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Nanotechnologies — Occupational risk management applied to engineered nanomaterials —

Part 1: Principles and approaches

Nanotechnologies — Management du risque professionnel relatif aux nanomatériaux manufacturés —

Partie 1: Principes et approches

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Foreword

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The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

In other circumstances, particularly when there is an urgent market requirement for such documents, a technical committee may decide to publish other types of document:

— an ISO Publicly Available Specification (ISO/PAS) represents an agreement between technical experts in an ISO working group and is accepted for publication if it is approved by more than 50 % of the members of the parent committee casting a vote;

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An ISO/PAS or ISO/TS is reviewed after three years in order to decide whether it will be confirmed for a further three years, revised to become an International Standard, or withdrawn. If the ISO/PAS or ISO/TS is confirmed, it is reviewed again after a further three years, at which time it must either be transformed into an International Standard or be withdrawn.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO/TS 12901-1 was prepared by Technical Committee ISO/TC 229, *Nanotechnologies*.

ISO/TS 12901 consists of the following parts, under the general title *Nanotechnologies — Occupational risk management applied to engineered nanomaterials*:

— *Part 1: Principles and approaches*

Introduction

The field of nanotechnologies continues to advance rapidly through the development of new materials, products and applications. At the same time, many questions have been raised relating to the potential risks to human health and to the environment of some of these new nanomaterials. Internationally, a large programme of research is underway to understand better and quantify these risks. Although some research is now published, this effort will need to continue for some time. However, those involved in the development and use of nanomaterials now still require to make assessment of the risks and to implement effective risk management approaches based on the best available evidence. International standardization on nanotechnologies should contribute to realizing the potential of this technology for the betterment and sustainability of our world through economic development, improving the quality of life, and also for improving and protecting public health and the environment.

This part of ISO/TS 12901 supports this by describing the principles of an occupational risk management framework and gives practical advice on its implementation based on the best current emerging evidence concerning the potential risks of nanomaterials. ISO/TS 12901-2, which is under development, describes a specific approach based on control banding to further support the implementation of good practice in this area.

Nanotechnologies — Occupational risk management applied to engineered nanomaterials —

Part 1: Principles and approaches

1 Scope

This part of ISO/TS 12901 provides guidance on occupational health and safety measures relating to engineered nanomaterials, including the use of engineering controls and appropriate personal protective equipment, guidance on dealing with spills and accidental releases, and guidance on appropriate handling of these materials during disposal.

This part of ISO/TS 12901 is intended for use by competent personnel, such as health and safety managers, production managers, environmental managers, industrial/occupational hygienists and others with responsibility for the safe operation of facilities engaged in production, handling, processing and disposal of engineered nanomaterials.

This part of ISO/TS 12901 is applicable to engineered materials that consist of nano-objects such as nanoparticles, nanofibres, nanotubes and nanowires, as well as aggregates and agglomerates of these materials (NOAA).

The term “NOAA”, as used in this part of ISO/TS 12901, applies to such components either in their original form or incorporated in materials or preparations from which they could be released to a certain extent during their lifecycle, including, as a result, downstream activities such as disposal.

2 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

2.1
agglomerate
collection of weakly bound particles or aggregates or mixtures of the two where the resulting external surface area is similar to the sum of the surface areas of the individual components

[ISO/TS 27687:2008, definition 3.2]

NOTE 1 The forces holding an agglomerate together are weak forces, for example van der Waals forces, or simple physical entanglement.

NOTE 2 Agglomerates are also termed secondary particles and the original source particles are termed primary particles.

2.2
aggregate
particle comprising strongly bonded or fused particles where the resulting external surface area may be significantly smaller than the sum of calculated surface areas of the individual components

[ISO/TS 27687:2008, definition 3.3]

NOTE 1 The forces holding an aggregate together are strong forces, for example covalent bonds, or those resulting from sintering or complex physical entanglement.

NOTE 2 Aggregates are also termed secondary particles and the original source particles are termed primary particles.

2.3
engineered nanomaterial
nanomaterial designed for a specific purpose or function

[ISO/TS 80004-1:2010, definition 2.8]

2.4
exposure
contact with a chemical, physical or biological agent by swallowing, breathing, or touching the skin or eyes

NOTE Exposure may be short-term (acute exposure), of intermediate duration, or long-term (chronic exposure).

2.5
hazard
biological, chemical or physical element or factor that adversely affect individuals, the environment, a process or a product

[ISO 14698-2:2003, definition 3.10]

2.6
health hazard
potential source of harm to health

[ISO 10993-17:2002, definition 3.7]

2.7
nanofibre

nano-object with two similar external dimensions in the nanoscale and the third dimension being significantly larger

[ISO/TS 27687:2008, definition 4.3]

NOTE 1 A nanofibre can be flexible or rigid.

