Cosmetics manufactured using nanomaterials are subject to the same legal requirements as any other cosmetics. Companies and individuals who market cosmetics are legally responsible for the safety of their products.
- In general, the processes currently in use for assessing safety are appropriate for cosmetics containing nanomaterials. However, data needs and testing methods should be evaluated in light of the properties or functions that may be exhibited by nanomaterials used in cosmetic products.

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/ucm300914.htm?source=govdelivery
Nanoscale Materials
Many nanoscale materials are regarded as "chemical substances" under the Toxic Substances Control Act (TSCA). To ensure that nanoscale materials are manufactured and used in a manner that protects against unreasonable risks to human health and the environment, EPA is pursuing a comprehensive regulatory approach under TSCA. This four-pronged approach includes: Premanufacture notifications; a Significant New Use Rule; an information gathering rule; and a test rule.

http://www.epa.gov/oppt/nano/
Nanosilver

“Currently, tracking products that contain nanosilver is getting to be difficult because the products are almost always packaged under numerous brand names, and current labeling regulations do not require that the nanomaterial be listed as an ingredient.”

Assess the cradle to grave cost/risk associated with any given product

- Life Cycle Assessment (LCA)
- Comprehensive Environmental Assessment (CEA)

Risk assessment paradigm, which includes hazard identification, dose-response assessment, risk characterization and exposure assessment

European Union is implementing a new Classification, Labeling and Packaging (CLP) Regulation. CLP includes the requirement that if the form or physical state of a substance is changed, an evaluation must be done to determine if the hazard classification should be changed.

http://www.understandingnano.com/nanotechnology-regulation.html
Nike currently restricts the use of nanomaterials within apparel, footwear, and equipment product lines.

**Products to which nanomaterials are applied must:**
- Not leach or release chemicals (or particles) in order to be effective or as a result of wear, unless safety data are available and acceptable
- Meet legislative standards (globally)
- Be appropriately registered (e.g., EU Biocide Directive, if used as bacteriostatic agent)
- If registration not required: Manufacturer/supplier has made available an analysis of consumer safety
- Pass a corporate toxicity review (conducted thru the Considered Chemistry team)
- Be proven effective (for our product types)
- Comply with the Nike Corporate RSL (Restricted Substances List)

Nike Restricted Substances List (RSL) and Sustainable Chemistry Guidance (SCG)
http://www.nikeresponsibility.com/rsl
Questions / Recommendations

➢ Are nanomaterials new substances?  
  YES

➢ Transparency about use in industry and consumer products

➢ Research / Standards for sampling and assessment

➢ Fate and transport – cradle to grave

➢ Human and Environmental health effects
“As crude a weapon as a cave man’s club, the chemical barrage has been hurled against the fabric of life.”

Rachel Carson – Silent Spring (1962)
“The “control of nature” is a phrase conceived in arrogance, born of the Neanderthal age of biology and the convenience of man.”

Rachel Carson – Silent Spring (1962)
Resources

http://depts.washington.edu/envdev/nanotox/
“When an activity raises threats of harm to human health or the environment, precautionary measures should be take even if some cause and effect relationships are not fully established scientifically.”

NIRT

Nanotechnology information, reporting and tracking (NIRT) review panel

Why a NIRT

Business in WA
- Track the use of nanotechnology in WA
- Help encourage business opportunities
- Encourage Nanotech R&D, manufacturing

Human health
- Many consumer product now use nanotechnology
- How much consumer exposure
- Individual vulnerability (children?)
- Worker health and safety

Environmental health
- Consumer and manufacture use
- Consequences of environmental exposure
Additional Information

- **Web Sites**
  - The International Council on Nanotechnology (ICON) [http://icon.rice.edu/](http://icon.rice.edu/)
  - Toxipedia – Nanotoxicology - [http://www.toxipedia.org/display/toxipedia/Nanotechnology](http://www.toxipedia.org/display/toxipedia/Nanotechnology)
Authorship Information

This presentation is supplement to “A Small Dose of Toxicology”

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Public Health and the Precautionary Principle

By Steven G. Gilbert

See: http://healthlinks.washington.edu/nwcphp/nph/nwph
Precautionary Principle

“When an activity raises threats of harm to human health or the environment, precautionary measures should be take even if some cause and effect relationships are not fully established scientifically.”

Central components

• Setting goals (Health indicators)
• Taking preventive action in the face of uncertainty
• Shifting the burden of responsibility to the proponents of an activity (Who benefits?)
• Exploring a wide range of alternatives to possibly harmful actions (Is it necessary?)
• Increasing public participation in decision making (transparency of information & environmental justice)