Nanosafety Guidelines

Preventing exposure to
Nanomaterials at the
Faculty of Applied Sciences

Workgroup Nanosafety & Authors	Andreas Schmidt-Ott Valérie Butselaar-Orthlieb Jos van Winsen Duco Bosma
Document version	Version 2 – September 2010
Contact info	Valérie Butselaar-Orthlieb Delft University of Technology – The Netherlands Faculty of Applied Sciences V.C.L.Butselaar-Orthlieb@tudelft.nl
Nanomonitor	Duco Bosma Delft University of Technology – The Netherlands Faculty of Applied Sciences D.Bosma@tudelft.nl

Contents

1. Introduction 3
2. Potential nanotoxicity 4
  2.1 Criteria for potential nanotoxicity 4
  2.2 Risk assessment on nanotoxicity 4
3. Recommendations for preventing workplace exposure to nanomaterials 5
  3.1 Strategy 5
  3.2 Measures for working with nanomaterials in liquids 5
  3.3 Measures for working with nanomaterials in gas phase reactors 5
  3.4 Explosion risk and pyrophoricity test 5
  3.5 Measures for working with nanomaterial powders 6
  3.6 Personal protective equipment 6
  3.7 Monitoring lab air and filter efficiency 7
  3.8 Cleaning procedures and spills 8
  3.9 Transport of nanomaterials 9
  3.10 Disposal of nanomaterials 9
  3.11 Summary flowchart 10
4. Background information on nanosafety 11
  4.1 Terminology of nanomaterials 11
  4.2 Nanotoxicity 11
  4.3 Regulations and guidelines 13

1. Introduction

Within Delft University of Technology, both nanotechnology and nanoscience are important research areas. They comprise engineering, design, synthesis and application of nanomaterials with novel properties. The introduction of these new materials into the workplace raises questions concerning occupational safety and health and generates the need for appropriate safety measures. The current debate on the risks of nanotechnologies and nanoscience tends to focus on the potential dangers on the work floor, notably inhalation exposure.

In safety context, the term nanomaterial is used as a general name for materials with primary particles in the nano range, confusedly also called free nanostructured materials, nano-objects, nanoparticles, nanopowders, nanosized material, nano-aerosols, ultrafine-dust, -particles or -aerosols or other names.
In this guideline, we refer to particles or structures with at least one primary dimension in the size range of 1 to 100 nm.

Scope
To protect the people from the Delft University of Technology from the potential dangers of nanomaterials, the present guidelines have been set up in view of research activities within the faculty of Applied Sciences (TNW) of the University.
The guidelines are sharpened periodically, taking into account gained knowledge on nanotoxicology as well as new domains of research activity within the faculty. The input of researchers is incorporated in the update of these guidelines.

2. Potential nanotoxicity

This chapter gives the criteria for being classified as nanomaterial in a safety context within the Faculty of Applied Sciences and a suggestion on how to asses the risks on potential nanotoxicity.

2.1 Criteria for potential nanotoxicity

The emphasis is primarily made on the possibility of the nanomaterial to become airborne and be inhaled, secondly on the possibility to penetrate the skin and cross other physiological barriers.

From what is presently known, it is advised to consider particles as (potentially) nanotoxic if each of the following 3 criteria are fulfilled:

1. The primary particles are between 1 and 100 nm at least in one dimension. This includes larger aggregates of these particles. Nanoparticles tend to form clusters rather than being isolated.

2. They are solid.

3. They are virtually insoluble in water or liquids of the organism or dissolve only very slowly.

It must be stressed that if only part of the three criteria above is fulfilled, materials can still be toxic but not specifically nanotoxic. For example, liquid or soluble nanomaterials. In these cases, the conventional safety precautions should be acted upon.
Nanotoxicity may also co-exist with toxicity due to nano specific physical and catalytic properties (see section 4.2 for more information).

2.2 Risk assessment on nanotoxicity

All nanomaterials must be considered as being nanotoxic until the contrary is proven.
Consult reliable internet sources for possible recent nanotoxicity data on your nanomaterial. when the nanomaterial has been purchased, consult the manufacturer.
If no trustworthy proof is given, consider as nanotoxic and prevent exposure according to the strategy given in chapter 3.

