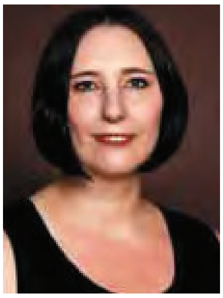
Nanoparticles: Why are they dangerous?



by Monique Muller

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1. What are nanoparticles

Nanotechnology sounds like novel modern technology although in fact it has been around since as evidenced by the Roman Lycurgus chalice. However, only in the past 20 years has nanotechnology been actively used to revolutionise our life and will continue to do so still far into the future.

So what is nanotechnology? Simply stated, it is the technology used to manipulate matter (such as carbon, gold, nickel, silver, silica or silicates as well as amalgamated chemicals) at a nanometer scale; thus the manipulated matter is called nanoparticles, abbreviated to NPs.

Due to their extremely small size - to all intents and purposes - NPs are "new" matter that displays new properties unassociated with the original source matter.

The development of NPs impacts many areas, for example:

- by improving disease diagnosis and treatment technologies in the healthcare and medicine sector;
- by creating smaller, lighter, stronger and more efficient products;
- by decreasing the impact of environmental pollution by improving water purification or energy conservation technologies.

Nanomaterial	Uses
Metal oxides	Electronics, consumer products, biomedical, environmental remediation
Carbon nanotubes	Textiles, consumer products, structural materials
Quantum dots	Optical properties, electrical applications
Fullerene-C60 (Buckyballs)	Lubricants, superconductors, solar cells

Table 1: Various applications of nanotechnology through the use of nanoparticles

As indicated NPs are normal chemical elements which are "ground" or "cut" up into very small pieces equal or smaller than one tenth of a micrometer (0.1 µm), otherwise indicated as being in the one to one hundred nanometer range (1 – 100 nm), hence their name. They can have various geometric shapes such as spheres, rods, tubes and more.

To fully grasp the concept of what a nanoparticle is consider the following:

- a sheet of paper is about 100 000 nm thick;
- a virus is approximately 100 nm in size; and
- fingernails grow about 1 nm per second.

Figure 1 gives an indication of the small scale of the particles referred to when discussing NPs. Source: Youtube video by the Centre of Nanomedicine (https://www.youtube.com/watch?v=38Vi8DmOkdY). Video generated by the AlloSphere Research Group.

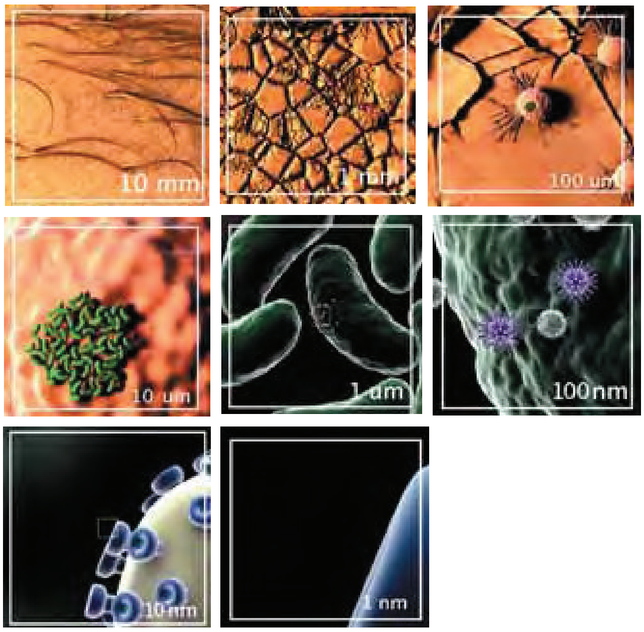

Figure 1: Illustration of nanoparticle size against other particles commencing top left with a 10 mm square of human skin surface and zooming in down to 1 nm square view of part of a key on a virus's surface.

Thus NPs can never be seen with the naked eye. Special microscopes such as Scanning Electron Microscopes or even Scanning Transmission Electron Microscopes or High Resolution Transmission Electron Microscopes are required to see objects of this size.