NOTE 2 The two similar external dimensions are considered to differ in size by less than three times and the significantly larger external dimension is considered to differ from the other two by more than three times.

NOTE 3 The largest external dimension is not necessarily in the nanoscale.

2.8
nano-object
material with one, two or three external dimensions in the nanoscale

[ISO/TS 27687:2008, definition 2.2]

NOTE Generic term for all discrete nanoscale objects.

2.9
nanoparticle
nano-object with all three dimensions in the nanoscale

NOTE 1 If the lengths of the longest to the shortest axes of the nano-object differ significantly (typically by more than three times), the terms nanorod or nanoplate are intended to be used instead of the term nanoparticle.

NOTE 2 Adapted from ISO/TS 27687.

2.10
nanoplate
nano-object with one external dimension in the nanoscale and the two other external dimensions significantly larger

[ISO/TS 27687:2008, definition 4.2]

NOTE 1 The smallest external dimension is the thickness of the nanoplate.

NOTE 2 The two significantly larger dimensions are considered to differ from the nanoscale dimension by more than three times.

NOTE 3 The larger external dimensions are not necessarily in the nanoscale

2.11
nanoscale
size range from approximately 1 nm to 100 nm

[ISO/TS 27687:2008, definition 2.1]

NOTE 1 Properties that are not extrapolations from a larger size will typically, but not exclusively, be exhibited in this size range. For such properties the size limits are considered approximate.

NOTE 2 The lower limit in this definition (approximately 1 nm) is introduced to avoid single and small groups of atoms from being designated as nano-objects or elements of nanostructures, which might be implied by the absence of a lower limit.

2.12
particle
minute piece of matter with defined physical boundaries

[ISO/TS 27687:2008, definition 3.1]

NOTE 1 A physical boundary can also be described as an interface.

NOTE 2 A particle can move as a unit.

NOTE 3 This general particle definition applies to nano-objects.

2.13
risk
combination of the probability of occurrence of harm and the severity of that harm

[ISO/IEC Guide 51:1999, definition 3.2]

3 Symbols and abbreviated terms

ADME	adsorption, distribution, metabolism and elimination
ACGIH	American Conference of Governmental Industrial Hygienists
BMD	benchmark dose
BMDL	benchmark dose lower confidence limit
CB	control banding
CNT	carbon nanotube
COSHH	Control of Substances Hazardous to Health Regulations
CPC	condensation particle counter
DMPS	Differential Mobility Particle Sizer
EDX	energy dispersive X-ray analysis

ELPI	electrostatic low pressure impactor
ES	exposure standard
GHS	Globally Harmonized System
HEPA	high-efficiency particulate matter
LCL	lower confidence limit
LEV	local exhaust ventilation
LOAEL	lowest-observed-adverse-effect-level
MWCNT	multi-wall carbon nanotube
NEAT	nanoparticles exposure assessment technique
NIOSH	National Institute for Occupational Safety and Health
NOAA	nano-objects, and their agglomerates and aggregates greater than 100 nm
NOAEL	no-observed-adverse-effect-level
OECD	Organization for Economic Cooperative Development
OEL	occupational exposure limit
OPC	optical particle counter
PB-ECL	performance based exposure control limit
PPE	personal protective equipment
RPE	respiratory protective equipment
SEM	scanning electron microscopy
SWCNT	single wall carbon nanotube
TEM	transmission electron microscopy
TEM EDX	transmission electron microscopy energy dispersive X-ray analysis
TEOM	tapered element oscillating microbalance
TLV	threshold limit value
WEL	workplace exposure limit

4 Nanomaterial types and characteristics

4.1 General

This clause describes some of the more common types of engineered nanomaterials to which this guide might be applied. It is not intended to provide a full and comprehensive guide or definition for these nanomaterials types.

4.2 Fullerenes

Fullerenes comprise one of four types of naturally-occurring forms of carbon, first discovered in the 1980s[6]. Their molecules are composed entirely of carbon and take the form of a hollow sphere. Fullerenes are similar in structure to graphite which comprises sheets of hexagonal carbon rings, but can also contain pentagonal or heptagonal rings which enable 3D structures to be formed. One of the most commonly described fullerenes is C60, known as a Buckminster fullerene or a buckyball. Fullerenes are chemically stable materials and insoluble in aqueous solutions. Potential applications include drug delivery, coatings and hydrogen storage[7].

