

# **Human Health and Nanomaterials in Consumer Products**

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Literature Review  
for the Region of Peel's Public Health Unit

By  
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The views expressed in this report are the views of the author and not necessarily those of the Region of Peel or its Public Health Unit.

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## Glossary of Key Terms

**Agglomerate** a collection of particles held together by weak forces resulting in a smaller external surface area than the surface area of its components.

**Aggregate** a collection of particles that are strongly bonded or fused together resulting in a smaller external surface area than the surface area of the component particles.

**Argyria** is a condition caused by the ingestion of elemental silver, silver dust or silver compounds that causes the skin and mucous membranes to permanently turn blue or bluish grey.

**Catalyst:** A substance, usually used in small amounts relative to the reactants, that modifies and increases the rate of a reaction without being consumed or changed in the process.

**Cytotoxicity** refers to the degree to which something is toxic to living cells.

**Engineered Nano-object or Nanomaterial (ENM)** is a nanoscale material that is deliberately engineered by man.

**Exposure assessment:** The determination or estimation (qualitative or quantitative) of the magnitude, frequency, timing, duration, route, and extent (number of people) of exposure to a chemical, material, or microorganism.

**Incidental or Natural Nanomaterials** are the by products of human activity, such as combustion, welding, or grinding or those that are produced naturally from forest fires and volcanoes.

**Nanotechnology** The application of scientific knowledge to control and utilize matter at the nanoscale where size related properties and phenomena emerge.

**Nanoscale** refers to having one or more dimensions in the size range of 1 - 100 nanometres.

A **nanometre** (nm) is one billionth of a metre.

**Nano-objects or nanomaterials** are materials with one, two or three dimensions in the range of 1-100 nanometres, which exhibit novel characteristics compared to the same material in its bulk form. (ISO, 2008)

**Nanoplates or nanolayers** are materials with one dimension in the nanoscale but are extended in the other two dimensions to form thin films or surface coatings (ISO, 2008).

**Nanofibre** is a nanoscale material with two dimensions less than 100 nm and is extended in one direction (ISO, 2008).

- **Nanorod** is a nanofibre with the shape of a solid rod.
- **Nanotube** is a nanofibre with the shape of a hollow tube.

- **Nanowire** is a nanofibre which conducts electricity.

**Nanoparticles** are materials that are nanoscale in three dimensions and have a shape similar to a ball (ISO, 2008).

**Nanoproduct** is a product that incorporates a nano-object.

**Nanoscaffold** a very fine lattice or scaffold made of nanoscale polymer fibres which act as a guide for cells to grab onto so they can begin to rebuild missing bones and tissue. The tissue grows through tiny holes in the scaffold. After the body part has regenerated, the scaffold breaks down, is absorbed into the person's body and disappears entirely.

# Human Health and Nanomaterials in Consumer Products

## 1.0 Project Purpose and Methodology:

### 1.1. Purpose:

The purpose of the literature review is to provide Peel Regional Public Health officials with an objective overview of the scientific research and results reported in the literature with respect to the impact of engineered nanomaterials on human health. The nanomaterials include those that have been developed or are being developed for use in consumer products such as food, cosmetics, drugs, general consumer products. This review will focus on the scientific results and the gaps in the scientific knowledge related to hazard identification and characterization, the potential of exposure to nanomaterials and the potential impact on human health. The literature addressing the safety assessment of these materials and oversight of the technology by governments and industry will also be reviewed.

### 1.2. Methodology:

#### 1.2.1. Literature Review Search Plan:

Sources: Review papers, referred journal articles, reports by government agencies and task forces, conference proceedings, reports by NGOs.

Key words: nanotechnology, nanomaterials, nanoparticles, health impacts, exposure, risk assessment, consumer products, cosmetics, drugs, food

Focus of search will be on review papers related to key words.

Internet Search Engines: PubMed, Google, Google Scholar,

#### 1.2.2. Criteria

*In assessing each piece, consideration will be given to:*

- The relevancy of the document to the subject,
- The author's credentials,
- Whether or not the author's arguments are supported by evidence (e.g. primary historical material, case studies, narratives, statistics, recent scientific findings),
- Whether or not the perspective presented is even-handed or prejudicial. (I.e. is contrary data considered or is certain pertinent information ignored to prove the author's point).
- Are the author's arguments and conclusions convincing?
- Does the work ultimately contribute to an understanding of the subject?

### 1.2.3. Search Plan:

#### **Web sites Specifically Related to Nanotechnology and Health**

These included sites such as International Council on Nanotechnology's data base on nanotechnology, Safenano, Woodrow Wilson International Center for Scholars' Project on Emerging Nanotechnologies, and Institutes, Universities and Organizations carrying out research and projects in the field of nanotechnology such as:

- (1) Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies
- (2) International Council on Nanotechnology's data base on nanotechnology
- (3) US National Initiative on Nanotechnology
- (4) Safenano
- (5) Royal Society and the Royal Academy of Engineering
- (6) UK Institute of Nanotechnology
- (7) Michigan State University, Institute for Food and Agricultural Standards
- (8) University of Toronto, Energenius Centre for Advanced Nanotechnology
- (9) University of Waterloo
- (10) National Institute of Nanotechnology of Canada

#### **Government Agencies and Quasi Government Organizations**

- (1) Commission of the European Communities
- (2) NIOSH Nanotechnology Research Center
- (3) US Environmental Protection Agency
- (4) US Food and Drug Administration
- (5) US Consumer Product Safety Commission
- (6) US Interagency Working Group on Nanoscience, Engineering and Technology, National Science and Technology Council
- (7) Health Canada
- (8) Environment Canada
- (9) Industry Canada
- (10) National Research Council
- (11) OECD
- (12) UN Organizations
- (13) WHO
- (14) ISO and British Standards Institute

#### **Consumer Organizations and NGOs**

- (1) Environmental Defence League
- (2) Consumer Union
- (3) Consumers Council of Canada
- (4) ETC Canada
- (5) Friends of the Earth
- (6) Greenpeace
- (7) Canadian Institute for Environmental Law and Policy

## 2.0 Introduction:

Nanotechnology is an emerging technology that involves manipulating substances at the nanoscale to create new classes of materials with novel and unique properties. These unique materials are commercially very useful and are being applied in many diverse sectors such as medicine, consumer products, food, agriculture, environment, energy, electronics and building materials. Currently, a number of products that Canadians buy from retail stores or order over the internet are enhanced by engineered nanomaterials. These engineered nanomaterials when added to products result in clothes that resist stains, socks that reduce odour producing micro-organisms, windows that never need cleaning and sports equipment that is much stronger and lighter. More importantly, are the products under development that have the potential to remove bacterial or chemical contamination from drinking water, to identify contaminated food products, to produce energy more efficiently, to diagnose disease and to deliver cancer drugs directly to the cancer cell reducing severe and painful side effects (UK RS/RAE , 2004).

The same unique properties that have the potential of providing so many significant benefits may also pose unanticipated risks to human health. Many scientists (Maynard, 2006a) (Stern & McNeil, 2008), governments (EC/HC, 2007) (E.C, 2004) and NGOs (ETC, 2005) (ICTA, 2007) have raised such concerns. Efforts are underway by scientists and governments to identify the exact impact of these materials and to ensure that any negative impacts on human health are effectively managed (Tigner, 2008)(EC/HC, 2007) (EC, 2004) (Maynard, 2006a).

The deliberate engineering and manufacturing of nanomaterials by humans was not envisioned until 1959 when Richard Feynman presented the idea that the manipulation of atoms and molecules could result in new technological advances (Feynman, 1959). It was not until the invention of powerful microscopes twenty years later that the development of engineered nanomaterials started to become a reality (CCA, 2008). However, the exposure of humans to nanoscale materials is not a new event. Nanoparticles have existed naturally for thousands of years in smoke from forest fires and as salt crystals in ocean air or, more recently, as incidental by products of cooking, heating and driving (UNESCO, 2006). In fact, nanotechnology has been used for many years in manufacturing without industry being aware that the desired properties were due to the presence of nanomaterials. When carbon black was added to tires, tire abrasion from the road was reduced but no one realized that the improved tire quality was due to enclosed ultra-small particles in the carbon black (Swiss Re, 2004).

### 2.1. What is Nanoscience and Nanotechnology?

Over the past ten years, many influential studies and reviews of nanotechnology have been published by the Royal Society and Royal Academy of Engineering of the UK (UK RS/RAEng, July 2004); Swiss Re one of the world's largest reinsurers (Swiss Re, 2004), the OECD in partnership with Allianz's insurance research group (OECD; Allianz, 2005), the Woodrow Wilson International Center for Scholars (Maynard, 2006 a) (Maynard, 2006 b) and by the Council of Canadian Academies (CCA, 2008). All of these reviews defined, described and explained matter created on the nanoscale and the reasons for its novel properties in the same way as described in this section.

**Nanoscience** involves research to discover new behaviours and properties of materials

with dimensions at the nanoscale which ranges roughly from 1 to 100 nanometres (nm) (NNI, 2008).

**Nanotechnology** refers to the application of scientific knowledge to control and utilize matter at the nanoscale where size related properties and phenomena emerge.

Other terms have been defined in a standard recently published by the International Standards Organization's Technical Committee on Nanotechnology (ISO, 2008 a)

**Nanoscale** refers to having one or more dimensions in the size range of 1 - 100 nanometres.

A **nanometre** (nm) is one billionth of a metre.

**Nano-objects**, often called **nanomaterials**, are materials with one, two or three dimensions in the range of 1-100 nanometres, which exhibit novel characteristics compared to the same material in its bulk form. For example, materials can have one dimension in the nanoscale but be extended in the other two dimensions to form thin films or surface coatings that are called nanolayers or nanoplates. If the nanoscale material has two dimensions less than 100 nm and is extended in one direction, it is defined as a nanofibre. Nanofibres can take the shape of a solid rod (nanorod), a hollow tube (nanotube) or conduct electricity (nanowires). Materials that are nanoscale in three dimensions and have a shape similar to a ball are called nanoparticles.

The preparation of nanomaterials normally involves either a "bottom up approach" such as chemical synthesis or self assembly where atoms or molecules arrange themselves into ordered nanoscale structures or by a "top down approach" such as grinding, etching or milling processes that reduce the size of a larger material. They also can be made from nearly any substance and their properties are dependent not only on their chemistry but also on a number of other characteristics such as size and structure. The most common substances used to produce nanomaterials are carbon, silver, silicon, silicate, titanium and various metals or metal oxides (OECD; Allianz, 2005) (Maynard, 2006b) (Powell & Kanarek, 2006). Usually, nanomaterials are not used by themselves but as raw materials, ingredients or additives to enhance the properties of other products.

The engineering of a common substance at the nanoscale level results in a material whose physical and/or biological properties differ significantly from those in its bulk form. They are normally more chemically reactive and display different electrical, optical and physical/mechanical properties. According to experts, the unique properties of nanomaterials are attributed to many factors such as particle size and size distribution, agglomeration state, shape, crystal structure, chemical composition, surface area, surface chemistry, surface charge, and porosity (Oberdoerstor & al, 2005) (EFSA, 2008). But the two principal factors are size and quantum effects as explained below (EPA, 2007) (Swiss Re, 2005). First of all, very small particles have a greater surface area compared to the same amount of material in its larger form. As a large form of a substance changes into smaller particles, its surface area increases while its mass and volume remain the same. The result is a greater proportion of atoms and molecules not being fully bonded on the surface of the particles. Since the surface is where contact is made with other substances and chemical reactions occur, the larger the surface area and the greater proportion of molecules or atoms on it mean that the chemical reactivity of the material dramatically

increases. Secondly, as materials become smaller especially in the range of 20 nm or less, the electronic nature of the substance changes. This change in the internal electronic properties alters the optical, electrical and magnetic properties and it is said that quantum effects rather than classical physics start to dominate. Quantum mechanics is a collection of natural laws which describe the behaviour of subatomic particles, such as electrons, protons and neutrons. The term 'quantum' indicates that the particles can only exchange discrete amounts of energy. For example, when the size of gold is in the nanoscale range, quantum effects lead to changes in its optical properties such that its colour changes as its size becomes smaller. This effect allows it to be used in pregnancy tests and imaging technologies (CCA, 2008).

In addition to the impact of size, the shape of the nanomaterial, such as whether it is a sphere, tube or film, and how it is used with other materials may also affect its properties (Oberdorster & al, 2005) (Oberdorster, 2008) (Maynard, 2006b). The impact of the shape on the toxicity of nanomaterials is for the most part unknown although initial work suggests that the shape of nanomaterials may affect the deposition and absorption in the body. For example, the results of a recent *in vitro* cytotoxicity study appear to suggest that single-wall nanotubes are more toxic than multi-wall nanotubes (Jia et al, 2005).

