NANOTECHNOLOGY AND HEALTH RISKS

Health & Environment Alliance (HEAL)

FACT SHEET

Nanotechnology is being hailed as the "next industrial revolution". Nanomaterials are now found in hundreds of products, from cosmetics to clothing to food products. Inevitably, these nanomaterials will enter our bodies as we handle nanomaterials in the workplace, eat nano-foods, wear nano-clothes and nano-cosmetics, use nano-appliances and dispose of nano waste into the environment. Early scientific studies demonstrate the potential for materials that are benign in bulk form to become harmful at the nanoscale. There is an urgent need for regulations to protect workers, the public and the environment from nanotoxicity's risks, for greater understanding of the short and long-term implications of nanotechnology for people's health and the environment, for consideration of nanotechnology's broader social implications and for public involvement in decision making regarding nanotechnology's introduction.

What is "nanotechnology" and how is it used?

"Nanotechnology" refers to the design, production and application of structures, devices or systems at the incredibly small scale of atoms and molecules – the "nanoscale". "Nanoscience" is the study of phenomena and the manipulation of materials at this scale, generally understood to be 100 nanometres (nm) or less[1]. To put 100nm in context, a single strand of DNA measures 2.5nm across, red blood cells measure about 7,000nm and a human hair is 80,000nm wide. Most observers do not make a distinction between nanotechnology and nanoscience and use the term nanotechnology to encompass production and use of nanoscale materials ("nanomaterials"). Nanomaterials are "first generation" products of nanotechnology and have already entered wide-scale commercial use. They include nanoparticles (eg metal oxides), nanotubes, nanowires, quantum dots and carbon fullerenes (buckyballs), among others.

The ability to manipulate matter at the nanoscale may create opportunities for profitable new uses of familiar substances. For example, the nanoscale arrangement of carbon atoms is the only difference between soft graphite, hard diamonds, or carbon nanotubes capable of conducting electricity[2]. The colour, solubility, material strength, electrical conductivity and magnetic behaviour of nanoparticles can be very different from those of larger particles of the same chemical composition[3]. For example, in nanoparticle form gold may be red or blue, carbon nanotubes conduct electricity as well as copper and aluminium explodes. Altered properties are a result of both the influence of "quantum mechanics" at the nanoscale and also the much greater relative surface area that nanomaterials have compared with larger particles. Because of their large reactive surface area, nanomaterials have increased chemical reactivity[4], making them attractive for use in medicine or as industrial catalysts. However their high chemical reactivity and their greater capacity to penetrate biological membranes also pose serious new toxicity risks.

There are now over 720 products that contain nanomaterials on the global market[5]. These include transparent sunscreens and cosmetics, odour and wrinkle-repellent clothing, long-lasting paints, electronic and sports equipment, fuel catalysts, building equipment, a small number of medicines, and even some food products[6]. In coming years and decades, "next generation nanotechnology" is forecast to bring more complex nanodevices, nanosystems, nanomachines and nanobiotechnology[7] that will transform manufacturing, agriculture, health care, military, communications and energy production[8]. In fact, the United States government suggest that in time nanotechnology will be "the next industrial revolution"[9].

The risks of nanotoxicity to human health and the environment

In the past, incidentally produced nano-sized particles have been a by-product of forest fires and volcanoes, and high-temperature industrial processes including combustion, welding, grinding and vehicle combustion. The widespread use of manufactured nanomaterials in consumer, industrial and agricultural products will dramatically increase our exposure to particles in this size range. Study of the negative health impacts of exposure to very small particles in air pollution, coal and silica dust, welding fumes and asbestos is informing the emerging field of nanotoxicology[10], but much more research is needed to understand the health risks of nanomaterials already used in hundreds of products world-wide.

Why do nanomaterials present greater toxicity risks than larger particles and materials?

The toxicity of nanomaterials is often linked to their extremely small size. Smaller particles have a greater reactive surface area than larger particles, are more chemically reactive and produce greater numbers of reactive oxygen species that include free radicals[11]. Reactive oxygen species production has been found in a diverse range of nanomaterials including carbon fullerenes, carbon nanotubes and metal oxides[12]. This is one of the primary mechanisms of nanoparticle toxicity; it may result in oxidative stress, inflammation, and consequent damage to proteins, membranes and DNA[13].

The extremely small size of nanomaterials also means that they are much more readily taken up by the human body than larger sized particles. Nanomaterials are able to cross biological membranes and access cells, tissues and organs that larger sized particles normally cannot[14]. Nanomaterials can gain access to the blood stream following inhalation[15] or ingestion[16]. At least some nanomaterials can penetrate the skin[17], especially if skin is flexed[18]. Broken skin is an ineffective particle barrier[19], suggesting that acne, eczema, shaving wounds or severe sunburn may enable skin uptake of nanomaterials more readily. Once in the blood stream, nanomaterials can be transported around the body and are taken up by organs and tissues including the brain, heart, liver, kidneys, spleen, bone marrow and nervous system[20]. Nanomaterials have proved toxic to human tissue and cell cultures, resulting in increased oxidative stress, inflammatory cytokine production and cell death[21]. Unlike larger particles, nanomaterials may be taken up by cell mitochondria[22] and the cell nucleus[23]. Studies demonstrate the potential for nanomaterials to cause DNA mutation[24] and induce major structural damage to mitochondria, even resulting in cell death[25].

