A Small Dose of Nanotoxicology
Or
An Introduction to the Health Effects of Nanomaterials

Chapter 21
A Small Dose of Toxicology - The Health Effects of Common Chemicals

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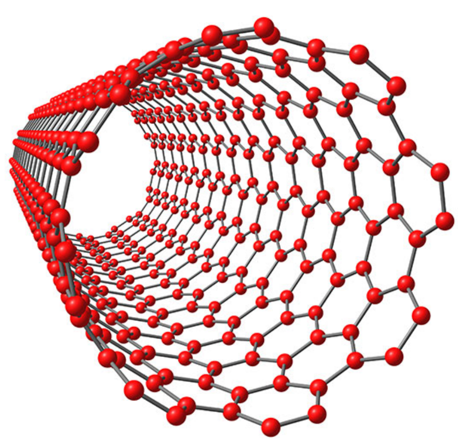
Supporting web sites
web: www.asmalldoseoftoxicology.org - "A Small Dose of Toxicology"



Carbon Nanotube – from NIOSH

Dossier

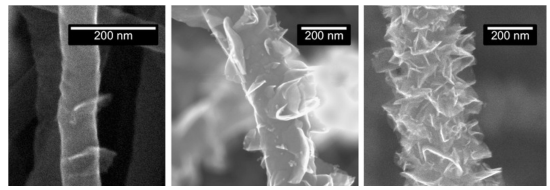
Toxicology of Nanomaterials

Name: Nanotoxicology
Definition of nanomaterials: materials sized from 1 to 100 nanometres (a nanometer is one billionth of a meter)
Use: wide range of chemicals, pesticides, plastics, flame retardants, medicine, paints, cosmetics, sunscreens, clothing, baby toys, and much more
Source: synthetic chemistry, plants
Recommended daily intake: none (not essential)
Absorption: intestine, respiratory system (lungs), skin
Sensitive individuals: fetus and children, workers
Toxicity/symptoms: endocrine system, mimic estrogen, anti-estrogenic, effects on hormone levels, sexual characteristics, reproduction, developmental effects
Regulatory facts: FDA and EPA are reviewing the use and potential hazards of nanomaterials
General facts: billions of pounds used every year in wide range of products
Environmental: widely distributed in environment and can affect wild life
Recommendations: minimize use, avoid exposure to children, and consider alternatives, expand research into toxicity, adopt precautionary approach

Case Studies

Carbon Nanotubes – Health Concerns?

Carbon nanotubes (CNTs) are typically created from one-atom-thick sheets of carbon, called graphene, that is rolled to form a hollow structure. Nanotubes can be either single-walled nanotubes or multi-walled nanotubes with a typical single-walled tube having a diameter of about 1 nanometer. CNTs are attractive to industry because they have multiple extraordinary properties including great hardness and strength, thermal and electrical conductivity, and optical properties as well as other capabilities depending on manufacture and other chemicals or elements that are added. CNTs are now common in industry processes as well consumer products such as skis, baseball bats, golf clubs, car parts, paints and others. There is a concern that CNTs may be hazardous to human and environmental health. The physical structure of nanotubes appears similar to that of asbestos fibers which appear to be long and sharp when magnified. Inhalation of asbestos can cause malignant mesothelioma a fatal lung cancer following a latency period of 20-40 years. Approximately 18,000 people died from malignant mesothelioma between 1999 and 2005. Animal studies using rodents have reported lung damage from CNTs similar to that caused by asbestos. This has important implications for people working with CNTs. The great variety in their ```size, shape, surface area, chemical coating make toxicology studies difficult to design and replicate. Some studies indicate that CNTs can cross cell walls and result in cell death.