Materials created by nanotechnology can start with molecules or atoms, such as carbon, titanium or gold, and be produced in various shapes to be added to consumer products. For example, carbon in the form of nanotubes is added to other materials to improve their strength or the clarity of display screens. The behaviour of the nano-enhanced material cannot be predicted solely from the chemical make-up of the added nanomaterial, its size or from its shape, because the structure and properties of the material to which it is added will have a major effect on its final properties (SCENIHR, 2006).

The unique properties which provide so many potential benefits could also mean that the same nanomaterials could pose new risks to humans and the environment. (Maynard, 2006b) Due to their increased reactivity, the toxicity of nanomaterials may be very different than the larger substance. It is also thought that their small size may allow them to cross cell membranes into the blood, organs or brain (Born & al, 2006) and be transported

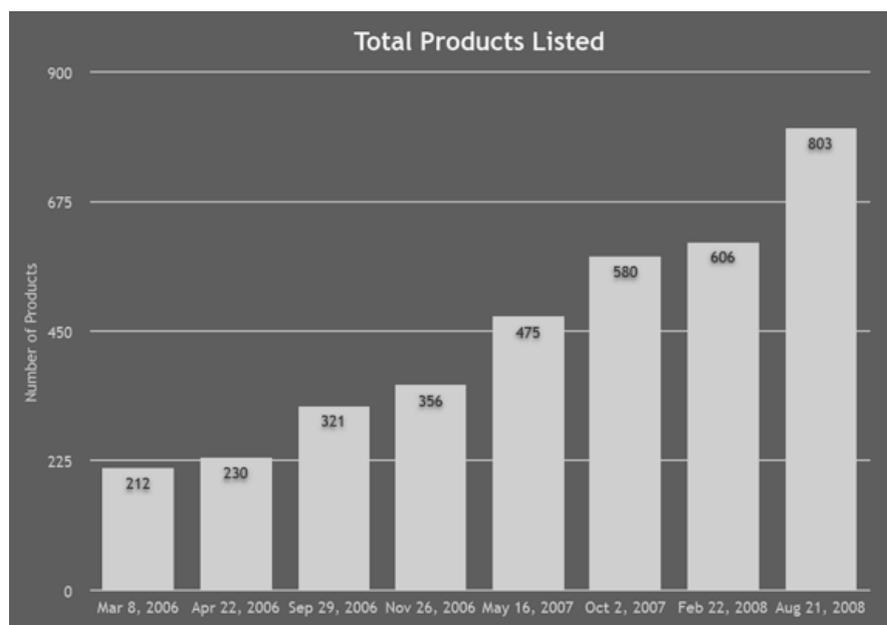
readily through the air and water. Indeed, some studies have demonstrated that the smaller particles have crossed the intestinal wall depending on their physio-chemical properties and the health status of the intestinal tract (Rieux & al, 2006) (EFSA, 2008).

Consideration has not been given to the potential risks these materials may pose to vulnerable groups such as children, seniors and those with health problems. This is of particular concern due to the number of products for children entering the market that contain or are coated with nanomaterials (Rejeski, 2007) (Treyer & al, 2006).

## **2.2. The Application of Nanomaterials in Consumer Products**

Nanotechnology as a platform technology like the steam engine or the internet has the potential of having a significant impact on all sectors of society and being used to improve the characteristics of a wide range of consumer products. Inventories of nano-enhanced

consumer products have been established by the European Union (Gleiche, 2006), the Woodrow Wilson International Center for Scholars (WWICS, 2008), the insurance industry (Swiss Re, 2004) and Friends of the Earth (FOE, 2006) (FOE, 2008). According to these inventories, everything from paints, cosmetics, sporting goods, textiles, construction materials, batteries, computer and cell phone components to food additives, drugs and children's toys containing nanomaterials are being marketed globally. For example, the inventory maintained by the Woodrow Wilson International Center for Scholars contains more than 800 consumer products enhanced by nanomaterials that are on the global market. Although, it is not known how many of the products listed in the inventory are actually available to Canadians, the information from the websites of the products listed indicates that many of them can be purchased through Canadian retailers and distributors or by ordering over the internet. The number of products that manufacturers have voluntarily listed in this inventory has almost tripled increasing from 212 in March 2006 to



803 in August 2008 as can be seen in this chart<sup>1</sup>. For almost 60% of these products, the chemical identity of the nanomaterials used could not be determined (Hansen & al, 2008). It is speculated that many more products containing nanomaterials are on retail shelves as many manufacturers particularly in the food and cosmetic industries are reluctant to identify

the presence of nanomaterials in their products (European Parliament, 2007) (FOE, 2008) (Which, 2008).

Table 1 below reproduced from the Consumers Council of Canada report (Nielsen, 2008) summarizes the current applications of nanoscale products in consumer products around the world.

<sup>1</sup> Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies

Table 1: Nanotechnology Based Consumer Products on the Global Market

<b>Automotive</b> <ul style="list-style-type: none"> <li>• Air and Oil Filters</li> <li>• Waxes, engine oil</li> <li>• Anti-scratch finishes</li> <li>• Car wax</li> <li>• Air purifiers</li> <li>• Catalysts to improve fuel consumption</li> <li>• Tires</li> </ul>	<b>Clothing and Textiles</b> <ul style="list-style-type: none"> <li>• Wrinkle and stain resistant apparel</li> <li>• Anti-bacterial and anti odour clothing</li> <li>• Anti-bacterial fabrics</li> <li>• UV resistant and protective clothing</li> <li>• Flame retardant fabrics</li> </ul>	<b>Cosmetics</b> <ul style="list-style-type: none"> <li>• Skin creams and moisturizers</li> <li>• Skin cleansers</li> <li>• Sunscreens</li> <li>• Lipstick, mascara, make-up foundations</li> <li>• Make up removal</li> </ul>
<b>Electronics</b> <ul style="list-style-type: none"> <li>• Batteries</li> <li>• Displays-electronics</li> <li>• Organic Light Emitting Diodes (OLED) and LEDs</li> <li>• Data memory</li> <li>• Anti-bacterial and anti static coatings on keyboards, mouse, cell phones</li> <li>• DVD coatings</li> <li>• MP3 players</li> <li>• Computer processors and chips</li> </ul>	<b>Food, Food Additives and Food Packaging</b> <ul style="list-style-type: none"> <li>• Energy drinks</li> <li>• Nutritional supplements</li> <li>• Food storage containers</li> <li>• Anti-bacterial utensils</li> <li>• Cutting boards</li> <li>• Plastic wrap</li> <li>• Food packaging</li> <li>• Nano-tea, chocolate shakes, canola active oil</li> </ul>	<b>Household</b> <ul style="list-style-type: none"> <li>• Anti-bacterial furniture and mattresses</li> <li>• Anti-bacterial coatings in appliances</li> <li>• Filters</li> <li>• Air purifiers</li> <li>• Self cleaning glass</li> <li>• Anti-bacterial, UV resistant paints</li> <li>• Irons, vacuums</li> <li>• Solar cells</li> <li>• Cleaning products</li> <li>• Disinfectant sprays</li> <li>• Fabric softeners</li> </ul>
<b>Personal Care/Health</b> <ul style="list-style-type: none"> <li>• Hearing aids</li> <li>• Contact Lenses</li> <li>• Body wash</li> <li>• Cellulite treatment</li> <li>• Tooth powder</li> <li>• Shampoos, hair gels</li> <li>• Deodorants</li> <li>• Insect repellents</li> <li>• Anti-bacterial creams</li> <li>• Bandages</li> <li>• Home pregnancy tests</li> <li>• Drug delivery patches</li> <li>• Man-made skin</li> </ul>	<b>Sports Equipment</b> <ul style="list-style-type: none"> <li>• Golf balls and clubs</li> <li>• Tennis rackets and balls</li> <li>• Baseball bats</li> <li>• Hockey sticks</li> <li>• Skis and snowboards</li> <li>• Ski wax</li> <li>• Bicycle parts</li> <li>• Wet suits</li> <li>• Shoe insoles</li> <li>• Anti fogging coatings</li> </ul>	<b>Toys and Children's Goods</b> <ul style="list-style-type: none"> <li>• Stain resistant plush toys</li> <li>• Anti-bacterial baby pacifiers, mugs and bottles</li> <li>• X-boxes and play stations</li> <li>• Anti-bacterial stuffed toys</li> </ul> <b>Medical Applications</b> <ul style="list-style-type: none"> <li>• Drugs</li> <li>• Medical Devices</li> </ul>

The most common nanoscale substance reported to be used in consumer products is nano-silver. It is being applied extensively for its anti-bacterial and anti-fungal properties to coat everything from baby bottle nipples, door handles, food contact products, to the interiors of refrigerators and washing machines. Manufacturers have also identified its use in clothing, bedding, paints, cleaning products, food storage containers, bandages, medical devices, mattresses, and children's teddy bears (Woodrow Wilson International Center for Scholars, 2008) (Luoma, 2008). Silver particles on the nanoscale cannot be seen or felt

but improve the products by preventing the growth of bacteria or fungi, thus reducing infection, odor, itchiness, sores and smelly feet. Nanosilver is even effective in killing some strains that have proven resistant to antibiotics (Luoma, 2008).

Carbon based nanomaterials are the second most common nanoscale materials found in consumer products. They are used due to their exceptionally high strength, light weight, and excellent electrical and thermal conductivity. To improve the strength of a product while reducing its weight, double walled carbon nanotubes are embedded in the various resins found in baseball bats, hockey sticks, skis or vehicle parts. The weakest areas in a traditional baseball bat or a snowboard are the tiny spaces between the fibers that contain only resin. To improve the strength of these areas, carbon nanotubes are dispersed throughout the resin making it tougher and stronger. Fullerenes, nanomaterials shaped like a soccer ball and composed of carbon, are used to impart increased strength to products, to improve the storage of power in batteries, to improve the moisturizing effectiveness of cosmetics and to deliver drugs (Maynard, 2006b).

Claims have been made that nanomaterials are being used extensively in many personal care products, sunscreens and cosmetics (FOE, 2006) (SCCP, 2007). In a recent study of personal care products, researchers at Which, a British consumer organization, were not able to clearly determine how and where nano materials are used in cosmetics since many manufacturers that use nanomaterials do not reveal it (Which, 2008). Similar results were found by scientists who carried out research for the European Parliament (Dekkers & al, 2007). According to Which, the types of nanomaterials that are used in personal care products include:

- Nano titanium dioxide and zinc oxide are used in nano form as UV filters in sunscreens to make the sunscreen transparent rather than white when the bulk form is used. It is also claimed that they are more effective when used in nano form.
- Nano emulsions and nanosomes are used to preserve active ingredients, such as vitamins and anti-oxidants, by encapsulating them and for their lightness and transparency.
- Fullerenes are used in face creams to increase their penetration into the skin and it is claimed that these tiny carbon spheres have anti-aging properties.
- Other materials used in nano size include nano gold in 'energizing' moisturiser and products using nano silver because of its anti-bacterial properties.

Key ingredients are being encapsulated or suspended in nanospheres or nanoemulsions to increase the penetration of the cosmetic ingredient into the skin. For example, L'Oreal has used polymer nanocapsules to deliver retinol or Vitamin A into the deeper layers of skin. Other companies using nanomaterials in skin products that were identified by Friends of the Earth include: Procter & Gamble's Olay brand, Mary Kay and Clinique from Estée Lauder, Neutrogena, from Johnson & Johnson, Avon and the Estee Lauder brand (FOE, 2006). Similarly, nanoemulsions and nanocapsules are used in hair products to carry active ingredients into hair shafts. Nano zinc and nano titanium can be found in sunscreens to make them transparent, less greasy, less smelly and more absorbable into the skin (Little & al, 2007).

In the medical field, nanoparticle agents that are deliberately ingested or injected can be found or are being developed for drug delivery purposes, biosensors, and imaging (Nanoforum, 2003)(Netherlands, 2006)(Lewinski & al, 2008). They are being used or considered for use in medicine since the pharmaceutical industry believes they will reduce

the toxicity of drugs and associated side effects. In addition, the potential ability to cross cell membranes or the blood brain barrier may result in more effective ways of delivering drugs into cells or the brain. A number of substances are being considered for drug delivery, including biological substances at the nano level like albumin, gelatine and phospholipids for liposomes and various polymers, carbon nanoparticles such as fullerenes and solid metal containing nanoparticles (Jong & al, 2008).