At present, no health-based occupational exposure limit exists for nanomaterials. As an alternative, the National institute for public health and the environment (RIVM) issued a report based on the expertise of KIR-nano (Knowledge and Information Centre Risks of nanotechnology) with provisional nano reference values (RIVM report 601044001/2010 Tijdelijke nano-refentiewaarden) that can be used as pragmatic benchmark levels to reduce exposure of nanomaterials to employees.
The derived values (see section 3.7) are only to be used as pragmatic benchmark levels - they do not guarantee that an exposure to nanomaterials below these values is safe. It therefore remains important to minimize the exposure to nanomaterials as much as reasonably practicable.

3. Recommendations for preventing workplace exposure to nanomaterials

Health hazards from nanomaterials in the present work of the faculty of Applied Sciences and in particular the department of Chemical Engineering are mainly limited to inhalation toxicity and skin contact. The focus lies on avoiding inhalation exposure which is the dominant exposure route, as well as contact with skin and eyes. Additionally to this guideline, always use good general laboratory safety practices.
The first section outlines the strategy to be followed. Afterwards, more concise instructions are given on how to handle nanomaterials in various cases. In any case, the lab air can be monitored before, during and after experiments with nanomaterials to asses the efficiency of the exposure restricting measures (see section 3.7).
Finally, a summary flowchart on the recommendations is given in section 3.11.

3.1 Strategy

The approach consists of the application of the Precautionary Principle, which is to minimize exposure levels to nanomaterial, As Low As Reasonably Practicable (ALARP principle) as long as the toxicity is classified as uncertain.

In order to realize minimal exposure, the Occupational Hygiene Strategy is used. This hierarchy of control for nanomaterials consists of the following steps:

1. Eliminate: do not work with nanomaterials.
2. Substitute: replace the nanomaterial by another material.
3. Isolate: immobilized in a matrix, on a substrate, contained in a closes system (reactor, glovebox)
4. Ventilate: work in a fume hood or a ventilated cabinet/area
5. Personal protective equipment: wear respiration protection and gloves.

Note the order of the steps to be applied. Personal protective equipment (PPE) is considered as last remedy if the foregoing steps did not fulfill to realize minimal exposure.

3.2 Measures for working with nanomaterials in liquids

Avoid spreading of the liquid by working in a spill container.
Wear gloves that are suited for the liquid that is handled.
Avoid the dispersion of liquid droplets in the lab air.
Directly clean-up spills, before evaporation or further spreading occurs.

3.3 Measures for working with nanomaterials in gas phase reactors

Work in a closed reaction vessel, preferably around atmospheric or lower than atmospheric pressure. Make sensitive leak checks between runs. When working in overpressure, obey the standard safety rules for pressurized vessels and put the vessel into an enclosed safety vessel. For small over-pressure set-ups a closed fume hood is sufficient.
Mount a HEPA filter (e.g. Emflon PFR filter from Pall, > 3 nm) on the exhaust side of the process before leading into the fume hood and the outside air.
Test this HEPA filter periodically with a nanomonitor (see section 3.7) and replace when needed.
Explosion safety: take notice of the information given in section 3.4 on pyrophoricity.

3.4 Explosion risk and pyrophoricity test

Due to their large surface-to-volume ratio and enhanced reactivity of a strongly curved solid surface, all oxidizable nanomaterials in the powder state must be considered as potentially pyrophoric when put in contact with air. Thus, explosive behavior is possible.
Asses the risk of an incident in a process where a large un-oxidized sample is momentarily exposed to air. In a process that produces nanomaterial from the gas phase, the particles tend to become cleaner and cleaner while the process runs, e.g. less oxidized. This should be considered!

Little is known about nano pyrophoricity, so we recommend to test the pyrophoricity by bringing a small quantity of material in contact with air before producing or handling quantities on the level of one gram or more.
Laboratory studies within the department of Chemical Engineering however, have revealed that pyrophoricity, can in some cases, be avoided if the particles have already formed an oxide layer before exposure to atmospheric oxygen. Therefore, be certain that the test is not performed on partially oxidized particles.