Nanosilver

Nanosilver has many interesting characteristics but it was added to consumer products because of its antibacterial properties. Over two thousand years ago, Hippocrates (460 BC – 370 BC) acknowledged the antimicrobial and healing properties of silver. By the early 1900s the antimicrobial properties of silver were well known and used in a number of medical treatments. For example, people placed silver coins in milk to preserve its freshness. Silver sulfadiazine was used successfully to treat external infections and as an antiseptic in the treatment of burns but is now being replaced by nanosilver products. The use of silver in medicine declined with the introduction of antibiotics. Recently, the use of silver-impregnated wound dressing has increased particularly for burn patients. The ability to more easily manufacture nanosilver particles has stimulated a range of applications in consumer products to take advantage of its antibacterial properties. The products range from nanosilver-impregnated socks to baby toys, kitchen tools, paint, sunscreen, cosmetics, and water treatment, to name just a few. While nanosilver is increasingly used in industrial and consumer applications, there has not been a systematic evaluation of environmental or human health hazards. Cell-based studies clearly demonstrate that nanosilver can be toxic to a variety of organ cells, such as lung, liver, kidney, and brain. There is also evidence that nanosilver particles are readily absorbed through inhalation or skin contact. In addition, there are concerns about environmental release of nanosilver when it is washed down the drain from consumer products. The toxic properties of silver are typical of heavy metals, but the advantage was that silver appeared to minimally toxic to humans, unlike other metals such as mercury, lead, or arsenic. Silver solutions, sometimes called colloidal silver, are marketed as alternative medicines with a variety of unsubstantiated beneficial effects.

Bear toy with nanosilver

Nanomaterials in Sunscreens

The ultraviolet radiation of the sun provides an excellent lesson in dose response in which a small dose is beneficial while a larger dose (exposure) to sunlight is hazardous. A small dose of or exposure to sunlight (ultraviolet UVB wavelength of 290-315 nanometers) is important for the production of vitamin D. The result of too much exposure of unprotected skin to the ultraviolet radiation of the sun is sunburn and is also associated with skin cancer, premature skin aging, and cataracts of the eyes. Sun exposure is mutagenic, causing damage to the cellular DNA, which can lead to cancer. To protect against the undesirable aspects of sunlight you can limit exposure, wear protective clothing, or apply sunscreens to unprotected skin. Sunscreens are made up of chemicals that absorb the UV radiation or of inorganic particles such as zinc oxide or titanium dioxide or a combination that reflect the UV radiation. Typical sunscreens block the UVB that causes sunburn but do not always block UVA ultraviolet light so it is recommended to use broad-spectrum sunscreens that block both UVA and UVB. Many sunscreens use nanosized zinc or titanium in part because the material becomes transparent at the nanoscale. Thus the white titanium appears clear instead of white. Chemicals can also be applied to the small particles, to enhance their effectiveness. The concern is that the nanosized particles may be absorbed through the skin or swallowed with unknown consequences. There is also concern that the material is washed off into the environment with unknown effects on the biotic community.

Introduction and History

Nanometer one billionth of a meter (10^{-9})
From the Greek nanos or 'dwarf'
Nanoparticle 1 – 100 nanometers

"Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications."
(see www.nano.gov)

Nanomaterials or nanoparticles are generally defined as being between 1 to 100 nanometers. At this scale, the physical and chemical properties of a material can change. For example, titanium, which is usually white, becomes clear at the nanoscale. The small size of nanoparticles means that there is a much greater surface area to volume ratio, which makes the material potentially more reactive. Nanoparticles can also be coated with chemicals that can react with the environment.

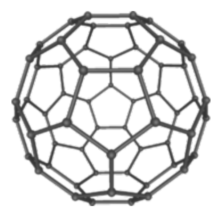
A nanometer in perspective

- 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 in diameter
- 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 (10^{-9}) of a millimeter

The use of nanomaterials dates back many centuries, when people unknowingly used them a variety of objects (see table below). For example, colloidal gold and silver was used to change the color of the glass in the Roman Lycurgus Cup, which looks opaque green but turns red when light shines from the inside. The famous steel of the Damascus swords was strengthened by carbon nanotubes that appeared during the rigorous shaping of the steel blade.