The future of nanomaterials in medicine was examined in a workshop organized by the Canadian Institutes of Health Research (Gordon & Sagman, 2003). Research and development was reported to be underway in many potentially beneficial applications including:

- Delivery of drugs directly to where they are needed without causing harsh side effects;
- Production of a range of materials with large surface areas to increase the adhesion, durability and lifespan of implants;
- Nanopolymers are being investigated as potential scaffolds to assist in tissue regeneration;
- New implantable and/or wearable sensing technologies that provide continuous and extremely accurate medical information such as blood pressure, temperature and blood glucose; and
- The development of smaller and potentially more powerful devices to restore lost vision and hearing functions. The devices collect and transform data into precise electrical signals that are delivered directly to the human nervous system.

Although many of these potential applications may take years before they become available, some of the first generation nano products in the area of medicine are being applied or marketed now. Examples include an anti-cancer drug, approved by Health Canada, containing a nanomaterial designed to find cancer cells, which attaches itself to the cells and then releases a chemical that kills them (Health Canada, 2008). Since the drug is only released when attached to the cancer cell, the toxic side effects associated with many drugs used for chemotherapy are reduced significantly. Another example is the United States military researchers who have used nanoscaffolds to rebuild tissues and organs (Pilioci, 2008). Since the use of nanomaterials in the medical area is intentionally designed to interact with cells, toxicity is a critical factor in evaluating their potential application (Lewinski & al, 2008).

Over the past few years, the food industry has started to develop and, in a small number of cases, uses natural and engineered nanomaterials in the food, additives and packaging it produces (ETC Group, 2004). It is anticipated that the use of these nanomaterials will result in a range of benefits, including new flavours and textures, less use of fat; enhanced absorption of nutrients; blockage of certain ingredients that contribute to elevated blood cholesterol; smart packaging that identifies contaminated food; the ability to trace food products; and improved safety of food (EFSA, 2008) (Netherlands, 2006). In the case of packaging materials, nanoscale sensors are under development for the purpose of identifying the presence of certain bacteria or the release of certain chemicals as food spoils. It is alleged that, as soon as the food starts to spoil, the packaging will change color to alert the consumer, a system that could be far more accurate and safer than sell-by dates. The challenge is to develop a system that will not only identify the presence of bacteria such as *Listeria* or *E. Coli* but also identify the strains of these bacteria that are

actually pathogenic. Food supplements to address mineral deficiencies such as colloids contain nanoparticles of various metals such as silver, gold, copper, and platinum. Colloids basically are solid, liquid, or gaseous substances made up of small particles that remain in suspension. They are being sold as all purpose medicines (Oberdorster, 2008).

Equipment and surfaces contaminated with microbes create safety problems in the food industry. Modification of the surfaces by nanomaterials is being studied as a way of preventing adhesion of the microbes to the surfaces and equipment (Netherlands, 2006). To achieve the same purpose, nanosilver is being used on food contact utensils and containers due to its anti-bacterial characteristics (WWIS, 2008). Nanomaterials are currently being used by a number of beer companies as coatings on their bottles to keep the beer fresher over a longer period of time (Wolfe, 2005) (Senik, 2007). The exact usage and quantity of nanomaterials in food is not known (EFSA, 2008).

The textile industry applies nanotechnology extensively to meet the demands of modern society. For example, it is used to produce fabrics and clothing that are resistant to stains. Fabrics have a tendency to absorb water and liquids which often result in stains on the fabric. If the water repellency of the fabric is increased by using fluorinated carbon chains that make the cloth more hydrophobic or water hating, this problem can be overcome. The industry is now increasing the fluorine content of the outmost fabric layer similar to Teflon in Gore-tex products to enhance water repellency. On many textile products, the terms "nanotex", "nano" and "nanotech" appear. These terms either refer to finishes which incorporate nanomaterials to provide the properties desired or nanofibres created through specialized spinning processes. The finishes and fibres can be designed to provide the fabrics with different stain, wrinkle resistant, antibacterial, and ultra violet radiation absorbency properties. In addition silver, titanium and zinc dioxide at a nano scale are being added to textile fibres to provide protection against bacteria and ultra violet radiation (Gleiche, 2006).

At present, there are only a few products enhanced with nanomaterials used in building or construction products. An excellent illustration of this is self-cleaning sheet glass based on a layer of titanium dioxide nanoscale particles. Nano titanium dioxide is fixed in layers onto glass which enables sunlight to break down any dirt making it easy for the rain to wash the dirt away. Some cordless power tools available in Canada are powered by batteries that contain phosphate nanocrystals to extend the time between recharging of the battery (WWICS, 2008). Nanoparticles can also be found in other building products in Canada including paints with improved adhesion and anti-mildew properties, insulation with increased insulating properties, in concrete and steel to increase strength and durability and in the production of glass that acts as a fire barrier (Nanoforum, 2006).

The Meridian Institute (Meridian Institute, 2005) and nanotech scientists (Schmidt, 2007) argue that nanotechnology has the potential of preventing water pollution and cleaning up contaminated water. Systems are under development to filter out bacteria and viruses and to remove lead, arsenic, and uranium from water. Moreover, it is claimed that nanomaterials will have the capability to help clean up the environment due to their enhanced surface area and reactivity, and their ability to segregate contaminants and remove them from soil. For example, iron nanoparticles can remove contaminants from soil and ground water by precipitating them and making them less mobile. Nanosized sensors also could improve the detection and tracking of contaminants (EPA, 2007).

### 3.0. Assessing the Impact on Human Health

“The novel properties of nanomaterials, however, may also give rise to new exposures and effects which need to be assessed for their potential impacts on human health and the environment.”

Environment Canada and Health Canada (EC/HC, 2007)

As more nanomaterials are developed and commercialized, the potential for adverse effects to human health increases. The rapid advancements in the development of nanomaterials have not been matched by research into the possible risks associated with them based on their increased reactivity and potential to cross traditional biological protective barriers. For these reasons, concerns have been raised by scientists (Poland et al, 2008)(Oberdorster, 2008) (Maynard, 2006b), government agencies (EC/HC, 2007) (European Commission, 2004) (EPA, 2007) and non governmental organizations (Balbus et al, 2005) (Born & al, 2006)(ETC, 2005) (Consumers Union, 2006) that the unique properties of nanomaterials may also have negative impacts on human health.

When assessing any potential risks to human health associated with nanomaterials, there are three main elements that need to be considered:

- the identification and characterization of the hazard that exists such as toxicity, flammability or explosive properties of the material or product;
- the probability of exposure of the public to the material from the time it is being developed, manufactured until its disposal which includes its intensity, frequency, duration and when exposure happens relative to development; and
- the consequences of exposure such as whether or not it causes an acute or chronic minor or major health problem.

Essential to any human health assessment is the generation, collection, analysis and interpretation of chemical, physical and biological data from scientific studies. Since no data or only limited data is available, it is very difficult to assess the potential risks. Experts in the field, research institutions, and governments have recommended and identified additional research that needs to be carried out on health effects (Born & al, 2006) (Maynard, 2006a) (CIHR, 2008) (CCA, 2008).

#### 3.1. Identification and Characterization of Potential Hazards

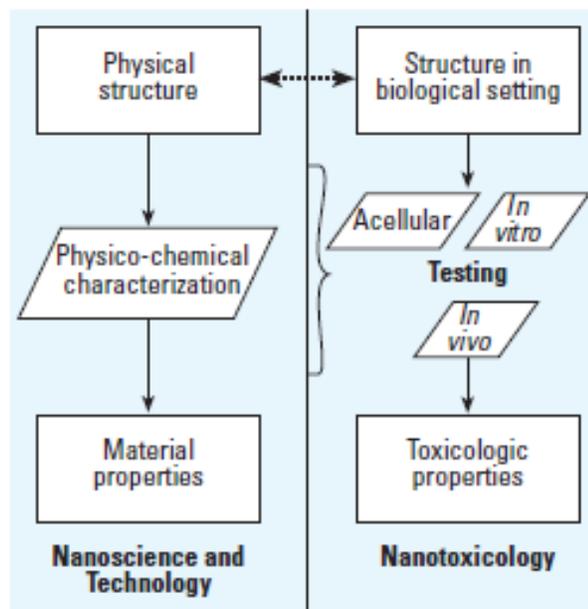
Hazards associated with a material are identified through epidemiological studies, in vitro experiments and in vivo research using animal models and/or humans. The characterization of the hazard involves determining the properties of the nanomaterial that influence the potential toxicity or hazard of a nanomaterial and cause adverse health effects in those who are exposed to the nanomaterial. The diversity and complexity of nanomaterials makes chemical identification and characterization not only important but also very difficult (Lewinski & al, 2008). Adding to the difficulty is the fact that many physicochemical properties are engineered into the nanomaterial and can be altered making it impossible to establish classes of nanomaterials based on composition or structural properties. Moreover, the properties of nanoparticles can change when they interact with living systems (ICON, 2008). As a result, there is considerable debate about

the critical information that is needed to evaluate the human health impact of nanomaterials and the ability of researchers using existing protocols to identify and characterize potentially hazardous materials. A number of hazard identification frameworks have been proposed and no consensus exists among experts with respect to which characteristics are critical to assessing any hazard posed and it has been suggested that new ways of evaluating hazards are required (Nel & al, 2006).

With respect to the parameters that need to be characterized when determining the toxicity of nanomaterials, some researchers (Oberdorestor & al, 2005) (Warheit, 2008) have proposed a set of properties that must be measured. The critical information required to characterize nanomaterials in order to assess any potential hazards were also identified by an expert working group and the U.S. EPA. The critical elements under oral, dermal, inhalation and injection routes of exposure (Oberdorestor & al, 2005) (EPA, 2007) include:

- Physicochemical Characteristics such as particle size and size distribution, agglomeration state, shape, crystal structure, chemical composition, surface area, surface chemistry, surface charge, and porosity.
- *In Vitro* Assays (cellular and non-cellular) which allow for the testing of specific techniques under controlled conditions to evaluate the toxicity of materials under different entry routes, and for different target organs.
- *In Vivo* Assays were proposed for the different routes of exposure to evaluate inflammation, oxidant stress, deposition and translocation in organs and tissues, biopersistence effects of multiple exposures; and potential effects on the reproductive system, placenta, and fetus; alternative animal models; and mechanistic studies.

Warheit (Warheit, 2008) who reviewed the importance of adequate characterization of nanomaterials on human health, Born (Born & al, 2006) who reviewed research on risks of nanomaterials and a meeting of experts that identified the information needed to assess any hazards (Balbus & al, 2007), agreed with the recommendations of the expert working group. The diagram taken from the report of a meeting to assess hazards of nanoparticles (Balbus & al, 2007) illustrates the relationship between material design (nanotechnology) and material testing (nanotoxicology). It shows both the importance of physical structure to material properties and the structure in a biological setting which can be different. In addition, Warheit along with others emphasised the importance of properly characterizing these physicochemical properties not only initially but repeatedly, so that variables affecting biocompatibility can be identified, transformations at the portal of entry and comparisons to other hazard identification studies can be made (Stern & McNeil, 2008) (Warheit, 2008) (Balbus & al, 2007).



Others have taken a different approach and recommended that the intended use of the material and its toxicity in relation to other substances or in a biological setting must also be considered when characterizing the hazard associated with a nanomaterial (Stern & McNeil, 2008) (ED-Dupont, 2007) (Jong & al, 2008). Hansen (Hansen & al, 2008), a researcher at the Technical University of Denmark, reviewed the research carried out on the physical and chemical properties of nanoparticles and the related effects. He found that there was in general a lack of categorization of the nanoparticles studied making it impossible to link specific properties of the nanoparticles to the observed effects. Hansen and his colleagues went on to suggest that in addition to assessing toxicity on the physical and chemical properties of nanomaterials they should be categorized on the basis of the location of the nanoscale structure in the system. This leads to three main categories:

- materials that are nanostructured in the bulk
- materials that have nanostructures on the surface
- materials that contain nanostructured particles such as liquids, solids or airborne.

In addition, the toxicity of nanoparticles cannot be predicted from the known properties of their macro sized counterpart (Hagens & al, 2007).

Lewiniki and colleagues (Lewinski & al, 2008), who reviewed the research in the area of cytotoxicity of nanoparticles used in medical applications, concluded that surface coatings can define much of the bioactivity of particles including their solubility. As a result, these coatings make it difficult to evaluate the potential toxicity of the core nanoparticles. Jong and associates (Jong & al, 2008) who reviewed hazards associated with nanoparticles in drug delivery systems came to the same conclusion based on the extensive use of coatings which have the potential of altering the toxicity of the nanoparticles.