3.5 Measures for working with nanomaterial powders

Handle free nanomaterial powder exclusively in a closed fume-hood or an enclosed vessel (glove box).
If handling outside a closed environment cannot be avoided, wear P3 certified respiratory protection (see section 3.6 on personal protective equipment).
For characterization purposes such as XRD analysis, envisage the use of a drop of oil to contain the powder and prevent it be become airborne.
Explosion safety: take notice of the information given in section 3.4 on pyrophoricity.
Clean all parts that have been in contact with nanoparticles and spills after use (see section 3.8).

3.6 Personal protective equipment

In accordance with the occupational hygiene strategy, all possible protective measures must be taken before preventing exposure to nanomaterials with personal protective equipment. Use respiration protection in case of inhalation exposure risk.

Mask
The following respiration protection are considered to be effective against airborne free nanomaterials:
Assisted breathing filter with full face shield such as the Dräger X-plore 7300 system.
Full face mask (also protects the skin and the eyes) with P3 certified filter cartridges.
Half face mask with P3 certified filter cartridges.
Considering the orders of magnitude between inhalation toxicity and skin or eye toxicity, half face masks may also be used. Take notice that for any mask, a lack of tightness between the face and the mask can lead to unnoticed exposure.

Gloves
Nanomaterials may penetrate through commercially available gloves. Glove material is not the only criterion; elaboration process and thickness are major issues as well. The advice given in the Nanosafe report on effectiveness of conventional protective devices is: use 2 layers of gloves to prevent nanomaterials to migrate through the gloves onto your skin or replace the gloves after a spill.

Lab coat
Non-woven fabrics such as high density polyethylene textile seem to give less penetration than cotton and paper. However, a lab coat cannot be considered as an effective protection against nanomaterial. Depending on the situation or in case of spills, a suitable protective coverall might be considered.

3.7 Monitoring lab air and filter efficiency

To asses inhalation exposure, it is advised to measure the concentration of airborne nanomaterial in the lab air shortly before, during and after the handling of nanomaterials and to compare the values to the issued provisional nano reference values as given below.

Table 1: Provisional nano reference values expressed as Benchmark Exposure limit (source: RIVM report 601044001/2010 Tijdelijke nano-refentiewaarden)

Category	Description	Proposed Benchmark Exposure limit (BEL)
A	Metals, metal oxides and other bio-persistent granular nanomaterials with density > 6000 kg/m^3 and a particle size in the range of 1 to 100 nm e.g: Ag, Fe, Au, Pb, La, TiO_2, CeO_2, ZnO, SiO_2, Al_2O_3, Fe_xO_y, SnO_2, CoO and nanoclay.	20.000 particles/cm^{3*}
B	Bio-persistent granular nanomaterials with density < 6000 kg/m^3 and a particle size in the range of 1 to 100 nm e.g.:C_{60}, carbon black, TiN, Sb_2O_5, polymers, polystyrene, dendrimers and carbon nanotubes for which asbestos like health effects have been excluded.	40.000 particles/cm^{3*}
C	Carbon nanotubes for which asbestos like health effects have not been excluded.	0.01 fibres/cm^{3**} (10.000 fibres/m^3) based on asbestos exposure risk ratio.

* 8 hours time weighed average increase with regards to background level.

** measured with a phase contrast microscope (PCM) or 20.000 fibres/m^3 when measured with a transmission electron microscope (TEM).

The proposed benchmark exposure limits are issued in order to minimize workplace exposure according to present knowledge and are not based on toxicological data. Health risks of workers exposed to these levels cannot be excluded. These benchmark limits may not be confused in any case with health based exposure limits on the workplace.

Background levels fluctuate by day and season and synthesized nanomaterials cannot be differentiated from industrial environmental nanomaterials such as soot, solid industrial air pollutants, viruses and bacteria. Therefore, it is important to measure (reference) concentrations just before, during and directly after the handling of nanomaterials to detect a significant rise in concentration.

The efficiency of filters and vacuum cleaner filters must be tested periodically by means of measurements. Badly placed, bypassed or damaged filters can become a major source of well dispersed nanomaterial.