The understanding of these interesting phenomena and the emergence of the new field of nanotechnology was only possible be steady advances in technology. In 1936 the field-emission microscope, allowing the experimentally observation of atoms, was invented by Erwin Müller (1911-1977). The next major advance was in 1981 when Gerd Binnig and Heinrich Rohrer at IBM's Zurich lab invented the scanning tunneling microscope, which allowed imaging surfaces at the atomic level, resulting in the ability to "see" individual atoms. In the intervening years nanotechnology was predicted by the physicist Richard Feynman in a lecture in titled "There's Plenty of Room at the Bottom," in 1959 (reference below). He predicated that someday there would be the technology to manipulate individual atoms and molecules, something that did in fact happen. In 1985 the "buckyball" was discovered. It is a structure of carbon atoms that resembles a soccer ball in shape, though much smaller, of course (see illustration). Shortly thereafter, in 1991 carbon nanotubes were discovered, tubular in shape, very strong and with a range of interesting properties. In the late 1990s nanomaterials begin to appear in consumer products. The U.S. government took noticed and established the National Nanotechnology Initiative (NNI) to coordinate federal research and development efforts and to promote nanotechnology (http://nano.gov/). Gradually, authoritative reports advocating the need to address potential health, environmental, social, ethical, and regulatory issues associated with nanotechnology began to appear. The challenge now is to assess the consequences of human and ecological exposure to nanomaterials and balance these against the benefits.

Roman Lycurgus Cup



Milestones in Nanotechnology *

Year	Event
~300 AD	Lycurgus Cup (Rome), dichroic glass, looks opaque green but turns red when light shines from inside, the result of colloidal gold and silver in the glass. http://www.nano.gov/timeline
~600-1500	Stained glass windows in European cathedrals contained nanoparticles of gold chloride and other metal oxides
~1200-1800	"Damascus" saber blades contained carbon nanotubes and cementite nanowires
1857	Nanogold solutions can appear as different colors depending on the lighting – demonstrated by Michael Faraday (1791-1867)

1936	Field emission microscope, allowed the experimental observation of atoms - invented by Erwin Müller (1911-1977)
1959	"There's Plenty of Room at the Bottom" - first lecture on technology and engineering at the atomic scale by Richard Feynman (1918-1988) of the California Institute of Technology
1981	Scanning tunneling microscope - allowed imaging surfaces at the atomic level permitting scientists to "see" individual atoms, invented by Gerd Binnig and Heinrich Rohrer at IBM's Zurich lab.
1985	Buckminsterfullerene (C60) or buckyball was discovered by researchers at Rice University, soccer ball in shape and composed entirely of carbon.
1986	Atomic force microscope invented – provided the ability to view, measure, and manipulate materials down to fractions of a nanometer in size
1991	Carbon nanotube (CNT) – very strong, with electrical and thermal conductivity, entirely composed of carbon but in a tubular shape
1999-to?	Consumer products appeared employing nanotechnology, from cars to golf balls to paint to clothing and more
2000	National Nanotechnology Initiative (NNI) – started by President Clinton to coordinate Federal R&D efforts and promote nanotechnology (http://nano.gov/)
2004	Nanoscience and Nanotechnologies: Opportunities and Uncertainties published by Britain's Royal Society and the Royal Academy of Engineering, advocating the need to address potential health, environmental, social, ethical, and regulatory issues associated with nanotechnology
2008 updated 2011	Nanotechnology-Related Environmental, Health, and Safety (EHS) Research published by the US NNI (http://nano.gov/node/681)`
	*For a more detailed list see http://www.nano.gov/timeline

Nanomaterials in Use

There are over 1,300 identified consumer products employing nanomaterials, according to a list compiled by the Project on Emerging Nanotechnologies (see http://www.nanotechproject.org/). The products include baby toys such as a baby bear and baby blanket impregnated with nanosilver, sun screens and cosmetics, kitchen utensils, socks and shirts, paint, computer products, golf clubs and much more. Silver nanoparticles are being used in a wide variety of products to kill bacteria. Nanosilver is touted as being natural and "clinically proven to fight against harmful bacteria, molds and mites". Nanoparticles in paint are advertised to improve adhesion and provide anti-mildew properties.

Nanomaterials are also widely used in university and industry research labs studying the properties of nanoparticles and trying to find new applications.