According to the report prepared by the Council of Canadian Academies (CCA, 2008) and reports of reviewers (Born & al, 2006) (Hansen & al, 2007) (Hagens & al, 2007), the identification of the behaviour of nanomaterials in biological systems requires that the following properties or ADME framework are considered:

- “Absorption – how readily can the particle cross biological barriers (e.g., skin, cell membranes and blood-brain barrier);
- Distribution – how easy is it for the particle to travel to other locations and what organs do the particles tend to target;
- Metabolism – does the material get broken down into further constituents; and
- Excretion – do the particles get excreted or do they accumulate in various tissues.”

As a result of these recommendations and the gaps in scientific knowledge about the factors that influence nanomaterial toxicity, in the test protocols to measure them, and consensus on the key properties that need to be measured, efforts are underway internationally to fill these gaps. The organizations involved and the work being carried out by them are described below.

- The International Organization of Standardization (ISO) has set up Technical Committee 229 on Nanotechnology. Currently, the following four working groups have been established: terminology and nomenclature; measurement and characterization; health, safety and environment; and material specification. The working groups are involved with the development of a range of documents from

technical reports to international standards on these various aspects of nanotechnology. Similarly, the International Electrical Technical Commission (IEC) has established a committee to deal with similar issues related to nanotechnology in electrical and electronic products.

- OECD has initiated under its Chemical Committee a Working Party on Manufactured Nanomaterials to carry out a research strategy and testing program that will test 14 of the most common nanomaterials that have been commercialized. The purpose of the research is to ensure that the approach to hazard, exposure and risk assessment of manufactured nanomaterials is of a high, science-based, and internationally harmonized standard (Tigner, 2008)(Oki, 2007).
- The World Health Organization and the Food and Agricultural Organization plan to convene a joint Expert Meeting in June 2009 to identify knowledge gaps including issues on food safety, review current risk assessment procedures, and develop global guidance on adequate and accurate methodologies to assess potential food safety risks that may arise from nanoparticles (Safenano, Dec 2008).

### 3.2. Exposure

The assessment of exposure is crucial to determine the risks posed by a nanomaterial. Irrespective of the toxicity or hazard of a material, if there is no exposure, the nanomaterial poses minimal or no risk. The main routes of exposure of humans to nanomaterials include (Born & al, 2006) (CCA, 2008) (Stern & McNeil, 2008) (EPA, 2007):

- inhalation of nanoparticles emitted or released into the air from products during manufacture, use or disposal such as occurs with aerosol sprays or decomposition of the materials after disposal;
- dermal route of exposure through the skin involving nanoparticles present in such products as cosmetics, sunscreens, and clothing or transferred from surfaces in the workplace;
- oral route of exposure by the intentional ingestion of food, drugs or oral hygiene products or unintentional ingestion of nanomaterials used in food packaging or mouthing of products coated or containing nanomaterials by infants;
- injection of a drug or implantation of a device for medical purposes; or
- release of nanomaterials in the environment leading to human exposure through the air, water or food.

Workers and scientists have the highest exposure to nanomaterials as they carry out their duties in research and production facilities (Born & al, 2006) (Netherlands, 2006). Although more research is needed to identify the effects of nanoparticle exposures on workers, occupational health and safety officials are recommending that employers take steps to minimize worker exposure until more is known about whether or not they actually pose a risk. For example, in the few airborne exposure studies that have been carried out in industrial settings, airborne concentration levels of carbon nanotubes were found to be quite low (Maynard & al, 2004) and were below the concentration of background incidental nanoparticles produced by heating systems or present in the environment (Peters & al, 2006). Nevertheless, the National Institute for Occupational Safety and Health (NIOSH, 2006), the International Organization of Standardization(ISO, 2008b), and the British Standards Institute (BSI, 2007) have all published guidance for employers on the best practices to follow in order to protect their workers based on available information. The research being carried out on nanomaterials in the workplace and their impact on workers

should provide valuable data on any hazards related to nanomaterials, ways of exposure, the effects on human health and ways to manage any effects that could damage health.

Although exposure of workers to nanomaterials is the focus of much of the research, potential consumer exposure needs also to be examined ((EFSA, 2008) (Hansen & al, 2008). This has been identified as a significant research need since many consumer products enhanced by nanomaterials are currently on the market (Treyer & al, 2006). Currently, studies on the exposure of the public to nanomaterials are very limited and it is very difficult to assess exposure since data is normally not available on the actual composition of the nanomaterial used, its concentration in an individual product and background levels of nanoparticles that exist naturally or as by-products of other human activities (Hansen & al, 2008) (Stern & McNeil, 2008).

Human and environmental exposure to nanoscale materials in consumer products can take place throughout the life cycle of the product from the production of the nanoscale materials and nano enhanced products, the use of the products to the release of nanoscale materials into the environment (through industrial emissions, leakage, recycling or disposal of consumer products) (EPA, 2007). Moreover, most toxicological studies deal with external exposure not the part of the external dose that actually translocates into the body and is able to interact with the cells or organs (Hagens & al, 2007). The parameters that need to be measured to assess public exposure have not been determined (Born & al, 2006).

It has also been argued that the chance of being exposed to nanoscale materials very much depends on the location of the nanomaterial in the product (Hansen & al, 2008). For example, the exposure scenarios for a free airborne nanoparticle will be much different than for a particle fixed in a solid. Hansen and his colleagues who examined the consumer products in the inventory maintained by the Woodrow Wilson International Center for Scholars found that in 19% of the products the nanoparticles were bound to the surface, in 37% they were suspended in liquids and in 13% the particles were suspended in solids. It is unlikely that many current applications in consumer products, such as computer chips, sports equipment or tools, will pose health or safety risks to humans during use. The nanomaterial is fixed in or etched onto a larger object that is enclosed or not in contact with a person. Similarly, in textiles, tires, automotive parts or construction products, the nanomaterials are fixed or embedded in stable resins. Therefore, it is thought that exposure will be minimal and mainly as a result of wear or disposal in the environment.

However, the lack of information on the concentration of nanoparticles, location of the nanomaterial and release during wear or use makes it nearly impossible to assess exposure and risk (Treyer & al, 2006).

In the case of manufactured nanomaterials that are free to move around as occurs in aerosols or cosmetics (European Commission, 2007), the potential of exposure is very different. The concern is that nanomaterials which are free could be inhaled, ingested or enter the body via the skin, and adversely affect the health of the individual. A working group of experts concluded that engineered nanomaterials presenting a potential risk to human health include those capable of entering the body and exhibiting a biological activity that is associated with their nanostructure (Oberdorster & al, 2005). The membrane structure and function is the primary barrier which protects a cell. A material must cross the cell membrane and its ability to do so very much depends on its physicochemical properties. One of the primary concerns regarding exposure to nanomaterials is their

reduced size and potential to overcome the biological protective membrane. This would provide them access to sensitive cellular processes that could result in enhanced toxicological effects (CCA, July 2008) (Born & al, 2006) (Royal Commission on Environmental Pollution, 2008).

A recent study comparing certain multi-walled carbon nanotubes with asbestos fibres suggested that carbon nanotubes which physically resemble harmful asbestos fibres also behave like asbestos fibres causing respiratory problems when inhaled in large amounts over long periods (Poland et al, 2008). From another perspective, the reliability of the design and execution of this study was evaluated to establish in a court of law that the inhalation of carbon nanotubes causes adverse health effects similar to. The lawyers (Monica, 2008) who evaluated this study argued that it would not be acceptable because “(i) the design and execution of the Poland Study are not generally accepted in the scientific community for the purposes offered; (ii) in order to reach the conclusion that inhalation of multi walled carbon nanotubes may cause mesothelioma, an expert would have to use the Poland Study in such a manner as to extrapolate from an accepted premise to an unfounded conclusion; and, (iii) the Study's authors failed to adequately account for obvious alternative explanations (confounders), including surface chemistry, sample contamination, sample comingling, spontaneous formation of granulomas, and possible mouse colony”.

When carbon nanotubes were injected rather than inhaled, it was shown by research carried out at Rice University that no immediate adverse health effects occurred and after one hour they were removed by the liver (Weisman B. & R. Smalley, 2007). According to Günter Oberdörster of the University of Rochester, in the context of potential nanomedical uses, it appears that in cells copper is highly toxic, silver quite toxic, titanium dioxide not very, and gold the least toxic (Oberdörster, 2008). The findings from these initial studies will need to be repeated by other scientists before definite decisions can be made about whether or not these materials actually pose a health risk.

As the production of nanomaterials and nano-enhanced products increases, it is expected that the release of nanomaterials into the environment will also increase. Some will result from accidental emissions during production while others will result from normal wear and tear or degradation following disposal into landfills or recycling of products. For example, recent research has shown that the silver nanoparticles to eliminate odour in socks can be

washed out by ordinary laundering (Benn et al, 2008). Once released into the environment, different types of micro-organisms, plants and species of fish and animals may be exposed to the anti-microbial nanosilver and the impact on them and eventually humans is unknown. As a result of these concerns, a coalition of consumer, health, and environmental groups filed a legal petition with the U.S. Environmental Protection Agency, demanding that the agency use its authority to regulate anti-microbial substances such as nano-silver under its pesticide legislation and to stop the sale of the more than 260 consumer products that contain nanosilver (ICTA, 2008).

### **3.3. Identification and Assessment of Risks to Health**

Traditionally, the field of risk assessment in the chemical sector is based on the assumption that there is a relationship between the impact on a biological system and the amount of material (dose) to which one is exposed and the duration of the exposure. A European

scientific committee concluded that the currently used risk assessment paradigm (hazard identification, hazard characterisation, exposure assessment and risk characterisation) is applicable for nanomaterials. Conventional toxicological testing methods should be used as a starting point to identify hazards from nanomaterials (SCENIHR, 2006.). They also concluded that additional issues specific for the properties of nanomaterials must also be considered. To establish the impact, both the amount of material to which one is exposed, the duration of exposure and the response to that material must be measured. In the case of nanomaterials, there are significant data gaps in terms of the hazard posed and the concentration and length of time of exposure which makes it difficult if not impossible to assess the potential risk (SCENIHR, 2006).

The number and diversity of nanomaterials complicates the assessment (Lewinski & al, 2008) since it probably means that nanomaterials will have to be assessed for risk to human health on a case by case basis. Maynard (Maynard, 2006b) proposed two additional criteria for identifying nanomaterials which present a potential of adversely affecting human health. These include:

- the ability of the nanomaterial to interact with the body in such a way that its nanostructure is biologically available; and
- having the potential to cause a biological response.

Data concerning the behaviour and toxicity of nanoscale particles mainly comes from studies on inhaled nanoparticles and pharmaceutical studies in which formulations involving nanoscale components are used to solve problems dealing with insolubility of drug formulations and delivery of drugs. Several of these studies indicate that some engineered nanomaterials may exhibit adverse effects such as cancer, heart disease and asthma similar to ultrafine particulates in polluted air (Powell & Kanarek, 2006) and cross the brain blood barrier (Oberdoster, 2004b). Even though experts argue that particle size and surface area seem to be the critical elements to determine the potential hazards, the scientific results and data that is available is limited (CIHR, 2008) (Maynard, 2006a) (Balbus & al, 2005). Moreover, in some cases the applicability of the results to human health has been questioned and caution should be taken in drawing any conclusions from the results until the hazards and exposures have been more clearly identified and defined (Born & al, 2006) (Stern & McNeil, 2008).

A review of *in vitro* cytotoxicity research results and test procedures that are used was carried out by Lewinski and colleagues (Lewinski & al, 2008). It was concluded by these reviewers that,

- different data about cytotoxicity of carbon-, metal-, and semiconductor-based nanoparticles was published due to differing experimental conditions and nanoparticle physiochemical properties;
- cells can survive short-term exposure to low concentrations (<10 mg mL<sup>-1</sup>) of nanoparticles;
- At high doses cytotoxic effects were found to appear in a dose- and time-dependent manner for all of the nanoparticles reviewed; and
- the generation of reactive oxygen species and the influence of cell internalization of nanoparticles are two common findings in terms of causes for the increase in cell death at higher doses and longer exposure times.