On founded suspicion of exposure to nanomaterials, a letter for your employee file can be requested with the Department Safety Officer or Safety & Health advisor, that describes the exposure event. Similar to asbestos exposure, this letter is a document in case of long term health effects.

The department of Chemical Engineering has a continuous nanomonitor available for these measurements (for more information see contact information in cover).

Figure 1: Philips Aerasense Nanotracer

3.8 Cleaning procedures and spills

Specifically watch out for exposure during cleaning operations.
Wear gloves and work in a fume hood if the equipment allows this. Clean the fume hood afterwards.
If needed, monitor the lab air nanomaterial concentrations during clean-up.
Wear respiration protection when working outside a fume hood or in an open fume hood and consider overall protection.
All contaminated material must be disposed of as chemical waste.

Materials and surfaces can be cleaned as following:
Wiped with a wet cloth (use water or solvent) where possible, rinsing off the cloth with water or dispose of it.
Vacuum cleaned, where the exhaust of the vacuum cleaner is equipped with a HEPA filter and isn't equipped with a pressure relief valve that bypasses this HEPA filter if blocked. Monitor the exhaust of the vacuum cleaner during operation (see section 3.7 on lab air monitoring). A malfunctioning filter can increase the exposure by dispersing the nanomaterial in the air.

Small spills can be cleaned as described above.
The clean up of a significant or large spill must be assessed individually. Inhalation and dermal exposure present the greatest risks during clean-up.
Inhalation exposure in particular will be influenced by the likelihood of the material to re-aerosolize and become airborne. In this context, a hierarchy of potential exposures exist, with dusts presenting a greater inhalation exposure than liquids, and liquids in turn presenting a greater risk than encapsulated or immobilized nanomaterials.
In case of a spill, contact your Department Safety Officer or Safety&Health advisor to set-up a cleaning procedure together. The level of personal protection and the cleaning methodology resemble those used for asbestos.
Due to the ambiguity of the measurement, a cleanliness declaration is difficult to give.

Any significant spill or incident with nanomaterial must be reported to the Department Safety Officer or Safety & Health advisor.

3.9 Transport of nanomaterials

Transportation of nanomaterials can be done in the same manner as normal chemicals, i.e.: use closed containers.

3.10 Disposal of nanomaterials

Quantities of nanomaterials (powders, colloids) exceeding the milligram range should be treated as chemical waste, if the particle solubility in water is very small (inorganic materials like metals, metal oxides etc.)
If the solubility is higher, the rules according to the toxicity class of the macroscopic material apply.
Milligram range nanomaterial residues in water from cleaning can be poured down the drain.

3.11 Summary flowchart

The recommendations of this chapter are summarized in a Nanosafety 'Quick Check'.