Figure 2 is a good illustration of what is meant by surface size. When a 1 cubic centimeter (cm) is filled with micrometer (µm) sized cubes – a trillion (10^{12}) of them, each with a surface area of 6 μm^2 – the total surface area amounts to 6 m^2, or about the area of the main bathroom in an average house. And when that single cubic centimeter of volume is filled with 1 nanometer

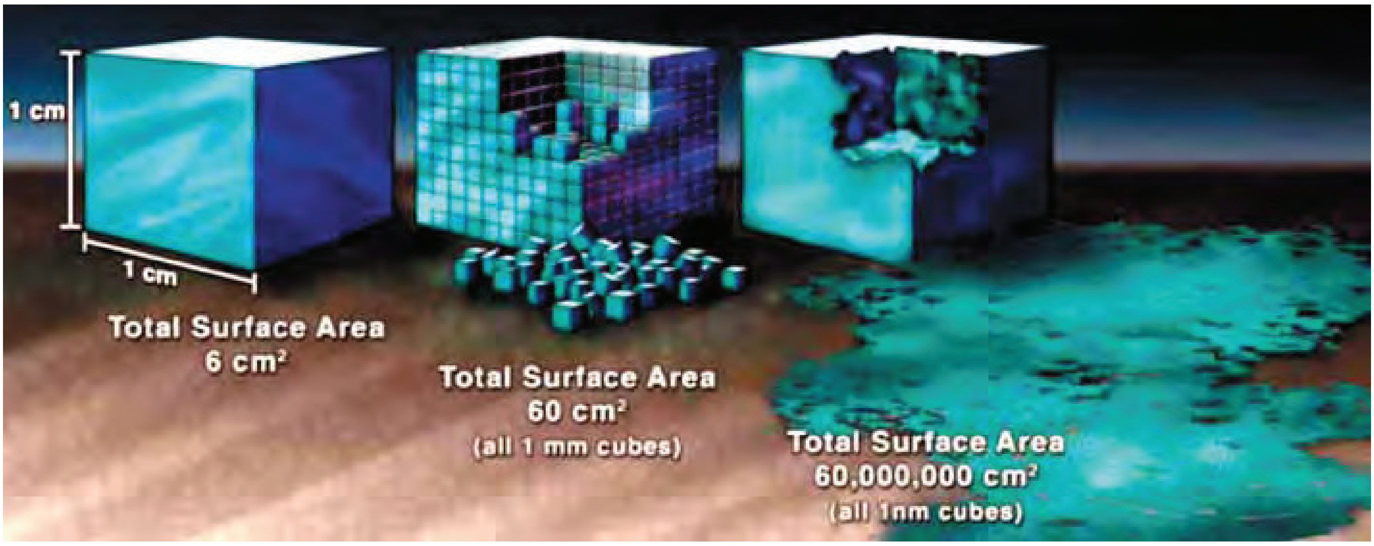

Figure 2: Comparison of Surface Areas at 1 cm, 1 mm and 1 nm scale. Source: www.nano.gov. Link: http://www.nano.gov/nanotech-101/special.

(nm) sized cubes – 10^{21} of them, each with an area of 6 nm^2 – their total surface area comes to 6 000 m^2, which is slightly smaller than a soccer field.

An NP's properties depend more on its surface area than on the particle's composition itself. Thus its relative surface area is one of the principal factors that enhance the NP's reactivity, strength and electrical properties. One benefit of greater surface area - and improved reactivity - of nanostructured materials is that they help to create better catalysts (a substance that increases the rate of a chemical reaction without itself undergoing any permanent chemical change).

2. Why might Nanoparticles be dangerous?

Although engineered nanomaterials seems to have limitless possibilities for use, they bring with them new challenges such as identifying and controlling potential safety and health risks to those exposed to them. The drawback of NPs is that anyone who works with or in the vicinity of where NPs are used or created is exposed to these particles and it is feared that these will have far reaching health effects on workers such as in the case of asbestos fibers.

Although scientists may be dealing with the same chemical substances, because of the role the surface area plays, they may have totally different chemical characteristics, including reactivity, electrical conductivity, strength, mobility, solubility, magnetic and optical properties. If the original chemical was already known to cause cancer or allergic reactions, NPs, due to their size, may cause similar affects but even more rapidly, and on a bigger scale, even at small quantities or doses. The chemical heath effect of NPs is called Nanotoxicity.

It has been determined that the impact on the human body will also depend on particle size, mass, chemical composition, the surface area and how the individual NPs aggregate, or clump, together. It is well known that toxicity of NPs increases with a decrease in particle size. It is also well known that the NPs involved in catalytic and oxidative reactions can induce a greater than normal cytotoxicity (the toxicity of a substance to a living cell).