Inhalation is thought to be one of the major routes of exposure to nanoparticles particularly

for workers. Nanoparticles of less than 100nm were found to be deposited deep in the lungs mainly in the alveolar region where it is more difficult to clear them resulting in a higher burden in the lungs (Hoet, 2004). Both animal and human data show that nanoparticles are able to cause acute and chronic effects in the lung ranging from inflammation, exacerbations of asthma to genotoxicity and carcinogenesis (Hoet, 2004). The tumour-related effects are unique to rats and have not been reported in rodent species such as mice or hamsters, under similar chronic conditions (Warheit D. B., 2004). Moreover, the relevancy of data from pulmonary studies in rats to impacts in larger mammals has been questioned (Warheit D. B., 2004)(Stern & McNeil, 2008). Available epidemiological data in workers exposed to titanium dioxide and carbon black ultrafine particles do not show increased risks for lung cancer (Born & al, 2006) (IARC, 2006). As mentioned earlier, a major study used established methods to see if specific types of nanotubes have the potential to cause mesothelioma -- a cancer of the lung lining that can take 30-40 years to appear following exposure. The results show that long, thin multi-walled carbon nanotubes that look like asbestos fibres, behave like asbestos fibres (Poland & al, 2008). The reliability of this study was questioned by lawyers who evaluated it in detail. (Monica, 2008 )

Unlike larger particles, nanoparticles potentially are capable of entering cells and disrupting cellular metabolism. Studies examining the possible translocation of nanoparticles from the lungs to other organs are mixed with some showing that translocation has occurred and others the opposite. In addition, the amount of material translocating differs among studies (Hoet, 2004). For example, Oberdorster and his colleagues (Oberdorster & al, 2002) found that carbon when inhaled by rats did translocate to the liver. With respect to the liver, it has been suggested that that low solubility, low toxicity nanoparticles stimulate the cells designed to remove and neutralize any potential pathogens resulting in oxidative stress that can interfere with bile formation and production of pro-inflammatory compounds associated with liver disease (Born & al, 2006). Also, nanoparticles were shown to enter the brain via the nasal mucous membrane and the olfactory nerves (Wanga & al, 2008). This significant study demonstrated that inhaled nano TiO<sub>2</sub> can travel from the nose to the brain and provided evidence that inhaling TiO<sub>2</sub> particles can damage brain cells at a relatively low exposure dose and within a short period of time. The quick transfer into the brain raises safety concerns for workers who may be exposed to ultrafine TiO<sub>2</sub> during its manufacture or application to numerous industrial and commercial products. There is less clarity about the extent to which nanomaterials are capable of entering the body through the skin (whether damaged or intact) and the digestive track (Born & al, 2006) (Stern & McNeil, 2008).

Within the body, nanoparticles may promote the formation of harmful substances, such as reactive oxygen compounds (Oberdorster & al, 2005). The particles cause inflammatory reactions which, if chronic, can lead to elevated and harmful levels of immuno-reactive substances in the blood. It also has been demonstrated that it is possible for engineered nanoparticles of different sizes to translocate across respiratory and gastrointestinal tracts into the blood system, nervous system, organs and cells (Born & al, 2006) (Stern & McNeil, 2008) (Sass, 2007). Hoet and his colleagues (Hoet, 2004) who reviewed the work carried out to investigate the impact on health of nanoparticles concluded that it is possible for nanoparticles to be taken up by the intestinal track. The nanoparticles also have the potential to alter the signalling that takes place in cells to control the cellular function and responses. These findings strongly suggest that nanoparticles can actively engage and mediate molecular processes essential to regulate cell functions (Jiang & al, 2008). After the penetration, the distribution of the particles in the body is a strong function of the surface characteristics of the particles (Hoet, 2004).

In the case of nanosilver, recent reviews (Panyala & al, 2008) (Senjen, 2007) of its impact on human health found that a number of studies showed that nanosilver was capable of entering the human body by way of inhalation, ingestion and skin contact in various ways. At concentration levels between 5-50ug/ml (Senjen, 2007), nanosilver was shown to accumulate in the liver, kidneys, spleen and the central nervous system and can potentially cause neurotoxic damage, damage to the sperm cells and the male reproductive system and cause cell membrane rupture. Although the reviewers could not determine from many of the studies that the adverse health outcome was definitiely associated with nanosilver, they did conclude that nanosilver can easily translocate into the body, can interact with cell membrane surfaces, and potentially have a toxic effect. When human skin cells grown in a Petri dish were exposed to nanosilver particles 7-20 nm in size, concentration-dependent changes to cell morphology including abnormal size, shrinkage and rounded appearance were observed at concentrations above 6.25 µg/mL. Another paper describes the result of exposure to nanosilver in a wound dressing used to treat a severe burn victim. After a week of treatment with a wound dressing impregnated with nanosilver, the patient developed reversible signs of liver toxicity and a greyish discoloration of his face similar to that found in patients diagnosed with argyria (a permanent blue-gray discoloration of the skin and deep tissues). The dose received by the patient was not measured but the patient's blood plasma and urine were found to have an elevated concentration of silver (107 and 28 µg/kg, respectively). When the wound dressing was removed, all clinical symptoms returned to normal within ten months.

The anti-microbial properties of nano-silver are dependent on the ability of the particles to denature proteins by precipitating reactive groups of proteins and by oxidative reactions that rupture the cell (Panyala & al, 2008). Other studies have explored the effectiveness of nanosilver-impregnated wound dressings in a variety of clinical settings (Gago & al, 2008) and found them to be effective in treating infected chronic wounds. Whether or not microbes acquire resistance to nanosilver has been raised as a concern (Senjen, 2007); however, no research has been published to substantiate these ideas. The Friends of the Earth in a report on the health and environmental impact of nanosilver called "for an immediate moratorium on the further release, and the immediate withdrawal from the market, of all products containing nanosilver". This position was based on the review findings that the toxicity risks were not well understood, the potential risks to the public and environmental systems, and the failure of regulatory systems to manage these risks (Senjen, 2007).

The pharmaceutical industry is applying and investigating the application of nanoparticles in drug delivery systems to reduce toxicity and the side effects of drugs. Until recently, they were not aware that these delivery systems could pose a risk to the patient particularly since their size may allow them to cross various biological barriers in the body. Unfortunately, the data required to assess the risks posed by these materials has not been generated and it is not possible to adequately assess the risks (Jong & al, 2008). However, Lewinski et al reviewing cytotoxicity studies involving carbon, metal an semiconductor based nanoparticles, concluded that cells can survive short-term exposure to low concentrations of nanoparticles studied. At high concentrations, several of the researchers reported cytotoxicity effects for all the particles studied (Lewinski & al, 2008).

Both *in vitro* and *in vivo* studies have been carried out to identify the toxicological hazards associated with carbon nanotubes. However, few of these studies can be compared

because of differences in the tubes and test protocols which have the potential to affect the results (Helland & al, 2007) (CCA, July 2008). In a review of the research on the possible risks to human health and the environment of carbon nanotubes, Helland and his colleagues concluded that carbon nanotubes cannot be considered a uniform group because there are so many different types and because of their bioavailability to organisms they can accumulate in the food chain and produce a toxic response when reaching the lungs in sufficient quantity. In addition, the studies reviewed showed that carbon nanotubes may cause oxidative stress, inflammation, cell damage, adverse effects on cell performance and in the long term pathological effects like granulomas, fibrosis and wall thickening (Helland & al, 2007) (Born & al, 2006).

Safety concerns over nanoparticles in cosmetics were raised initially by the Royal Society in a report in 2004 (UK RS/RAE , 2004). The interaction of nanoparticles with the skin is receiving increasing attention due to the extensive use of nanoparticles in clothing and in cosmetic preparations applied to human skin, such as sunscreens and moisturizers. In addition, airborne particles have a tendency to settle on surfaces where dermal contact is possible. Mortensen et al who reviewed a number of papers on the subject of the ability of nanoparticles to penetrate healthy skin found that the issue is being debated. Studies that they reviewed suggested that titanium dioxide which is used extensively in sunscreens when suspended in an emulsion does not penetrate the skin (Mortensen & al, 2008) (Netherlands, 2006). This was also the conclusion reached by the International Agency on Cancer Research (IARC, 2006) and the Scientific Committee on Consumer Products (SCCP, 2007). The SCCP found that soluble nanoparticles normally disintegrated when applied to the skin while insoluble particles did not. It is primarily the insoluble particles if available on a persistent basis such as from repeated applications that are of concern. It is possible that they could translocate and accumulate in other organs. The SCCP also called for a re-evaluation of nano titanium dioxide and zinc oxide used in sunscreens, particularly in relation to damaged skin and to assess the effects of mechanical action from rubbing in the lotion or flexing the skin. One study carried out to address the question of whether or not the situation is the same when the skin is damaged or impacted by ultraviolet radiation raised concerns about potential increased penetration when the skin is damaged (Mortensen & al, 2008). Fullerenes which are used as ingredients in many face creams were found to cause brain damage in fish (Oberdorester, 2004a) and toxic effects in human liver cells (FOE, 2006).

Cosmetic companies are taking different approaches to the safety assessment of nanomaterials in their products. Many companies carry out their own risk assessments on nano-enhanced products or base their assessments on the information provided on Material Safety Data Sheets (Which, 2008). One of the recommendations of the Scientific Committee on Consumer Products (SCCP, 2007) in its evaluation of the safety of nanomaterials in cosmetics was that the data industry submits to government to demonstrate safety should be made available to the public.

#### **4.0. Scientific and Research Gaps**

There are significant gaps in our knowledge of the environmental, health, and ecological implications associated with nanotechnology (UK RS/RAEng, 2004) (Swiss Re, 2004). A Canadian Workshop on Multidisciplinary Research on Nanotechnology (CIHR, 2008) brought together experts to identify the knowledge gaps that pose major challenges to Canadian society and government in their efforts to manage and address the issues related

to nanotechnologies. The potential risks to human health and the response of the body to nanomaterials have yet to be determined. Similarly with respect to the environment, the impact of nanomaterials on different species, the fate of nanomaterials and how they are transported through the environment is for the most part unknown. This data is required to identify, to understand and to manage any risks to the environment posed by nanomaterials. From a practical perspective, new test procedures need to be developed to detect, to characterize, to measure and to monitor nanomaterials. Another area where gaps exist is related to risk assessment methods. Questions have been asked about whether the methods in existence are appropriate to evaluate any risks associated with nanomaterials or to evaluate their new uses and properties. The workshop also identified the need to carry out research into the ethical, economic, legal and social impacts of nanotechnology. This research would involve studying the effect of the technology on society, on an individual's privacy, the ethics of enhancing human physiological characteristics and industrial dislocations (CIHR, 2008).

All of the papers (Stern & McNeil, 2008) (Maynard, 2006a) (Balbus & al, 2007) (ICON, 2008) and government assessments (EFSA, 2008) (EPA, 2007) (SCENIHR, 2006) (CCA, 2008) of the risk associated with nanomaterials have concluded that there are a number of gaps in our knowledge essential to identify and characterize any associated hazards, to determine both external and internal exposure, and to assess any potential risks. These include the lack of :

- Internationally accepted definitions and nomenclature systems of nanotechnology and nanomaterials;
- Suitable test protocols and instrumentation to characterize the materials, measure its purity, measure any hazards, determine exposure and determine potential accumulation and persistence of the material in the body;
- Reference materials to validate test results;
- Data on the sources of exposure from diverse applications and tools to measure exposure;
- Measurement protocols to characterize, detect and measure engineered nanomaterials;
- Reference materials for the purpose of precise and reproducible categorization and detection.
- Available toxicology data and risk assessment methods to assess toxicity and risks associated with nanomaterials;
- Knowledge about how nanomaterials enter body and the physiological responses to them;
- Data on adverse health outcomes due to exposure throughout life cycle of nanomaterials;
- In vitro and in vivo studies that use other routes of exposure and animal models that apply to human systems;
- Data on the changes in the nanoparticle physico-chemical characteristics that may occur under local environmental conditions.
- Research into safety aspects of nanomaterials such as flammability and explosive properties; and
- Accurate information on current usage and availability.

The Council of Canadian Academies also identified the need for the development and resourcing of a strategic research agenda:

- to improve understanding of the risks associated with the different classes of nanomaterials;
- to develop test procedures to identify and measure the presence of nanomaterials;
- to identify the properties of nanomaterials that are linked to human health and the health of the environment; and
- to identify effective monitoring and surveillance strategies.

There appears to be a major research gap with respect to the impact of nanoparticles on vulnerable groups such as children, seniors and those whose health is compromised. Only a very limited number of papers discuss the issue related to children (Rejeski, 2007) (Treyer & al, 2006), none mention seniors and the impact of health status is only rarely raised (Panyala & al, 2008). The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR, 2006.) concluded that the available data suggested that some vulnerable groups with pre-existing diseases such as allergies, cardiovascular disease and immune diseases or the very young and elderly may be more susceptible to the adverse effects of nanoparticles.

## 5.0. Oversight of Nanotechnology and Nanomaterials

### 5.1. Regulatory

“If you think that any existing regulatory framework can keep pace with this rate of change, think again” (Rejeski, 2004).

Most Canadians are ready to embrace nanotechnology but they also want the new products to be safe and the regulatory process to assure their safety. However, the rapid development and commercialization of nanomaterials makes it very difficult for regulators to keep pace. A number of reports over the last few years have identified potential gaps in current knowledge and regulations and recommended that governments carry out research and review existing regulations to ensure that human health and the environment are protected. Many experts also recommended that nanomaterials be treated as new substances (UK RS/RAEng, 2004) (Davies, 2007) while another report actually recommended that a new law to manage the risks of nanotechnology be established (Davies, 2005).