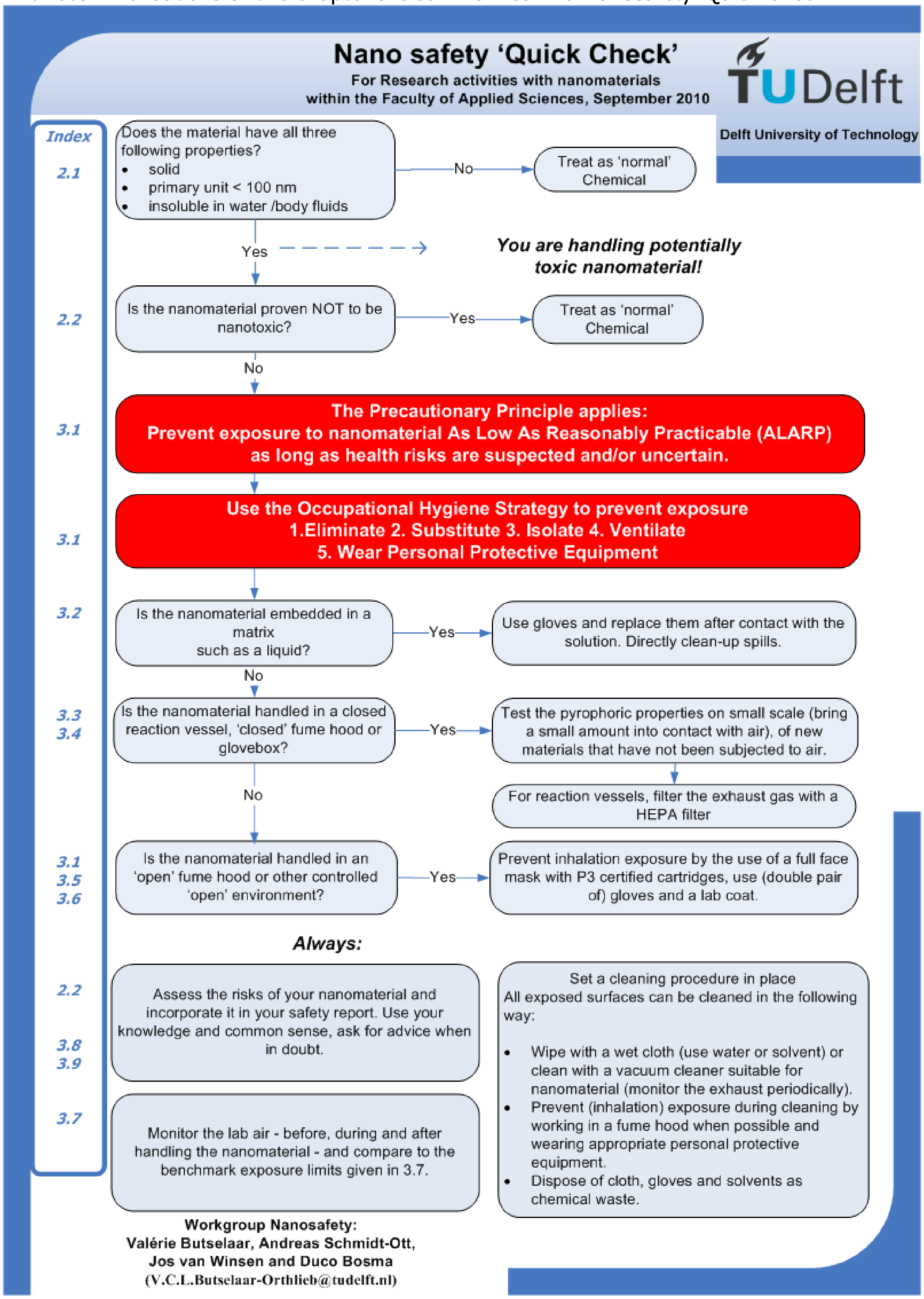

Figure 2: The summary of these guidelines in a 'Quick Check'

4. Background information on nanosafety

This chapter provides information on terminology, toxicity and regulations for nanomaterials.

4.1 Terminology of nanomaterials

Nanomaterials have recently been given a standard terminology. They encompass nano-objects and free nano-structured materials. Nano-objects are defined as particles with three (nanoparticle), two (nanofibre) or one (nanoplate) external dimensions in the nanoscale, between approximately 1 and 100 nm. See figure 3 for a hierarchy of terms.

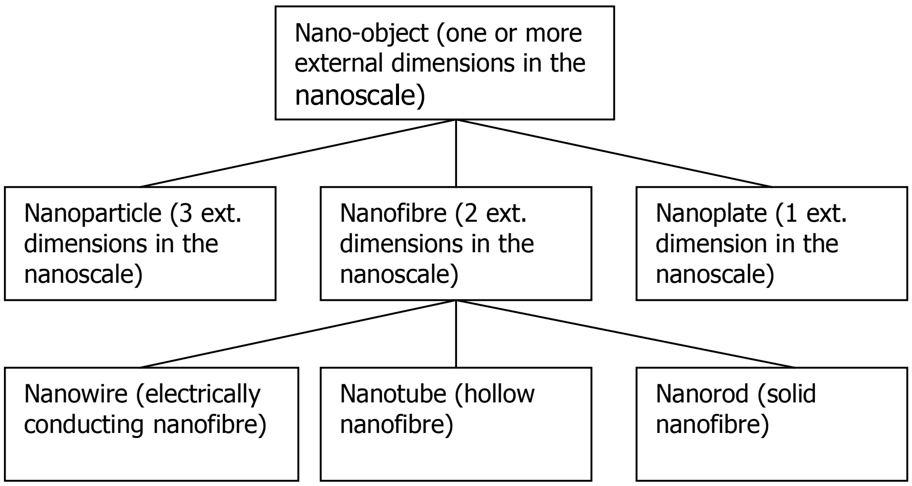

Figure 3: Hierarchy of terms related to nano-objects.