Inhalation is believed to be the primary route of human exposure to nanoparticles. The different compartments of the human respiratory tract (nose, larynx, airways and lungs) all act as a filter for NPs. The smaller the particle size, the more likely its chances of reaching the alveoli in the lungs. The NPs typically cause lung scarring and the thickening of the lung walls. As a result the oxygen supply from the lungs to the blood is reduced and persons with this condition are nearly always short of breath. Lung tissue scarring can also lead to inflammation of the lungs or cause lung tumours.

Researchers suggest a normal room contains 10 000 to 20 000 NPs per cm^3 or as high as 50 000 NPs per cm^3 in a forest and 100 000 NPs per cm^3 in an urban street. At these concentrations it can be inferred that we breathe in millions of NPs. It can be assumed that half of these reach the alveoli and may therefore also travel through to our bloodstream. At present it is not known to what extent the engineered NPs contribute to these overall numbers and what the concentrations in an uncontrolled work environment where NPs are manufactured or being used will be.

Other body and organ systems (immune, endocrine and cardiovascular) can be affected after long term exposure as the NPs travelling through the bloodstream will eventually reach various organs and organ cells. NPs can cause oxidative stress and/or activation of pro-inflammatory cytokines in the lungs, liver, heart and brain. NPs cause pro-thrombotic and adverse effects on the cardiac function; causing heart attack or adverse effects on the heart rate. Abnormal blood coagulation may even occur increasing the risk of blood clots, the chances of a heart attack or a stroke. It is of great concern that NPs can cross cell membranes (internally and externally) and can thus interact with sub-cellular structures causing oxidative damage and may eventually impair cell functions causing damage to the organs and finally to an entire system.

Although there is scant research on the following issues, the possible outcomes cannot be ignored:

a. NPs are not membrane bound and have direct access to the intracellular proteins, organelles and DNA of the cell and thus cause chaos inside the cells.
b. NPs can pass through the blood-brain barrier, causing neurotoxicity i.e. damage to the nervous system tissue that transmits and processes signals in the brain and to other parts of the body.
c. NPs can deposit in the nasal region when inhaled and enter the brain by travelling via the sensory nerves (including the olfactory and trigeminal nerves).
d. NPs can cross the placenta, causing the poisoning, genetic defects, cancer and disfigurement of the embryo. They may result in embryonic death, abnormal development of one or more body systems or being born with an incurable fatal disease; it can be harmful to the mother's health too.

Other issues:
a. When NPs are released into the atmosphere, they may cause external pollution
b. NPs may initiate catalytic reactions previously not anticipated, causing fire or an explosion; the explosion risk of some metals increases significantly as their particle size decreases
c. Particles may spread from work area to work area and even neighbouring businesses or communities and if work is not completed under a negative pressure and high-efficiency particulate arrestance (HEPA) filters are not installed.

Exposure to NPs at the workplace may occur in research and development facilities in the nanotechnology sector, in chemical and pharmaceutical companies, in facilities where paints, cement, and other products involving powder handling are manufactured and where NPs are by-products of processes such as baking, welding and polymer processing.

Unfortunately, data on occupational exposure is scarce. To detect NPs, both in gases and in liquids, is difficult due to their size and they can only accurately be detected by special microscopes as mentioned earlier. Testing is very expensive and retention of uncontaminated samples is virtually impossible. Furthermore, no validated sampling methods currently exist. Lastly it may be difficult (even on special microscopes) to distinguish between ambient NPs and those NPs being used in the workplace. Instruments able to detect and analyse particles of a few nanometers were only developed recently, therefore currently there is no or only little toxicology data; that which does exist has been garnered mostly from tests on animals.

Currently no occupational exposure standards and guidelines exist anywhere in the world. There is no clear opinion on which parameter(s) – mass, number of particles and/or surface area – should be measured as the most appropriate method of assessing exposure. The available portable instrumentation for nanoparticle exposure is inadequate and new sampling techniques and strategies for assessing exposure at the workplace and in the environment needs to be set up.