A basic issue is determining what products or facilities are using nanoparticles, the type of nanoparticles, and the quantity. As noted by the US EPA "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 nanomaterials be listed as an ingredient." Maps that detail nanomaterials use and consumer product information are available (see http://www.nanotechproject.org/inventories/map/). Some organizations are working on a cradle-to-grave cost / risk evaluation for products using nanoparticles, that would access potential hazards across manufacture, use, and disposal (see U.S. EPA State of the Science Literature Review: Everything Nanosilver and More – August 2010 - https://www.epa.gov/chemical-research/research-nanomaterials). The European Union is implementing a new approach to nanomaterials called Classification, Labeling and Packaging (CLP) Regulation. CLP stipulates 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.

Health and Environmental Effects of Nanomaterials

Introduction

A basic principle of toxicology is that risk of harm is related to hazard, exposure, and individual sensitivity. The assessment of any of these parameters is complicated by the large variety of nanoparticles and nonmaterials, and the unique characteristics related to a nanoparticles small size and large surface area, which changes physical properties, as well as other applied chemicals. In addition, procedures for the analytical measurement of specific nanoparticles must be developed and validated for a variety of media such air, water, soil, tissue, blood or urine. Consideration must be given to other characteristics of the nanoparticles beyond just concentration to include size, shape, surface charge, crystal structure, surface chemistry, surface transformations, and chemical coatings. Most importantly the small size and the large surface area to volume ratio means that nanomaterials have unique physiochemical properties compared to materials of the same kind only larger. The challenge is determining how the nanomaterials interact with biological systems. The classic questions of persistence and bioaccumulation in animals, humans, or the environment must also be addressed. The development of a standard set of procedures to assess the potential hazards of nanoparticles is urgently needed (see papers by Maynard et al. 2006 and 2011). Below are examples of the challenges associated with addressing the nanotoxicology of specific nanoparticles.

Distribution, exposure, and absorption

Given the wide range of products using or incorporating nanomaterials there is a growing distribution and potential for exposure to nanomaterials. In some products the nanomaterials are tightly bound or are a structural part of the product and thus not bioavailable. In products such as sun screens, however, the nanosized titanium dioxide or zinc oxide are applied to the skin where there is the potential for dermal absorption or oral ingestion. A variety of cosmetics are now employing nanomaterials, which increases the possibility of absorption through the skin. Breaks in the skin, sunburn, eczema, rashes, condition of skin, cut or scrape, or age of skin can accelerate absorption of the nanoparticles into the blood stream. There is also concern that these materials can be washed off the skin into the environment. There are similar concerns with nanosilver when used a bactericide because the nanomaterials must be bioavailable to be affective. Nanosilver particles may turn up in the water waste-stream and affect sewage treatment.

The manufacture of nanomaterials or their use in product manufacture presents important challenges for occupational exposure. For example, the inhalation of carbon nanotubes my result in damage to lung tissue and possibly lead to lung cancer as occurs with the inhalation of asbestos fibers. There have been calls for greater monitoring and control of potential exposure to nanotube materials. The unintended production of nanomaterials in diesel exhaust or soot (combustion-derived nanoparticles) can be a serious hazard to workers or those near the source of the exhaust, such as trucks, trains, or ships. The small size of these nanomaterials means that they can move deep into the lungs, resulting in acute effects such as asthma or long term damage. The nanoparticles can carry other chemical contaminants on their surface, such polycyclic aromatic hydrocarbons (PAHs), deep into the lungs.

Ultimately, there must be more information on the manufacture, use, fate, and transport of nanomaterials to better assess human exposure and ecological distribution of nanomaterials.