4.2 Nanotoxicity

Toxicological research has generated a great deal of information on the relationship between the physical and chemical properties of fine particles and their adverse effect on our health. The knowledge on these interactions is however far from complete.
The question facing scientists today is to what extent the current knowledge on 'traditional' fine particles is applicable to the new generation of nanomaterials. Due to their small size, odd shapes and high reactivity, their effect on the metabolism cannot easily be predicted.

Figure 4 gives a qualitative "formula" for nanotoxicity, which summarizes the three criteria. It introduces nanotoxicity as a new category of toxicity, which may be superimposed on conventional toxicity.
Conventional toxicity ($Tox_{conventional}$) basically implies dissolution, i.e. molecular dispersion of the toxin in the liquid of the organism, while nanotoxicity ($Tox_{nano\ cat}$ and $Tox_{nano\ phys}$) is related to properties of the undissolved particles, $Tox_{nano\ phys}$ being a purely physical property and $Tox_{nano\ cat}$ a chemical interaction by heterogeneous catalysis.

Thus conventional- and nanotoxicity can only coexist, if the solubility of the material is very small or if the particles are a mixture of soluble and insoluble components. For example: the release of silver ions from silver due to slow dissolutions would be defined as conventional toxicity, however the effect per unit mass is strongly increased if the particles are small, because the dissolution rate is related to the surface.
The formula does not describe any synergy effects between the categories, which could also occur.

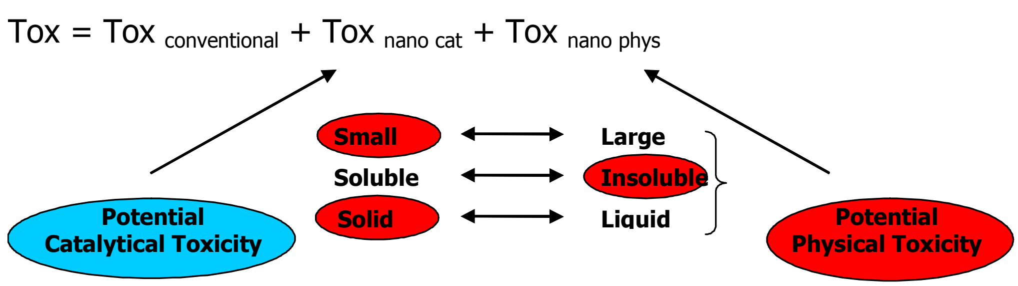

Figure 4: Nanotoxicity formula

Fine dust particles are known to penetrate deep into the lungs. Free nanomaterials are even able to bypass and damage the clearing mechanism of the lungs. If they do not readily dissolve or break down, they may accumulate and cause more damage. Because of the minute size of free nanomaterials, they are able to enter cells and disrupt cellular metabolism. Their ability to cross barriers enables them to enter the circulation system via the lungs or even enter the brain via the nasal mucous membrane. Inside the body, they can promote the formation of harmful substances such as reactive oxygen compounds. Additionally, they can evoke inflammatory reactions which eventually lead to harmful levels of reactive substances in the blood, derived from the immune system. It is believed that these mechanisms form the basis for the observed relationship between the presence of fine dust particles in the air and disorders in the respiratory and circulatory system in humans.

Less is known about the ability of nano sized particles to penetrate though the skin or digestive tract. Until more research on this subject has been done, care should be taken. At present time, the people most at risk are those who synthesize and work with these particles, in various research centres.

Figure 5 shows the deposition number percentage of particles in specific regions of the human lungs.