Size is clearly a key factor in determining the potential toxicity of a particle. However it is not the only important factor. Other properties of nanomaterials that influence toxicity include: chemical composition, shape, surface structure, surface charge, aggregation and solubility[26], and the presence of "functional groups" of other chemicals[27]. The large number of variables influencing toxicity means that it is difficult to generalise about health risks associated with exposure to nanomaterials – each new nanomaterial must be assessed individually and all material properties must be taken into account in safety assessment.

What evidence is there that commonly used nanomaterials pose serious toxicity risks?

Preliminary scientific studies indicate that nanomaterials now used in consumer products could present serious risks to human health and the environment. The Scientific Committee on Emerging & Newly Identified Health Risks (SCENIHR) issued a preliminary opinion on *"The appropriateness of the risk assessment methodology in accordance with the Technical Guidance Documents for new and existing substances for assessing the risks of nanomaterials*" in March 2007 [http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_004c.pdf]

In general, the report concluded that it is "**unclear**" whether existing EU risk assessment methods could capture **the potential environmental impacts** of nanomaterials, though it was **"generally likely" to identify risks to human health**.
The following conclusions (Page 51, 4.3.1. Conclusions of human health chapter) are specifically relevant to human health, and also single out certain vulnerable groups:

> *"… there is evidence that nanoparticles may cross the blood – brain barrier under some circumstances, that they may be associated with long term inflammation in several different types of tissue and organ and may be associated with cardiovascular effects. Although this data is still limited, these possibilities have to be taken into account. Similarly, the available evidence suggests that certain subpopulations, particularly those with pre-existing disease such as asthma and cardiovascular disease may be more*

susceptible to the adverse effects of nanoparticles, which again should be considered in the assessment of human health hazards."

Focus on vulnerable groups

"There are different human exposure scenarios during the life cycle of nanoparticles, including those during production, processing and distribution, use and application, storage, and waste disposal and recycling. Humans may also be exposed indirectly through contamination of the food chain by manufactured nanoparticles. If long term stability of a nanoparticle is proven, this may have consequences: for the general public and for potentially vulnerable subpopulations, including the embryo, the very young, and the elderly, beyond that associated with the exposure of workers. Furthermore the role of predisposition factors of individual humans, such as their genetic background and their pre-existing diseases such as allergies, cardiovascular disease and immune diseases needs to be taken into account."

Section 3.5.2. Potential risks to human health, SCENIHR Preliminary Opinion (see title above), 29 Mar. 2007

Nanoparticles of titanium dioxide are used in large numbers of sunscreens, cosmetics, personal care and food products. Titanium dioxide is a known photocatalyst. But even in the absence of UV light and at low doses, in a test tube experiment 20nm nanoparticles of titanium dioxide caused complete destruction of supercoiled DNA[28]. Also in the absence of UV, in another test tube experiment titanium dioxide produced reactive oxygen species in brain immune cells[29]. Pilot data from test tube experiments show nanoparticle titanium dioxide exposure negatively affected cellular function[30] and caused death of brain immune cells after 24 hours exposure[31]. The potential for nanomaterials in sunscreens and cosmetics to result in harm is made greater as production of reactive oxygen species and free radicals increases with exposure to UV light[32]. Photo-activated nanoparticle titanium dioxide has been demonstrated to cause oxidative damage to DNA in cultured human fibroblasts[33]. In test tube experiments, photo-activated titanium dioxide nanoparticles were toxic to skin fibroblasts and nucleic acids[34] and to human colon carcinoma cells[35].

Nanoparticles of silver are now used in toothpastes, soaps and face creams, food packaging, clothing, household appliances, disinfectants and wound dressings. Silver nanoparticles have a potent ability to kill bacteria[36]. In fact, the manufacturers of a washing machine which uses silver nanoparticles claim that their product will kill over 650 different bacteria[37]. However there are concerns that silver nanoparticles may also kill beneficial bacteria in environmental systems. The United States Environmental Protection Agency has announced plans to regulate as pesticides products that contain silver nanoparticles and which make antimicrobial claims[38]. At the same time, silver nanoparticles may also compromise our ability to control harmful bacteria. Harmful bacteria may become resistant to silver nanoparticles, but because of the type of resistance mechanism developed, they may also potentially develop resistance to 50% of commonly used antibiotics (beta-lactams)[39]. Silver nanoparticles may also be toxic to humans: test tube studies show that silver nanoparticles are highly toxic to rat brain cells[40], mouse stem cells[41] and rat liver cells[42].