A complex regulatory framework involving many federal and provincial government departments and agencies exists in Canada to manage the diverse products containing nanomaterials. At the Federal level, Environment Canada (EC), Health Canada (HC), the Pest Management Regulatory Agency (PMRA), the Canadian Food Inspection Agency (CFIA) and Industry Canada (IC) are all involved. Provincial and municipal agencies administering legislation in the areas of occupational health and safety, public health, safe drinking water, and management of the environment also are or will be involved in managing products of nanotechnology.

In Canada, existing legislation requires that many products containing nanomaterials be assessed for safety and efficacy before entering the market. These products include novel foods, drugs, and biological health products, natural health products, and medical devices that are regulated under the *Food and Drugs Act* and pesticides regulated under the *Pest Control Products Act*. Enforcement of these regulations involves not only the assessment

before the product enters the market but also surveillance and monitoring of these products or any problems that may result after they are on the market. The diversity of the properties of nanomaterials and the products in which they are used or will be used means that they will probably have to be assessed on a case by case basis. Since cosmetics, personal care products and sunscreens are not classified as drugs unless the manufacturer makes health claims, these products may or may not be exempt from pre-market review. The same situation exists for products that contain nano-silver. The pre-market assessment of products containing nanosilver under pesticide regulations will only take place if the manufacturer makes a specific claim of anti-microbial properties. Other products including children's toys, textiles, sporting goods, paints and household chemicals regulated under the *Hazardous Products Act* do not require such pre-market evaluation. The safety of these products is dealt with through the development of regulations and surveillance and monitoring of the product on the market. No requirements for labelling of products that contain nanoscale materials exist in Canada or other countries.

One of the primary statutes that deals with the assessment and oversight of chemicals is the *Canadian Environmental Protection Act* (CEPA). As a result of concerns raised about whether or not nanomaterials are new chemical substances requiring assessment, and whether the current trigger levels and data requirements are suitable for nanomaterials, Environment Canada and Health Canada have undertaken a process to ensure adequate oversight exists. Consultations on the approach proposed have taken place. The approach involves continuing to work with international partners to develop scientific and research capacities; informing companies involved with products of nanotechnology of their regulatory responsibilities under current regulations; developing initiatives to gather information from industry on uses, properties and effects of nanomaterials; and consider where amendments to CEPA and its regulations would need to be made to facilitate the risk assessment and management of nanomaterials. This will be very similar to the initiative launched by the US Environmental Protection Agency called the Nanoscale Materials Stewardship Program (EPA, 2008) whose purpose is to provide a firmer scientific foundation for regulation by asking industry to voluntarily provide available information on the products they produce or utilize and in some cases develop data and carry out testing over the long term.

The major challenges that government regulators face are the lack of definitions, and a nomenclature system to categorize them, test procedures to measure and identify them, limited information on the properties of these materials and their impact on humans and the environment and the diversity of the products being developed. As Lori Sheremeta from the National Institute of Nanotechnology in Edmonton said "If we can't define what we're talking about accurately, how are we going to regulate it?" (Metzger, 2007). Developing the basic tools and information needed by regulators for the purpose of developing and enforcing regulations to manage this technology and the resulting multitude of products will take a considerable amount of time.

Recently, an expert panel established by the Council of Canadian Academies on behalf of the Minister of Health assessed the state of knowledge with respect to the properties of existing nanomaterials and their potential impact on human health and the environment. The emphasis of the study was on research, risk assessment and surveillance which could underpin regulatory perspectives (CCA, 2008). The panel found that, although it was not necessary to establish new regulatory regimes to address the novel characteristics of nanomaterials, "the existing regulatory mechanisms could and should be strengthened in a

variety of ways". In particular, they recommended that an interim classification system be developed, the current regulatory criteria which determines when a substance is assessed needs to be reviewed, information on the proper handling of nanomaterials be developed to protect workers, a life cycle approach be adopted and meaningful ways of involving the public be established. Similar conclusions were reached by several other recent studies (Monash University, 2007) (Laursen, 2008) (Breggin & R, 2008) which recommended that that existing regulatory mechanisms need to be reviewed and strengthened and that nanomaterials cannot be considered the same chemical substance as their larger counterparts. The overall conclusion of the panel was that the any potential risks associated with this new technology will be managed by the precautionary approach followed by Canadian regulatory regimes.

Davies, in a paper providing advice to the new US administration presents a somewhat different view (Davies, 2008). He stated in his paper that "Unfortunately, federal agencies currently have to draw on decades-old laws—many of which are woefully out of date—to ensure the safe development and use of these technologically advanced products. Federal officials need 21st century tools for cutting-edge technologies. Anything short of that is unacceptable and may leave the public unprotected from emerging risks." He also recommended that the Food and Drug Administration require premarket testing of food and cosmetic ingredients and forbid the marketing of any cosmetic containing an ingredient which is not safe. Since much of the legislation in Canada, is similar to that which exists in the United States, this advice could also apply to the Canadian situation. The Royal Commission of the United Kingdom who investigated nanotechnology also was concerned that existing regulations could not be depended on to detect and manage adverse effects that these materials may cause (Royal Commission on Environmental Pollution, 2008).

The European Commission due to its concern about the potential risk of engineered nanomaterials has established three non-food scientific panels to provide opinions on specific issues related to nanotechnology to help in the development of public policy. These are the Scientific Committee on Consumer Products, the Scientific Committee on Health and Environmental Risks and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The European Food Safety Authority provides advice on issues related to food.

Consumer groups have recommended to governments nationally and internationally that pre-market assessment of nano enhanced products be made mandatory and that governments require disclosure through labelling of the use of nanomaterials in consumer products (CCC, 2008) (CIELAP, 2008) (Hansen, 2008) (Sass, 2007). A number of public interest groups even recommended that a moratorium be placed on nano enhanced food and cosmetic products until they are shown not to pose a risk to the public (ICTA, 2008) These reports and concerns are essentially calling for a precautionary approach, and for investing more resources into research on the potential risks generated by products of nanotechnology. The potential hazards and unknown risks and the growing number of nanotech products already on the market have made management of the technology more urgent.

Oversight of nanotechnology is also being considered by certain municipal public health Units in the United States due to the slow pace of federal government action. Berkeley California was the first to adopt and enforce an ordinance that requires those dealing with nanomaterials to report on the toxicity of the materials, if known, and what is being done to

manage the risk to workers, the public and the environment (Keiner, 2008). Cambridge Mass. evaluated such an approach and has decided not to proceed at this time (Cambridge, 2008) since data on health effects is limited. Four potential actions that could be taken by American states or municipalities include:

- requirements for the disclosure of potential health, safety, or environmental hazards;
- adoption of standards that are expert-driven, such as the nanotechnology workplace standards being developed the International Organization for Standardization;
- control or prevention of releases of nanomaterials; or
- establishment of joint regional standards or approaches for overseeing the safe development of nanotechnology. (Keiner, 2008)

The major problem of such approaches is the patchwork nature of the oversight requirements across the country. No such strategies are being considered by Canadian provincial or local governments at this time.

## 5.2. Standards

Government efforts to develop the best regulatory approaches are complemented by domestic and international standard setting that is being asked to develop workable definitions, categorization systems, tests to identify and measure their properties and risk assessment protocols suitable for nanomaterials. The International Organization for Standardization (ISO), the Organisation for Economic Co-operation and Development (OECD) and the British Standards Institute (BSI) are in the forefront of the international work to develop such standards. ISO formed a committee to develop the standards that are essential to support regulatory activity and the assessment of the materials. This committee is in the process of developing standards for terminology and nomenclature, measurement and instrumentation; material specifications; and to address health, safety and environmental issues (Hatto, 2007). Canadian experts representing government, research organizations such as the National Research Council, the private sector and consumers are taking lead roles in this work. BSI has published nine documents for nanotechnology terminology and guidance for the United Kingdom, addressing nanotechnology terminology, health and safety issues, and product labelling (BSI, 2008).

The OECD has established two committees to address issues related to nanotechnology (OECD, 2008b). The first committee which is responsible for the health and environmental safety implications of manufactured nanomaterials initiated a program to test fourteen nanomaterials currently in commerce. The test program is concerned with the identification of the materials, measuring their physical and chemical properties, their environmental fate, mammalian and environmental toxicology, and their safety. The nanomaterials to be evaluated (OECD, 2008a) include:

- Fullerenes (C60)
- Single-walled carbon nanotubes (SWCNTs)
- Multi-walled carbon nanotubes (MWCNTs)
- Silver nanoparticles
- Iron nanoparticles
- Carbon black
- Titanium dioxide
- Aluminum oxide

- Cerium oxide
- Zinc oxide
- Silicon dioxide
- Polystyrene
- Dendrimers
- Nanoclays

Having decided on the nanomaterials to be tested, the next stage is to determine and understand the basic properties that are relevant in the assessment of exposure and health and environmental effects.

The purpose of the second committee is to advise on emerging policy-relevant issues in science, technology, and innovation related to the responsible development of nanotechnology. It is examining social/economic issues, public participation and perceptions, international collaborations on research, and the potential for nanotechnology to address global challenges such as clean water. Both Environment Canada and Industry Canada are involved in leading the work of some of these committees (Tigner, 2008).

An internationally recognized certification body, TUV SUD, has developed the first standard to uniformly assess the manufacturing processes of a company producing nano-products. It is titled Good Manufacturing Practices for Nano-Products. Certification to this standard confirms that a company is able “to manufacture specific nano-products to a consistent quality and offering the features stated” (TUV SUD, 2008). TUV in partnership with the Innovation Society has also developed CENARIOS®, the first certifiable nano-specific risk management and monitoring system. This risk assessment system is designed to ensure that the health, safety and environmental risks related to a nano-product are assessed to “State-of the Art” standards and new findings from science and technology (TUV SUD, 2006). The purpose of both these initiatives is to assist industry in producing nano-products posing risks As Low As Reasonably Possible (ALARP) through the responsible assessment and management of any potential risks..

### **5.3. Voluntary Industry Action**

The importance of voluntary industry action towards the responsible development and commercialization of engineered nanomaterials has been raised and a few programs have been developed. These programs will help in the interim to fill the current gaps in regulations and, in the future, could be used to complement any regulations developed.

To promote the responsible development of engineered nanoscale materials, Environmental Defense in partnership with DuPont developed a framework, the Nano Risk Framework, for the purpose of indentifying and managing any potential risks to human health or the environment (ED-Dupont, 2007). The framework is designed to enable the responsible development, manufacture, use and disposal of engineered nano materials through a systematic and disciplined process. The steps in the six step process include:

- describing the nanomaterial and its intended uses from available information or that generated by the developer;
- development of lifecycle profiles of the properties (characterization of the physical and chemical properties), inherent hazards and opportunities for exposure of the nanomaterial;
- the information provided by the lifecycle profiles is assessed to determine the

- nature, magnitude and probability of the risks posed;
- the risk management options are identified and evaluated and a course of action recommended;
- decision on whether to proceed with the development, documents the decisions and acts accordingly; and
- through regular reviews the risk evaluation is updated and if necessary revised.

In addition, the framework provides guidance on and illustrates through case studies the questions that an organization may have or need to consider:

- when developing nanomaterial applications or when using nanomaterials provided by external suppliers;
- when determining the information to be collected or produced in order to make risk management decisions;
- when dealing with uncertainty such as situations where there is little information;
- in order to communicate information and decisions to stakeholders.

A number of case studies to illustrate how the framework can be used were prepared by Dupont and can be found at [www.nanoriskframework.org](http://www.nanoriskframework.org).

The UK Royal Society and its partners initiated a project to develop a Responsible Nano Code and established a working group to develop the code. The working group finalised the *Seven Principles of the Code* and a series of *Examples of Good Practice* to assist industry in using the code (Responsible Nano Code, 2008). The main principles include: accountability of a company's board, stakeholder involvement, minimization of health and safety risks to workers and the public, minimization of risks to the environment, and transparency and disclosure. If followed by a company, the principles would go a long way to addressing the concerns of the public and environmental groups.

In response to a coalition of public health, educational, religious, labour, women's, environmental and consumer groups and new ingredient standards in Canada and Europe, the cosmetic industry has established a voluntary program, Compact for Safe Cosmetics. Under this initiative companies pledge to phase out hazardous materials in cosmetics and personal care products within three years, and to meet the new tough European Union cosmetics ingredients standards worldwide. According to a report prepared for the Investor Environmental Health Network, 500 manufacturers, distributors and retailers have signed the pledge. However, many of the larger companies, including Avon, Estée Lauder, and Procter & Gamble have refused to do so (Little & al, 2007).