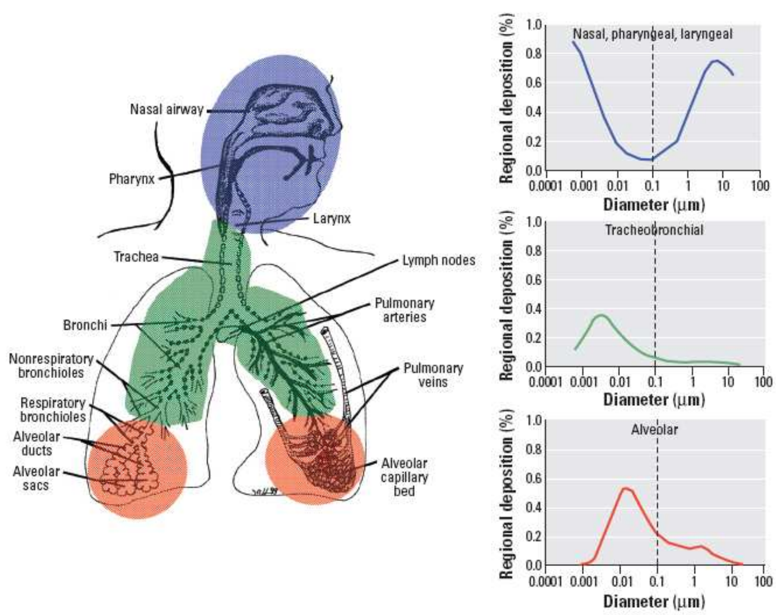

Figure 5: Predicted fractional deposition (number%) of inhaled particles in specific regions of the human respiratory tract during nose breathing [Oberdörster et al., 2005]

With limited toxicity data and little exposure data, it is currently unclear how exposure to nanomaterials should be monitored and regulated most appropriately. There is strong toxicity-based evidence that surface area is an appropriate exposure metric for low solubility nanomaterials, however there are also indications that in some cases a number count within specific size ranges may be important. Recent studies on particle translocation have indicated a size dependency on the likelihood of deposited particles moving from the respiratory tract to other organs.

4.3 Regulations and guidelines

Numerous international organizations like NIOSH, SCENIHR, UNEP, UNIDO, UNESCO, ISO, IUPAC, CAS, OECD, ILO and the WHO are currently working on legislation and guidelines for nanomaterials. A document with descriptions of recommended "best practices" and frameworks (WK8985) is under development by ASTM international. This document will describe standards and guidance for health and safety in the nanotechnology industry.
A committee of the Health Council of the Netherlands has issued a monograph in English with the title "Health Significance of Nanotechnologies" in early 2007.
BSI (British Standards) published a useful guide to safe handling and disposal of manufactured nanomaterials in 2007 (PD 6699-2:2007).
The recent report on provisional nano reference values is based on the IFA approach (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung').

Many publications recognize that there is considerable uncertainty about many aspects of risk assessment of nanomaterials.
The Social economic Council in the Netherlands issued an advisory report in 2009 on health and safety precautions for the use of nanoparticles in the workplace. Their main advise is to apply the precautionary principle as long as uncertainty exists. That is, all nanomaterials are considered potentially hazardous unless sufficient information to the contrary is obtained.

Relevant references:

SER (2009a) Veilig omgaan met nanodeeltjes op de werkplek. Advies van de Commissie Arbeidsomstandigheden. Sociaal Economische Raad, Den Haag. Available on: http://www.ser.nl/~/media/DB_Adviezen/2000_2009/2009/b27741.ashx

RIVM report 601044001/2010 'Tijdelijke nano-refentiewaarden, bruikbaarheid van het concept en van de gepubliceerde methoden'.

IFA (date unknown). Criteria for assessment of the effectiveness of protective measures. Available on: http://www.dguv.de/ifa/en/fac/nanopartikel/beurteilungsmassstaebe/index.jsp

BSI (2007) Nanotechnologies - Part 2: Guide to safe handling and disposal of manufactured nanomaterials, PD 6699-2-2007. British Standards Institution, Londen. Beschikbaar op: http://www.bsigroup.com/en/sectorsandservices/Forms/PD-6699-2/Download-PD6699-2-2007/

NPR-ISO/TR 12885 'Health and safety practices in occupational settings relevant to nanotechnologies'.

OSHA-EU report 'Workplace exposure to nanoparticles'.

More literature references on nanotoxicity and nanosafety can be obtained with the authors (see contact information in cover).