Carbon fullerenes ("buckyballs"), currently used in some face creams and moisturisers, have been found to cause brain damage in fish[43], kill water fleas[44] and have bactericidal properties[45]. Test tube studies have found that even low levels of exposure to water soluble fullerenes are toxic to human liver cells, carcinoma cells and skin connective tissue[46]. This is cause for serious concerns given the capacity of fullerenes to enter human cells and to localise within cell nuclei[47]. Fullerene-based amino acid damaged human skin cells[48]. In test tube studies in the presence of biological reducing agents (eg NADH) similar to the concentrations found in biological systems, photo-activated fullerenes destroyed supercoiled DNA[49].

What are the potential sources of nano-exposure?

Members of the general public face exposure to nanomaterials through use of products that contain nanomaterials, for example cosmetics, sunscreens, clothing or cling wrap, or through ingestion of products that contain nano-ingredients, for example foods, beverages, nutritional supplements or lipstick. Occupational exposure to nanomaterials is of particular concern as workers may be exposed at much higher levels than the general public and on a more consistent basis[50]. Workers may experience nano-exposure in the production, manufacture, packaging or transport of products that contain nanomaterials, or in cleaning or maintenance work. Environmental exposure to nanomaterials is likely to increase as the industry expands. Waste containing nanomaterials will be released into the environment from households and industry, and products containing nanomaterials will disposed of in landfill. Even nanomaterials that are "fixed" in products, for example lights, car parts or building equipment, may enter waste streams as "free" nanomaterials following product disposal or recycling. Large quantities of nanomaterials may also be released into the environment intentionally, for example for agriculture, military or remediation. There is a complete lack of data for current human and environmental exposure to manufactured nanomaterials[51].

Broader social issues associated with nanotechnology

This fact sheet is focussed on the health risks associated with nanotoxicity. However it is important to note that nanotechnology also raises important social issues and ethical challenges. Proponents suggest that a nanotechnology-enabled "revolution" will bring far-reaching changes to economic, social and ecological relations. The United States National Nanotechnology Initiative predicts: "If present trends in nanoscience and nanotechnology continue, most aspects of everyday life are subject to change"[52]. Yet to date there has been a dearth of critical discussion about public interest issues associated with the predicted nanotechnology "revolution" and in particular what role civil society should have in decision making.

Nanotechnology governance – EU action so far

The European Commission recognised the need for early regulation of nanotechnology's risks in 2004: "Appropriate and timely [nanotechnology] regulation in the area of public health, consumer protection and the environment is essential, also to ensure confidence from consumers, workers and investors"[53]. Also in 2004, the United Kingdom's Royal Society and Royal Academy of Engineering made very explicit recommendations for the precautionary management of nanotoxicity's risks: nanomaterials should be treated as new chemicals under REACH; be subject to new safety assessments *prior* to their inclusion in consumer products; factories and research laboratories should treat nanomaterials as if they were hazardous; and until the environmental impacts of nanomaterials are better known, their release into the environment should be avoided as far as possible[54]. However there are still no nanotechnology-specific regulations anywhere in the European Union – or indeed at a national level anywhere in the world.

In its 2006 report[55], the EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) recognised the systemic failure of existing chemicals regulatory frameworks to manage the risks of nanomaterials. Existing regulations do not require manufacturers to treat nanomaterials as new chemicals, thereby triggering the need for safety testing of nanoproducts prior to releasing these products into the market. Regulations remain based on the flawed assumption that materials are substantially equivalent whether in bulk or nanoparticle form – despite the known higher reactivity, and often greater toxicity, of nanomaterials. This means that if a nanomaterial has already been subject to safety assessment in bulk form – as many have – there is no trigger for new safety assessment. SCENIHR also recognised that the use by existing chemicals regulations of tonnage as the dose metric is inappropriate for nanomaterials that can be toxic even at low mass; it recommended that particle number and total surface area be used instead[56]. Finally, regulatory regimes must be updated to require assessment of nanomaterial characteristics such as shape, surface structure, charge etc in affecting toxicity.

New regulations are urgently required to manage nanomaterials: a recent survey suggests that industry has failed to undertake voluntary risk assessment. 138 Swiss and German companies that use nanomaterials were surveyed; of the 40 companies that responded 65% perform no risk assessments[57].

HEAL recommendations

HEAL calls for a strongly precautionary approach to manage nanotechnology:

- The assessment of nanomaterials as new chemicals
- Mandatory safety testing of nanomaterials prior to their inclusion in commercial products
- Requirements for product labels to indicate the presence of manufactured nano materials/particles
- The consideration of nanotechnology's broader societal implications alongside questions of basic safety
- Public participation in decision-making regarding nanotechnology's introduction and in determining priorities for public spending on nanotechnology research and development

Recognising that concern has been expressed at the highest scientific levels about the health risks of nanomaterials, until such time as these actions are taken to manage nanotechnology's risks, we support a moratorium on the further commercial sale of products that incorporate manufactured nanomaterials.

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6 For examples of specific products, visit the Consumer Products Inventory hosted by the Woodrow Wilson Center for International Scholars' Project on Emerging nanotechnologies: http://nanotechproject.org

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