4.3 Carbon nanotubes

Carbon nanotubes[8] are allotropes of carbon with cylindrical structure, high-aspect ratio different tube diameters and lengths as well as tube structures *principally* consisting of one to many layers of tubular graphene-like sheets[9]. The principal types are usually grouped into SW (single-walled), DW (double-walled), and MW (multi-walled) CNT. Diameters may vary from around 1 nm for SWCNT to more than 100 nm for MWCNT. Their lengths can exceed several hundred µm. Commercial CNT can often contain a significant amount of other carbon allotropes and inorganic nanoparticle catalysts.

4.4 Nanowires

Nanowires are small conducting or semi-conducting nanofibres with a single crystal structure, a typical diameter of a few 10s of nm and a large aspect ratio. Various metals have been used to manufacture nanowires, including cobalt, gold and copper. Silicon nanowires have also been produced. Potential applications include inter-connectors in nano-electronic devices, photovoltaics and sensors.

4.5 Quantum dots

Quantum dots are small (2 nm to 10 nm) assemblies of semiconductor materials with novel electronic, optical, magnetic and catalytic properties. Typically containing 1 000 to 100 000 atoms, quantum dots are considered to be something between an extended solid structure and a single molecular entity. Semiconductor quantum dots exhibit distinct photo-electronic properties which relate directly to their size. For example, by altering the particle size, the light emitted by the particle on excitation can be tuned to a specific desired wavelength. Applications include catalysis, medical imaging, optical devices and sensors.

4.6 Metals and metal oxides, ceramics

This category includes a wide range of compact forms of nanoparticles, including ultrafine titanium dioxide and fumed silica. Such nanoparticles can be formed from many materials, including metals, oxides and ceramics. Although the primary particles have compact form, these materials are often available only in agglomerated or aggregated form. They can be composites having, for example, a metal core with an oxide shell, or alloys in which mixtures of metals are present. This group of nanoparticles is generally less well defined in terms of size and shape, and likely to be produced in larger bulk quantities than other forms of nanoparticles. Applications include coatings and pigments, catalysis, personal care products, cosmetics and composites.

4.7 Carbon black

Carbon black is virtually pure elemental carbon in the form of particles that are produced by incomplete combustion or thermal decomposition of gaseous or liquid hydrocarbons under controlled conditions. Its physical appearance is that of a black, finely divided powder or pellet. Its use in tyres, rubber and plastic products, printing inks and coatings is related to properties of specific surface area, particle size and structure, conductivity and colour. The primary particle size of carbon black is most commonly less than 100 nm, but commercial forms are aggregated, typically with dimensions greater than 100 nm. Carbon black is one of the top 50 industrial chemicals manufactured worldwide, based on annual tonnage.

4.8 Dendrimers

Dendrimers are polymer particles in which the atoms are arranged in a branching structure, usually symmetrically about a core. Dendrimers are typically monodisperse with a large number of functionalizable peripheral groups. They are currently being evaluated as drug delivery vehicles.

4.9 Nanoclays

Nanoclays are ceramic nanoparticles of layered mineral silicates. Nanoclays can be naturally occurring or engineered to have specific properties. Naturally occurring forms include several classes such as: montmorillonite, bentonite, kaolinite, hectorite, and halloysite. Nanoclays also include organo-clays, i.e. clays that have been subjected to cat-ion exchange, typically with large organic molecules, which partially or completely de-laminates the primary sheets.

5 Nanomaterial hazard, exposure and risk

5.1 General

It has been established for many years that inhalation exposure to many types of particles, including nanoparticles, can cause ill health in individuals or exposed populations. These data are from studies in workers, animals, and the general population exposed to particulate air pollution. The lung effects depend on the particle dose, physicochemical properties and the susceptibility of the individuals. Animal studies have shown that nanoparticles can be more potent at causing adverse lung effects on a mass basis than larger respirable particles due to their greater surface area per unit mass[10]. There are many instances of adverse lung effects relating to exposure from industrial activity and environmental pollution. For example, in an occupational setting, exposure to coal dust is clearly linked to the onset of lung diseases, such as pneumoconiosis and chronic obstructive pulmonary disease (COPD), and exposure to asbestos is clearly linked with asbestosis, mesothelioma and lung cancer. In an environmental context, studies have reported associations between particulate air pollution and increased morbidity and mortality from respiratory and cardiovascular effects, primarily in susceptible populations such as the elderly or those with pre-existing conditions[11].