## **6.0. What are the public's concerns about nanotechnology?**

So far, there has not been wide-spread public pressure in Canada to regulate products of nanotechnology. This is not surprising since most Canadians aren't even aware what nanotechnology is or that nanomaterials can be found in a number of products they use regularly. This was illustrated in recent surveys which found that more than 70% of Canadians knew little or nothing about nanotechnology or what the government was doing about it (CCC, 2008) (Walker, 2005). As the commercialization of products of nanotechnology continues to expand into the Canadian market, it is anticipated that more and more consumers will become aware of the technology, show an interest in it, expect information about the technology, and adequate oversight and regulation of the resulting products.

Divergent views with respect to nanotechnology are held by the public who are aware of nanotechnology. One sector believes that nanotechnology will be very beneficial to society bringing improvements to many products and addressing many of the major issues of the day. Another sector believes that nanotechnology will increase global inequalities, cause social disruption and pose risks to humans and the environment. A report prepared by Greenpeace presents these opposing views. It indicates that there will be benefits in medicine, the production of clean energy and pollution prevention and remediation while possibly impacting human health and the environment and increasing the divide between rich and poor (Arnall, A. H. 2002).

A number of recommendations have been presented by public interest groups such as the Canadian Institute for Environmental Law and Policy (CIELAP, 2008), Friends of the Earth (2008), (Which, 2008) and the Consumers Council of Canada (CCC, 2008). They have all published reports or articles recommending that the oversight and regulation of nanomaterials should be based on the following approach:

- Full life cycle independent environmental, health and safety impact assessments as a requirement for commercialization;
- Testing and regulating manufactured nanoparticles as if they were a new substance;
- Increasing scientific research to address health safety and environmental issues;
- Building of overall capacity within the government to deal effectively with nanotechnology;
- Developing a public engagement strategy with a strong commitment to government openness and transparency; and
- More information and labelling of consumer products that contain nanomaterials and are ingested or applied to the skin so consumers can make informed choices.

These recommendations are the same as the recommendations from most public interest groups internationally. Other organizations have recommended that a moratorium be placed on the use of nanomaterials in all new products (ETC, 2005) or in cosmetics and personal care products (FOE, 2006).

The report prepared for Her Royal Majesty on nanotechnology (Royal Commission on Environmental Pollution, 2008) summarized the reason for concern among the public very astutely when it stated "It is a matter of concern that we were repeatedly told by competent organisations and individuals that we do not currently have sufficient information to form a definitive judgement about the safety of many types of novel materials, particularly many types of nanoparticles".

## **7.0. Conclusion.**

Despite concerns raised by individuals (both scientists and non-scientists), the few studies that have been conducted specifically with engineered nanoscale materials do not yet suggest a clear pattern of harm. Some evidence of biological response or elevated reactivity has been presented, but others suggest that it is not appropriate to use these narrow experimental observations alone to support a conclusion that such materials and products pose a threat under real-world conditions.

The review of nanotechnology safety concerns carried out by Stern and McNeil (Stern & McNeil, 2008) concluded that for the most part the lungs, skin and gastrointestinal systems

act as a formidable barriers to nanomaterials. The exception to this were certain nanomaterials like carbon nanotubes that display potentially significant pulmonary toxicity. They also concluded that until the hazards, exposures and impact on human health are clearly identified that the cautious development and implementation of nanotechnology would be the prudent course to follow.

While engineered nanoparticles, such as carbon nanotubes, may share the nanoscale size with combustion-generated ultrafines, studies that associate chronic respiratory and cardiac problems to combustion-related particle exposures are assessing exposures to heterogeneous particles (comprised of organic compounds, metals, and other impurities) and hazardous gases that are simply not present in engineered nanoscale materials. Despite these differences, many valuable evaluation methods and principles describing transport (movement into and through the body) derived from this body of work have contributed to the study of nanotoxicology.

Although research is ongoing, there are a few important observations about engineered nanomaterials that can be found in the existing toxicological literature:

1. There is emerging evidence that biological effects observed in some studies are tied to various properties, including size, surface area, shape, surface chemistry, and electric charge of nanoscale particles. Some nanoscale particles that do not have special surface charges or reactive sites have been found to elicit inflammation at lower concentrations than would be expected with similar materials produced in larger dimensions (e.g. bulk graphite vs. carbon nanotubes). This has led to the observation that *total surface area* can sometimes be a better predictor of toxicity with certain classes of nanomaterials than mass concentration.
2. Some nanoscale materials appear to be associated with cellular oxidative stress (free radical mechanisms) once inside a cell. This process results in the release of unstable forms of charged molecules and is tied to genetic damage and cellular dysfunction. While this insight may become important in understanding the precise molecular mechanism of harm, it will not help scientists predict the likelihood of these materials finding their way from the place of initial contact into the bloodstream and then inside certain cells.
3. Important questions remain about the ability of inhaled nanoscale materials to be transported into the bloodstream and then to specific organs, or for nanoscale materials to penetrate the skin directly. Specific concerns have been raised about the possibility that engineered nanoparticles, like other nano-sized particles such as viruses, welding fumes, and diesel exhaust particulates, may be able to *translocate* directly into the bloodstream from the surface of the skin or along the olfactory nerve into the brain. There is only limited evidence that these uptake routes may be of potential significance for humans, and some evidence that direct translocation through the skin is not taking place.
4. It is essential not to presume that effects exhibited by “parent” materials (large-scale) can be extrapolated to the effects of the derived nanoscale equivalent (e.g. engineered nano-gold vs. simple gold dust). Efforts to predict nanoscale effects from existing toxicology data have been found to be less than useful in many cases.

5. While ultrafine particle studies, along with earlier toxicological and clinical investigations, have laid the foundation for the nascent field of nanotoxicology, there are some fundamental questions about the impact of engineered nanoparticles on human health that earlier research did not resolve, such as:
- Can human exposures to engineered nanomaterials be prevented? If not, what is a safe threshold for exposure and what are the likely exposure levels that might be encountered by workers, researchers, and consumers?
  - How are engineered nanoparticles taken up by the human body and how are they metabolized? Do they reach organs and tissues that larger, less reactive particles are not able to reach? Do they interfere with cellular signalling in consequential ways? Does the immune system treat materials on that scale differently?
  - Are there chronic (long-term) health effects associated with exposure to engineered nanoparticles that cannot be evaluated with acute (short-term) and sub acute (medium-term) studies? How can long-term effects be assessed without allowing people to be exposed to uncertain risks?
  - Are there meaningful differences between the health effects of *engineered* nanoscale materials and those of *naturally occurring* or *incidental* materials with similar chemical composition? If there are different risks posed by engineered nanomaterials, then these materials must be evaluated separately and researchers cannot rely on toxicity values and mechanisms identified in previous studies.
  - How do physical, chemical, and electrostatic forces alter the transport dynamics, physical separation, and surface charge of these materials after they are released during processing or manufacturing? How can experimental conditions be defined and controlled so that health effects studies are measuring exposure to discrete nanoscale materials rather than larger clumps of material likely to form over time?
  - What is the probability (or risk) that a given individual will experience adverse health effects after being exposed to engineered nanoparticles for a limited period of time? What latent (or delayed) health risks might emerge years after the exposure has ended?
  - What is the impact of nanotechnology on vulnerable groups such as young children, seniors, those who are ill, or disabled?

## Bibliography

Arnall A. (2002). *Future Technologies Today's Choices Nanotechnology, Artificial*

*Intelligence and Robotics*. Greenpeace Environmental Trust.

Balbus & al, (2007). Meeting Report: Hazard Assessment for Nanoparticles - Report from an Interdisciplinary Workshop. *Environmental Health Perspectives*, Vol 115 (11).

Balbus J. & al. (2005). *Getting Nanotechnology Right the First Time, Position of Environmental Defense*.

Benn T., & al, (2008). *Nanoparticle Silver Release into Water from Commercially Available Sock Fabrics*. *Environmental Science and Technology*, Vol. 42, 4133-4139.

Born P., & al, (2006). *The potential risks of nanomaterials*. A review carried out by ECETOC. *Particle and Fibre Toxicology*, 3:11.

Breggin L., & R, P. (2008). *Application of the Toxics Release Inventory to Nanomaterials*. Research Brief No. 2, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars.

BSI (2007). *Nanotechnologies-Part 2 Guide to Safe Handling and Disposal of Manufactured Nano-materials*. BSI Published Document 6699-2 2007.

BSI (May 2005). *Publically Available Standard PAS 71:2005 Vocabulary - Nanoparticles*. British Standards Institute.

BSI (2008). *Publications for Nanotechnology*. [www.bsi-global.com](http://www.bsi-global.com): BSI.

Cambridge N. A. (2008). *Report to the Cambridge City Manager, Recommendations for a Municipal Health and Safety Policy for Nanotechnology*. Cambridge: City of Cambridge.

CCA (2008). *Small is Different: A Science Perspective on the Regulatory Challenges of the Nanoscale, Report of the Expert Panel on Nanotechnology*. Ottawa, Canada: Council of Canadian Academies.

CIELAP (March 2007). *Discussion Paper on a Policy Framework for Nanotechnology*. Toronto, Canada: Canadian Institute of Environmental Law and Policy, [www.cielap.org](http://www.cielap.org).

CIELAP (2008). *Update on a Framework for Canadian Nanotechnology Policy; A Second Discussion Paper*.

CIHR (2008). *Canadian Workshop on Multidisciplinary Research on Nanotechnology: Gaps, Opportunities and Priorities*. Edmonton: Canadian Institute of Health Research.

Consumers Union (Oct 2006). Presentation at the Food and Drug Administration's Public Meeting on *Regulated Products Containing Nanotechnology Materials*. FDA Report pp 62-69

Davies C. (2005). *Managing the Effects of Nanotechnology*. Woodrow Wilson International Center for Scholars, Project on Nanotechnologies.

Davies J. C. (2007). *EPA and Nanotechnology, Oversight for the 21st Century, PEN 9*. Washington: Project on Emerging Technologies, Woodrow Wilson International Center for Scholars.

Davies J. C. (2008). *Nanotechnology Oversight: An Agenda for the Next Administration*. Woodrow Wilson International Center for Scholars.

Dekkers S., & al, (2007). *Nanomaterials in Consumer Products, Availability on the European Market and Adequacy of the Regulatory Framework*. Brussels: European Parliament's Committee on the Environment, Public Health and Food Safety.

Donaldson K., & al, (2004). *Nanotoxicology*. *Occup. Environ. Med.*, 61, 727-728.

EC/HC (2007). *Proposed Regulatory Framework for Nanomaterials Under the Canadian Environmental Protection Act, 1999, Workshop on a Proposed Regulatory Framework for Nanomaterials under CEPA 1999*. Ottawa: Environment Canada and Health Canada.

ED-Dupont (2007). *Nano Risk Framework*. Environmental Defense and Dupont.

EFSA (2008). *Draft Opinion of the Scientific Committee on the Potential Risks Arising From Nanoscience and Nanotechnologies on Food and Feed Safety*. Brussels: European Food Safety Authority.

EPA (2008). *Nanoscale Materials Stewardship Program*. Washington: Environmental Protection Agency, [www.epa.gov/oppt/nano/stewardship.html](http://www.epa.gov/oppt/nano/stewardship.html).

EPA (Jan. 2008). *Nanoscale Materials Stewardship Program*. In U.S. Government, *Federal Register* (pp. Vol. 73, No.18, p 4861).

EPA (2007). *Nanotechnology White Paper*. Washington: Environmental Protection Agency.

ETC (2005). *A Tiny Primer on Nanoscale Technologies, and The Little Bang Theory*. Ottawa: ETC Group.

ETC Group. (Nov 2004). *Down on the Farm: The Impact of Nano-scale Technologies on Food and Agriculture*. ETC Group.

EC (2004). *Nanotechnologies: A preliminary risk analysis on the basis of a workshop organized in Brussels 1-2 March 2004 by the Health and Consumer Protection Directorate General of the European Commission*. Brussels: European Commission.

Feynman R. (Dec 1959). *There is Plenty of Room at the Bottom*. Annual Meeting of the American Physical Society. California Institute of Technology.

FOE (2006). *Nanomaterials, sunscreens and cosmetics: Small Ingredients Big Risks*. Friends of the Earth.

FOE (2008). *Out of the Laboratory and on to our Plates: Nanotechnology in Food and Agriculture*. Friends of the Earth.

Gago M., & al, (2008), A Comparison of Three Silver-containing Dressings in the Treatment of Infected, Chronic Wounds, *Wounds*, 20(10):273-278.