It should be remembered that people are at the highest risk of exposure when:

1. Opening and manually handling bulk nanomaterials
2. Pouring or mixing of liquid NP solutions
3. A high degree of agitation of NPs is involved
4. Generating NPs in non-enclosed systems, cabinets or cupboards
5. Handling (weighing, blending, spraying) powders of NPs
6. Conducting maintenance on equipment and processes used to produce or fabricate nanomaterials as it disturbs NP "dust"
7. Cleaning up or removing of spills of NPs and waste material containing NPs
8. Cleaning dust collection systems used to capture NPs such as HEPA filters
9. Working with no or inadequate personal protective equipment (PPE) and clothing
10. Machining, sanding, drilling or causing other mechanical disruptions of materials containing NPs
11. Operating of high-energy processes such as milling, sonication, grinding, and high-speed blending may cause the release of NPs

3. What can be done?

If this is the case, what can be done to minimise exposure risk? It is obvious that exposure to various NPs and especially when working in an uncontrolled environment with any of these NP substances will eventually have a deleterious effect on an individual's health. The employer can help by implementing a hierarchy of controls, for example:

1. Assume that all NPs are toxic, until health studies prove differently.
2. When purchasing NPs commercially obtain their Material Safety Data Sheet (MSDS) and share the information with the health and safety committee and the workers, through training and toolbox talks.
3. Work with NPs in a solution, liquid or slurry form, or attached to substrates so that the dry material is not released easily.
4. Install local exhaust systems, such as extraction arms at the point of operation. The vents should assist air to flow from low hazardous to high hazardous areas, thus usually from entrance to back of work space and create a negative pressure between NP areas and other work spaces.
5. HEPA filters must be installed in the extraction system to trap the NPs. The filters must be checked once a month, serviced and replaced as needed.
6. If local extraction is not possible consider installing enclosed HEPA filtered hoods or even rooms in where NPs are used.
7. Work surfaces should be non-static, easily cleanable and floors be made of concrete covered with a seamless pre-finished heat welded sheet vinyl, epoxy coatings (SANS 10109), or polished concrete with dustproof hardener. Covings between floors and walls are recommended to facilitate clean-up in case of spillages.
8. The walls shall be non-porous and painted with a durable, impervious finish in such a manner to facilitate cleaning and decontamination. A glossy acrylic or epoxy or equivalent coating is recommended (SANS 10305).
9. Set up Standard Operating Procedures (SOPs) for each activity and equipment being used which will include the safety procedures to be followed. Short versions of the SOPs should be displayed properly.

10. Ensure workers and any visitors to these areas wear the proper PPE - nitrile gloves {double}, a closed chemical protective overall, safety protective glasses, respirator with appropriate cartridges (Class P2 and P3 glass fibre/HEPA filters) and even closed shoe covers need to be considered.
11. It is strongly advisable to install a safety shower eye wash station combination close by.
12. Conduct annual inductions covering the potential hazard identification, proper techniques/procedures for activities and waste disposal with workers.
13. Post signs to communicate appropriate warnings and precautions regarding chemical containers at entrances to the chemical/raw material storage facilities. It should also include the emergency after hour contact details.
14. Introduce proper hygiene, maintenance and housekeeping procedures:
    a. Use HEPA-filtered local capture/extraction hoods.
    b. All extraction units must contain HEPA filters to capture the NPs.
    c. No cellphones to be used in the NP areas.
    d. Prevent ingestion by prohibiting eating and drinking in these areas.
    e. Clean and maintain all equipment and areas / benches / floors regularly i.e. daily or after use.
    f. Vacuum areas and equipment by using a HEPA-filtered vacuum cleaner.
    g. Wet wipe the area with paper towels.
    h. Clean spills immediately - have a special chemical spill kit ready for use.
    i. Collect clean-up materials in a tightly closed container and handle them as hazardous waste.
    j. Ensure a proper maintenance schedule of equipment is set up and followed.
    k. Label all chemical containers with the identity of the contents and include term "nano" in the descriptor as well as the hazard warning and chemical concentration.
    l. An inventory of all chemicals, including NPs must be in place and updated at least 6 monthly.
    m. Store NPs in a well-sealed container or room that when opened causes minimal agitation of the NPs contents. A preferred solution is to store all NP containers in an enclosed HEPA filtered box and work and weigh in this box.
    n. Wash hands frequently with the proper hand washing method.
    o. Remove gloves when leaving work area.
    p. Overalls, coats can be washed in-house or via a specialised laundromat. Store dirty coats in a biohazard bag until such time they are collected for washing.

Acknowledgments

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