However, many millions of the population are exposed to particles in environmental pollution on a daily basis without any apparent ill effects. For any material, the risk, or likelihood, of illness increases with increasing dose. Dose broadly refers to 'how much' gets to an organ and 'how long' it stays there. Toxicity, specifically for relatively insoluble particles, appears to relate to the total surface area of the particles. However, there are other physicochemical factors which can influence the toxicity of nanomaterials, such as the fibre-like toxicity of some carbon nanotubes[12].

5.2 Potential risk considerations to health from inhalation of NOAAs

More than 30 major reviews and position papers have discussed the potential risks to health and to the environment from exposure to NOAAs[13]. The potential risks to health from inhalation of NOAAs, specifically bio-persistent NOAAs[1)], may be summarized as follows:

a) Due to their small size, nano-objects can reach parts of biological systems which are not normally accessible by larger particles. This includes the increased possibility of crossing cell boundaries, or of passing from the lungs into the blood stream and so on to all of the organs in the body, or even through deposition in the nose, directly to the brain. This process is known as translocation and, in general, nano-objects can translocate much more easily than larger structures.

b) NOAAs have a much higher surface area than the same mass of larger particles. To the extent that surface area is a driver for toxicity, this clearly implies potentially increased toxic effects.

1) If particles are readily soluble, they will be taken up in the body the same way as other chemicals and classical toxicity, and particle toxicity will follow.

c) An important rationale for developing nanomaterials is that they will have new, improved or enhanced properties compared to larger particles of the same material. Altered chemical and/or physical properties might be expected to be accompanied by altered biological properties, some of which could imply increased toxicity.

d) A specific issue relates to comparisons between biopersistent high aspect ratio (ratio of length to diameter), NOAAs (e.g. some forms of carbon nanotubes or nanowires) and asbestos. Some biopersistent fibrous particles cause disease because they can be inhaled and enter the alveolar region of the lung and are not easily removed because (i) their physical dimensions mean they cannot be removed by lung clearance mechanisms, and (ii) they are highly durable and do not dissolve in the lung lining fluids. Hence they remain in the lung for a long period of time, causing inflammation and ultimately disease. Asbestos is an example of such a biopersistent fibre. High aspect ratio NOAAs of similar morphology (shape and rigidity) and durability are therefore likely to persist in the lungs, if inhaled.

e) In addition, for some NOAAs, reduction in size has been shown to relate to increased solubility. This effect might lead to increased bioavailability of materials which are considered to be insoluble or poorly soluble at larger particle sizes[2)].

Along with increasing production volumes, lower costs and an increased general presence of nanomaterials in industry and commerce, these issues indicate that more needs to be done to assess the potential risks associated with these NOAAs and that a suitably cautious approach should be taken in their handling and disposal.

The likelihood (or risk) of disease occurring depends on the physicochemical properties of the nanomaterial and the dose in the organ where disease can occur. Dose in humans is not assessed directly, but is estimated from the exposure, which for airborne particles is a combination of the concentration of particles in air, the inhalation rate, the particle size-specific deposition efficiency in the respiratory tract, and the length of time the exposure lasts. If there is no exposure, no dose will accumulate and, despite the potential toxicity of the particles, there will be no risk to health.

An appropriate response to the potential risks from NOAAs, particularly when hazard information is unavailable, is to understand the potential exposures which could occur throughout the life cycle of the nanomaterial and to put in place measures to eliminate or minimize these exposures. In this way the risks can be controlled.

5.3 Potential risk considerations to health from dermal exposure or ingestion

Concerns have also been raised about the potential risks to health arising from dermal exposure to some types of NOAAs, in particular nano-objects, based on the possibility of these materials penetrating the skin and entering the bloodstream. To date there have only been a few studies of this effect on skin models[14][15] and these have not demonstrated skin penetration by NOAAs to any extent. However, the studies are preliminary and have not considered, for example, the effect on damaged skin.

A recent paper found that small amounts of Zn from ZnO particles in sunscreens applied outdoors are absorbed through human skin[16]. In this study, volunteers applied two sunscreen products, one 'nano sunscreen' containing 19 nm nanoparticles and 'bulk sunscreen' containing > 100 nm particles. Stable isotope tracing was used to detect the presence of zinc. A small excess in blood and urine was detected. However it is not known whether ^{68}Zn has been absorbed as ZnO particles or soluble Zn or both.

Other studies are currently underway but, until consensus emerges, a prudent approach would be to limit exposure to the skin.

Potential health effects due to ingestion have also been postulated based on the possibility of nanoparticle transfer across the gastro-intestinal wall. However, there is presently no direct evidence of adverse health effects from ingestion of NOAAs but it would be prudent to minimize exposure by this route.

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2) If particles completely dissolve and the substance acts only by its molecules or ions, then classical toxicology comes in and particle effects are no longer relevant.