Gleiche M. (2006). *Nanotechnology in Consumer Products*. Nanoforum.

Gordon N., & Sagman, U. (2003). *Nanomedicine Taxonomy Briefing Paper*. CIHR Institute of Neuroscience, Mental Health and Addiction Workshop on Nanoscience and nanohealth. Montreal: Canadian Nanobusiness Alliance.

Hagens W., & al, (2007). *What do we (need to) know about the kinetic properties of nanoparticles in the body?* Regulatory Toxicology and Pharmacology, Vol 49(3) 217-229.

Hansen, & al, (2007). *Categorization framework to aid hazard identification of nanomaterials*. Nanotoxicology, 1:3 243-250.

Hansen S., & al, (2008). *Categorization framework to aid exposure assessment of nanomaterials in consumer products*. Ecotoxicology, 17: 438-447.

Hatto P. (2007, April). *Nanotechnologies*. ISO Focus, p. 1.

Health Canada (2008). *Abraxane for injectable suspension*. Health Canada's Drug Data base.

Helland A. & al (2007). *Reviewing the Environmental and Human Health Knowledge Base of Carbon Nanotubes*. Environmental Health Perspectives, 115(8): 1125-1131.

Hoet P & al. (2004). *Nanoparticles: known and unknown health risks*. Journal of Nanobiotechnology, Vol. 12; 2.

IARC. (2006). *Titanium Dioxide Summary of Data Reported*. Vol 93: 1-4.

ICON (2008). *Towards Predicting Bio-interactions. An international assessment of nanotechnology environment, health and safety research needs*. Houston: International Council on Nanotechnology, Rice University.

ICTA (2007). *Broad International Coalition Issues Urgent Call for Strong Oversight of Nanotechnology*. International Center for Technology Assessment.

ICTA (2008). *Petition for Rulemaking Requesting the EPA to Regulate Nano-silver Products as Pesticides*. International Center for Technology Assessment, Washington, D.C.

ISO (2008a). *Nanotechnologies - Terminology and definitions of nano-objects - Nanoparticle, nanofibres and nanoplate*. ISO/TS 27687. Geneva: International Standards Organization.

ISO (2008b). *TR 12885 2008, Nanotechnologies Health and Safety Practices in Occupational Settings*. Geneva: ISO.

Jia G. & al. (2005). *Cytotoxicity of carbon nanomaterials: single wall nanotube, multi-walled nanotube and fullerene*. Environ Sci Technol, 1:39(5) 1378-83.

Jiang & al, (2008). *Nanoparticle-mediated cellular response is size-dependent*. Nature Nanotechnology, Vol 3, 145-150.

Jong W., & al, (2008). *Drug Delivery and Nanoparticles: Applications and Hazards*. International Journal of Nanomedicine, Vol 3(2), 133-149.

Keiner S. (2008). *Room at the Bottom? Potential State and Local Strategies for Managing the Risks and Benefits of Nanotechnology*. Washington: Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars.

Laursen H. (2008). *The European Commission's Review of Existing Regulations. 10th Meeting of the Nanotechnologies Stakeholders Forum*. DEFRA.

Lewinski, N., & al, (2008). *Cytotoxicity of Nanoparticles*. Small, Vol 4(1) 26-49.

Little T., & al, (2007). *Beneath the Skin: Hidden Liabilities, Market Risks and Drivers of Change in the Cosmetics and Personal Care Products Industry*. Falls Church, Virginia: Investor Environmental Health Network.

Luoma S. (2008). *Silver Nanotechnologies and the Environment: Old Problems or New Challenges*. Washington: Woodrow Wilson International Center for Scholars' Project on Emerging Nanotechnologies.

Maynard A. (2006a). *Nanotechnology A Research Strategy for Addressing Risk*. Washington: Woodrow Wilson International Center for Scholars.

Maynard A. (2006b, October). *Nanotechnology: The Next Big Thing or Much Ado about Nothing?* Annul. Occup. Hyg., Vol 51, 1, 1-12.

Maynard A., & al, (2004). *Exposure to carbon nanotube material: Aerosol release during the handling of unrefined single-walled carbon nanotube material*. J. Toxicol. Environ. Health Part A, 67, 89-100.

Meridian Institute (2005). *Nanotechnology and the Poor: Opportunities and Risks Closing the gaps within and between Sectors of Society*. [www.nanotandthepoor.org](http://www.nanotandthepoor.org).

Metzger P. (2007). *Nanotechnology Small Science Generates Big Questions*. CBC News In Depth Science.

Monash University (2007). *A Review of Possible Impacts of Nanotechnology on Australia's Regulatory Framework*. Australian Government.

Monica J. Jr. (2008). *A Nano-Mesothelioma False Alarm*. Nanotechnology Law and Business, Vol 5, 3.

Mortensen L., & al, (2008). *In Vivo Skin Penetration of Quantum Dot Nanoparticles in the Murine Model: The Effect of UVR*. Nano Letters, Vol 8(9) 2779-2787.

Nanoforum (Nov 2006). *Nanotechnology and Construction*.

Nanoforum (2003). *Nanotechnologies and its implications for the Health of EU Citizens*. Nanoforum.

Nel A., & al, e. (Feb, 2006). *Toxic Potential of Materials at the Nano level*. Science Vol 311 (5761), 622-27.

Netherlands. (2006). *Health Significance of Nanotechnologies*. Hague: Ministry of Health, Welfare and Sports.

Nielsen E. (2008). *Nanotechnology: Its impact on Consumers*. Toronto: Consumers Council of Canada.

NIOSH (2006). *Approaches to Safe Nanotechnology: An Information Exchange with NIOSH*. Washington: CDC.

NNI National Nanotechnology Initiative. 2007. Research and Development Leading to a Revolution in Technology and Industry, Supplement to the President's FY 2008 Budget.

Oberdorster G., & al, (2002). *Extrapulmonary translocation of ultrafine carbon particles following whole-body inhalation exposure of rats*. Toxicol. Environ. Health Part A, 65, 1531-1543.

Oberdorster E. (2004). *Manufactured Nanoparticles (Fullerenes C60) induce oxidative stress in the brain of juvenile largemouth bass*. Environmental Health Perspectives, Vol. 112:10, 1058-1062.

Oberdorster G. (2004). *Translocation of Inhaled Ultrafine Particles to the Brain*. Inhalation Toxicology 16

Oberdorster G., & al, (2005). *Principles for characterizing the potential human health effects from exposure to nanomaterials: Elements of a screening strategy*. Particle and Fibre Toxicology, Vol 2:8

Oberdorster G. (2008). *Potential Health Risks of Engineered Nanoparticles*. IRSST-CSA-IAPA Nanoparticles and Nanomaterials: Health, Safety and Standardization. Montreal Canada.

OECD (2008a). *Series on the safety of manufactured nanomaterials, List of manufacturer materials and list of endpoints for phase 1 of the OECD Test Programme*.

OECD (2008b). *Nanotechnologies at the OECD, Sixth Session of the Intergovernmental Forum on Chemical Safety*. Paris: OECD.

OECD; Allianz. (2005). *Small Size Opportunities and risks for Nanotechnologies*. Allianz Centre for Technology, [www.allianzgroup.com](http://www.allianzgroup.com).

Oki N. (2007). *Report to ISO TC 229 on the Safety of Manufactured Nanomaterials*. Singapore: OECD.

Panyala N., & al, (2008). *Silver or silver nanoparticles: a hazardous threat to the environment or human health?* J. Appl. Biomed. , Vol. 6, 117-129.

Peters, A., & al, (2006). *The mapping of fine and ultrafine particle concentrations in an engine machining and assembly facility*. Ann. Occup. Hyg. 50 249-257, 50, 249-257.

Pilieci, V. (2008) *Scaffolds Let Humans Grow Replacement Limbs Organs*. Ottawa Citizen, November 7.

Poland C., & al, (2008). *Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study*. Nature Nanotechnology 3, 423-428.

Powell M., & Kanarek, M. (2006). *Nanomaterial Health Effects - Part 1: Background and Current Knowledge*. Wisconsin Medical Journal Vol. 105(2).

Rejeski D. (2004). *The Next Small Thing*. pp. 2-49.

Rejeski D. (2007). *Who Put the Nano in my Teddy Bear?* Nanotechnology Columns.

Responsible Nano Code (2008). *The Responsible Nano Code Update of May 2008*.

Rieux D., & al, (2006). Nanoparticles as potential oral delivery systems of proteins and vaccines: a mechanistic approach. *J Control Release*, 116(1), 1-27.

Royal Commission on Environmental Pollution (2008). *27th Report, Novel Materials in the Environment the case of nanotechnology*. Norwich: TSO.

Safenano (2008). *WHO and FAO examine food safety implications of nanotechnology*, December.

Sass J. (2007). *Nanotechnology's Invisible Threat Small Science, Big Consequences*. Washington: Natural Resources Defense Council.

SCCP (2007). *Opinion on the Safety of Nanomaterials in Consumer Products*. Brussels: Scientific Committee on Consumer Products of the European Commission.

SCENIHR (2006.). *Opinion on the Appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies*. Brussels: European Commission Health and Consumer Protection Directorate- General.

Schmidt K. (2007). *NanoFrontiers Visions for the Future of Nanotechnology*. Pen 6, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars.

Senjen R. (2007). *Nanosilver: A threat to soil, water and human health?* Friends of the Earth Australia.

Stern S. & McNeil, S. E. (2008). *Nanotechnology Safety Concerns Revisited*. *Toxicological Sciences*, 101(1), 4-21.

Swiss Re. (2004). *Nanotechnology. Small matter, many unknowns*. Zurich: Swiss Re.

Tigner J. (2008). *Organization for Economic Co-operation and Development Activities on*

*Nanotechnology*. IRSST-CSA-IAPA Nanoparticles and Nanomaterials, Health, Safety and Standardization. Montreal.

Treye T. & al, (2006). *Research strategies for safety evaluation of nanomaterials. Part VII Evaluating consumer exposure to nanoscale materials*. *Toxicol. Sci.*, 91: 14-19.

TUV SUD. (2006). *Cenarios Nanospecific Risk Management and Monitoring System*. St. Gallen: TUV and Innovation Society.

TUV SUD. (2008). *Good Manufacturing Practices for Nano-Products*. Munich: TUV SUD.

UK RS/RAEng. (July 2004). *Nanoscience and Nanotechnologies: Opportunities and Uncertainties*. Royal Society and Royal Academy of Engineering.

UNESCO. (2006). *The ethics and politics of nanotechnology*. Paris: United Nations Educational, Scientific and Cultural Organization.

Walker J. (2005). *Report on a Study of Emerging Technologies in Canada and the US. Prevailing Views, Awareness and Familiarity. First Impressions: Understanding the Public's Views on Emerging Technologies*.

Wanga J. & al, (2008). *Time-dependent Translocation and Potential Impairment on Central Nervous System by Intranasally Instilled Ti O<sub>2</sub> Nanoparticles*. *Toxicology*, Vol 254, Issue 1-2, 82-90.

Warheit D. B. (2004). *Nanoparticles: Health Impacts*. *Materials Today*, pp. 32-35.

Warheit D. (2008). *How meaningful are the results of nanotoxicity studies in the absence of adequate material characterization*. *Toxicological Sciences*, Vol. 101 (2): 183-185.

Wellcome Trust. (2005). *Big Picture on Nanoscience*. *Big Picture*, Issue 2.

Which (2008). *Small Wonder: Nanotechnology and Cosmetics*. Which.

Wolfe J. (2005). *Safer and Guilt-Free Nano Foods*. *Forbes/Wolfe Nanotech Report*.

WWICS. (2008). *The Nanotechnology Consumer Products Inventory*. Woodrow Wilson International Center for Scholars, [www.nanotechproject.org](http://www.nanotechproject.org).

## Websites Related to Nanotechnology

British Standards Institute	<a href="http://www.bsi-global.com/en/standards-and-publications/industry-sectors/nanotechnologies/nano-download">www.bsi-global.com/en/standards-and-publications/industry-sectors/nanotechnologies/nano-download</a>
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Environmental Protection Agency	<a href="http://www.epa.gov/oppt/nano">www.epa.gov/oppt/nano</a>
ETC Group,	<a href="http://www.etcgroup.org">www.etcgroup.org</a>
European Commission's Nanologue	<a href="http://www.nanologue.net">www.nanologue.net</a>
European Food Safety Authority	<a href="http://www.efsa.europa.eu">www.efsa.europa.eu</a>
European Nanotechnology Gateway	<a href="http://www.nanoforum.org">www.nanoforum.org</a>
Food and Drug Administration	<a href="http://www.fda.gov/nanotechnology">www.fda.gov/nanotechnology</a>
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