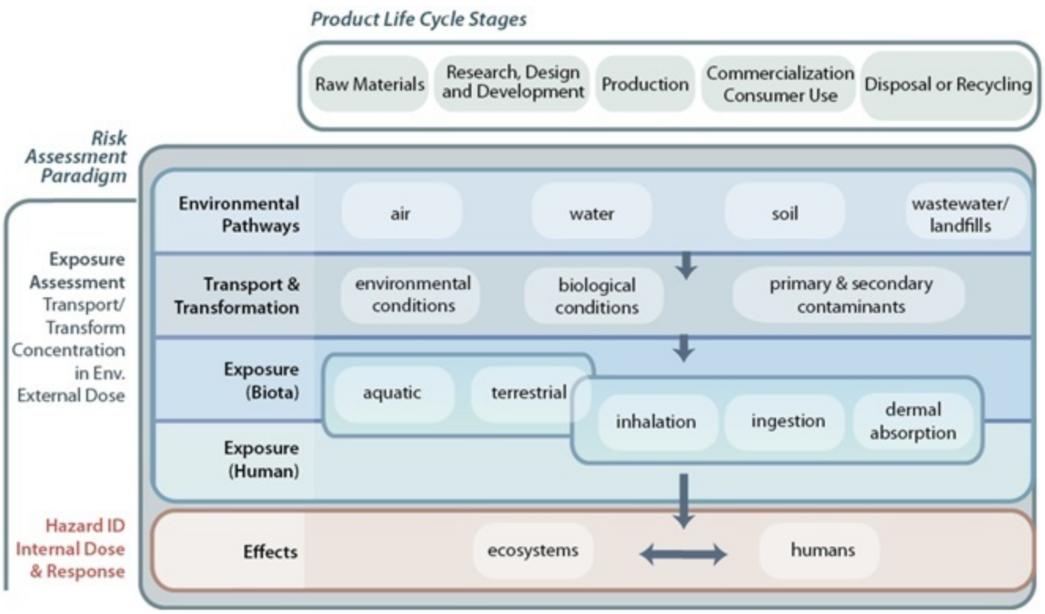
Health Effects

The potential health effects of nanoparticle exposure to humans or other organisms are just beginning. Studying the toxicity of nanoparticles is complicated by a host of factors such as the variety of substances, variation in size and surface area, chemical charge, chemical coating and other factors. An additional challenge is developing the analytical methodology for measuring the amount of nanomaterials in the tissue or biological fluid, to permit the assessment of tissue distribution or even cellular exposure. There are similar problems in evaluating distribution of the nanoparticles in the environmental media of air, water, or soil. It is known, that once in the body, nanoparticles can distribute into all organs and cross cell boundaries. Once inside the cell, the nanoparticles may interact with cellular DNA or cell proteins, thus interfering with normal cell function or resulting in an inflammatory response. An area of some study is the ability of nanoparticles to increase the production of reactive oxygen species (ROS), including free radicals, which can result in oxidative stress, inflammation and other cellular damage. It should be remembered that nanosilver is useful precisely because it kills bacterial cells. Little is known about potential immunological effects of nanoparticles other than some reports of allergic response to nanosilver particles. Studies in fish exposed to nanoparticles in the water indicated that the nanoparticles were readily absorbed and caused brain damage and affected the liver. The consequences of ecological exposure to small organisms is poorly studied and could be significant because for a small organism a small exposure represents a big dose and potential serious consequences.

Persistence and bioaccumulation of the various nanomaterials in their many forms, shapes, and coating is not well understood. There has been very little study on the potential developmental effects of nanomaterial exposure. In summary, there are many challenges to assessing the risks of nanomaterials to human health or the environment and a lot more research needs to be done. The history of toxicology is replete with examples in which the application of technology got ahead of the understanding and/or regulation of its health and environmental effects. The results of some of these cases have been devastating.

Evaluation summary

The chart below from nano.gov provides a good summary of the challenges and areas of concern.



from: http://nano.gov/you/environmental-health-safety. The risk assessment paradigm (on left) integrated with nanomaterial life cycle stages (across top). (Design credit: N.R. Fuller of Sayo-Art.)

Reducing Exposure

Reducing exposure is predicated on knowing if there is exposure. It is currently very difficult even to know if there are nonmaterials in a given product. When they are present, their potential bioavailability may be unknown. As a result, exposure cannot be predicted or quantitively evaluated.

Regulation of nanotechnology

Currently there is no comprehensive regulation that addresses industrial process or consumer products that use nanomaterials or nanotechnology. Despite the rapid increase in the use nanoparticles in consumer products from socks to sunscreens and the potential for human and ecological exposure there is no consistent approach or requirement to evaluate potential hazardous effects. The US EPA is struggling to adapt the 1976 Toxic Substances Control Act (TSCA) to address the potential hazards of nanoparticles. The U.S. Food and Drug Administration (FDA) is challenged to address the use of nanomaterials in products it regulates, such as foods, cosmetics, drugs, devices, and veterinary products. The FDA has released draft guidance related to nanotechnology applications in cosmetics and food substances (see reference below). The laws governing the Consumer Product Safety Commission do not mandate pre-marketing product approval, thus the CPSC can only address potential risk after public distribution of the product. The statement below is a good reminder of the problems faced by regulatory agencies as they try to address the use of nanomaterials. The workplace is an area of potentially high exposure to nanomaterials through inhalation, ingestion, or dermal exposure. The US Occupational Safety & Health Administration (OSHA) and National Institute for Occupational Safety and Health (NIOSH), that regulate and research occupational health and safety issues, attempt to address workplace exposures. For agencies and consumers, the failure to require adequate labeling of the use nanomaterials makes health assessments very difficult.

> Consumer Product Safety Commission
>
> 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.
>
> CPSC Nanomaterial Statement -
> http://www.cpsc.gov/LIBRARY/CPSCNanoStatement.pdf

A basic issue is determining what products or facilities are using nanoparticles, the type of nanoparticles, and the quantity. As noted by the U.S. EPA "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 nanomaterials be listed as an ingredient." Maps that detail nanomaterials use and consumer product information are available Some organizations are working on a cradle to grave cost / risk evaluation for products using nanoparticles that would access potential hazards across manufacture, use, and disposal (see US EPA State of the Science Literature Review: Everything Nanosilver and More – August 2010 - https://www.epa.gov/chemical-research/research-nanomaterials). The European Union is implementing a new approach to nanomaterials called Classification, Labeling and Packaging (CLP) Regulation. CLP stipulates 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.

Recommendation and Conclusions

Nanomaterials have interesting properties and have tremendous potential in many areas. Their use in industrials processes and consumer products is expanding rapidly. The huge challenge is making sure we understand the potential risks and that we properly balance the risks and the benefits. More research is needed on the potential human and ecological effects of nanomaterials. It is critical that our understanding and mitigation of potential adverse effects does not fall substantially behind the use of these materials.

More Information and References

Slide Presentation

- A Small Dose of Nanotoxicology presentation material and references online: www.asmalldoseoftoxicology.org
  Web site contains presentation material related to the health effects of nanomaterials.

European, Asian, and International Agencies

- Nanowerk - http://www.nanowerk.com/ (accessed 10 October 2020) – Food Safety - http://www.nanowerk.com/spotlight/spotid=25256.php
  Committed to educate, inform and inspire about nanosciences and nanotechnologies..

- World Health Organization - WHO Food Safety – Nanotechnology – “State of the art on the initiatives and activities relevant to risk assessment and risk management of nanotechnologies in the food and agriculture sectors”. FAO/WHO technical paper 9 September 2013. Report Online: (accessed 14 October 2020)

North American Agencies

- The National Nanotechnology Initiative (NNI) Online at http://nano.gov/ (accessed: 14 October 2020)
  U.S. Government Initiative on Nanotechnology is a federal R&D program established to coordinate the multiagency efforts in nanoscale science, engineering, and technology.

- The National Nanotechnology Initiative (NNI) Timeline Online at http://www.nano.gov/timeline (accessed: 14 October 2020)
  U.S. Government Initiative on Nanotechnology time line of milestones in the development of nanotechnology.

- NASA Ames Center for Nanotechnology. Online at https://www.nasa.gov/centers/ames/research/technology-onepagers/ames_nanotech.html (accessed: 14 October 2020)
  Started in early 1996 the research work focuses on experimental research and development in nano and bio technologies (also great images).

- Nanotechnology at PNNL. The Pacific Northwest National Laboratory (PNNL), operated by Battelle for the U.S. Department of Energy. Online at http://www.pnl.gov/nano/ (accessed: 14 October 2020).
  Overview of nanoscience, nanoengineering and nanotechnology.

- Understanding Nanotechnology - http://www.understandingnano.com/ (accessed: 14 October 2020) also Regulation of Nanotechnology Materials and Productshttp://www.understandingnano.com/nanotechnology-regulation.html
  Web site dedicated to making nanotechnology concepts and applications understandable by anyone. Website is owned and published by Hawk's Perch Technical Writing, LLC.

- US EPA State of the Science Literature Review: Everything Nanosilver and More – August 2010Online: https://www.epa.gov/chemical-research/research-nanomaterials (accessed: 14 October 2020).

- US FDA Nanotechnology: Science and Research. Online: https://www.fda.gov/science-research/science-and-research-special-topics/nanotechnology-programs-fda (accessed: 14 October 2020).

- US OSHA Nanotechnology - Department of Labor - Occupational Safety & Health Administration (OSHA) - Online at http://www.osha.gov/dsg/nanotechnology/nanotechnology.html (accessed: 14 October 2020).
  Address worker safety and health issues related to the use or production of nanomaterials.

- US NIOSH Nanotechnology - Centers for Disease Control and Prevention - The National Institute for Occupational Safety and Health (NIOSH) - : http://www.cdc.gov/niosh/topics/nanotech/ (accessed: 14 October, 2020).

Does research on worker safety and issues related to the use or production of nanomaterials.

- The Center for Integrated Nanotechnologies (CINT) at Sandia National Laboratories is a Department of Energy/Office of Science Nanoscale Science Research Center (NSRC). Online at http://cint.lanl.gov (accessed: 14 October, 2020).
  "Our vision is to become a world leader in nanoscale science by developing the scientific principles that govern the design, performance, and integration of nanoscale materials."

Commercial / For profit Organizations

- Nanotechnology Now (NN) http://www.nanotech-now.com/ (accessed: 14 October, 2020) Nanotechnology Glossary http://www.nanotech-now.com/nanotechnology-glossary-N.htm
  NN was created to serve the information needs of business, government, academic, and public communities. And with the intention of becoming the most informative and current free collection of "nano" reference material.

Non-Government Organizations

- Nano-silver policy failure puts public health at risk by Friends of the Earth. Sept. 2011. Online at http://www.foe.org/news/archives/2011-09-nano-silver-and-bacterial-resistance (accessed: 14 October, 2020).
  A critical look at the use of nanosilver materials in a consumer products.

Wikipedia

Nanotoxicology – Online: https://en.wikipedia.org/wiki/Nanotoxicology. (accessed: 14 October 2020).
Nice summary of the intersection of nanomaterials and toxicology.

Nanotechnology – Online: https://en.wikipedia.org/wiki/Nanotechnology. (accessed: 14 October 2020).
Overview of nanotechnology and access to many wiki based articles on Nanotechnology.

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- Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials. DHHS (NIOSH) Publication Number 2009-125. March 2009. http://www.cdc.gov/niosh/docs/2009-125/pdfs/2009-125.pdf (accessed: 14 October 2020).

- A Research Strategy for Environmental, Health, and Safety Aspects of Engineered Nanomaterials - National Academy of Sciences ISBN-10: 0-309-25328-4 free as pdf Online: http://www.nap.edu/catalog.php?record_id=13347 (accessed: 14 October 2020).

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Andersen , Dermont C. Bouchard , Robert M. Burgess , Elaine A. Cohen Hubal , Kay T. Ho , Michael F. Hughes , Kirk Kitchin , Jay R. Reichman, Kim R. Rogers, Jeffrey A. Ross , Paul T. Rygiewicz, Kirk G. Scheckel , Sheau-Fung Thai, Richard G. Zepp & Robert M. Zucker (2017): A comprehensive framework for evaluating the environmental health and safety implications of engineered nanomaterials, Critical Reviews in Toxicology. To link to this article: http://dx.doi.org/10.1080/10408444.2017.1328400.

- Nanosilver: Weighing the Risks and Benefits. Environmental Health Perspectives. volume 121 | number 7 | July 2013. http://dx.doi.org/10.1289/ehp.121-a220.