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Nanotechnologies — Occupational risk management applied to engineered nanomaterials —

Part 1: Principles and approaches

Nanotechnologies — Gestion du risque professionnel appliquée aux nanomatériaux manufacturés —

Partie 1: Principes et approches

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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This document was prepared by Technical Committee ISO/TC 229, *Nanotechnologies*.

This second edition cancels and replaces the first edition (ISO/TS 12901-1:2012), which has been technically revised.

The main changes are as follows:

— clauses have been updated and new references have been added to reflect recent research findings;

— a new subclause dedicated to graphene has been introduced in Clause 5;

— Clause 6 has been reorganized and eye exposure and accidental injection risks have been added for potential risk considerations from other potential routes of exposure;

— subclause 6.3 has been expanded and reorganized into two subclauses;

— Figure 1 has been added to Clause 7;

— text related to protection from ocular exposure has been added in 11.2 and substantial changes have been made to the personal protective equipment subclause;

— a new subclause, 11.3.4, has been introduced, focusing on safety by design;

— In 11.3.5 concerning state-of-the-art approaches, the reference to Clause A.1 has been removed and replaced with references to ISO/TR 12885 and other relevant documents;

— in 11.4, which discusses the evaluation of control measures, Clauses A.2 to A.4 have been removed and references to ISO/TR 18637:2016 and other relevant documents have been incorporated;

— Tables 1, 2 and 3 have been added;

— significant changes have been implemented in Clause 15;

— Annexes A, B and C have been added.

A list of all parts in the ISO 12901 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

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. Several research programs have been launched at the international level to better understand and quantify these risks. Although some research is already published, this effort will need to continue for some time, as those involved in the development and use of nanomaterials need to assess the risks of nanotechnologies 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 document supports this aim by describing the principles of an occupational risk management framework for nano-objects, and their aggregates and agglomerates (NOAA) greater than 100 nm and gives practical advice on its implementation based on the best current emerging evidence concerning the potential risks of nanomaterials. ISO/TS 12901-2 describes a specific approach based on control banding to further support the implementation of good practice in this area[1].

This document applies to such components, whether in their original form or incorporated in materials or preparations from which they can be released during their life cycle. However, as for many other industrial processes, nanotechnological processes can generate by-products in the form of unintentionally produced NOAAs, that can be linked to health and safety issues that need to be addressed as well.

Nanotechnologies — Occupational risk management applied to engineered nanomaterials —

Part 1:
Principles and approaches

1 Scope

This document provides guidance on occupational health and safety measures relating to materials that contain and release engineered or manufactured NOAA during their life cycle, 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 document is intended to be used 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 these materials.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
agglomerate
collection of weakly or medium strongly bound particles where the resulting external surface area is similar to the sum of the surface areas of the individual components

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

Note 2 to entry: Agglomerates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO 26824:2022, 3.1.2]

3.2
aggregate
particle comprising of strongly bonded or fused particles where the resulting external surface area is significantly smaller than the sum of surface areas of the individual components

Note 1 to entry: The forces holding an aggregate together are strong forces, for example covalent or ionic bonds, or those resulting from sintering or complex physical entanglement, or otherwise combined former primary particles.

Note 2 to entry: Aggregates are also termed secondary particles and the original source particles are termed primary particles.

[SOURCE: ISO 26824:2022, 3.1.3, modified —"or ionic" has been added to Note 1 to entry.]

3.3
engineered nanomaterial
nanomaterial designed for a specific purpose or function

[SOURCE: ISO 80004-1:2023, 3.1.8]

3.4
exposure
contact with a chemical, physical or biological agent by swallowing, breathing, or touching the skin or eyes

Note 1 to entry: Exposure can be short-term (acute exposure), of intermediate duration or long-term (chronic exposure).

3.5
harm
injury or damage to the health of people, or damage to property or the environment

[SOURCE: ISO/IEC Guide 51:2014, 3.1]

3.6
hazard
potential source of harm

[SOURCE: ISO/IEC Guide 51:2014, 3.2]

3.7
health hazard
potential source of harm to health

3.8
nanofibre
nano-object with two external dimensions in the nanoscale and the third dimension significantly larger

Note 1 to entry: The largest external dimension is not necessarily in the nanoscale.

[SOURCE: ISO 80004-1:2023, 3.3.5]

3.9
nano-object
discrete piece of material with one, two or three external dimensions in the nanoscale

[SOURCE: ISO 80004-1:2023, 3.1.5]

3.10
nanoparticle
nano-object (3.9) with all external dimensions in the *nanoscale* (3.12)

Note 1 to entry: If the dimensions differ significantly (typically by more than three times), terms such as *nanofibre* (3.8) or *nanoplate* (3.11) are preferred to the term nanoparticle.

[SOURCE: ISO 80004-1:2023, 3.3.4]

3.11
nanoplate
nano-object with one external dimension in the nanoscale and the other two external dimensions significantly larger

Note 1 to entry: The larger external dimensions are not necessarily in the nanoscale.

[SOURCE: ISO 80004-1:2023, 3.3.6]

3.12
nanoscale
length range approximately 1 nm to 100 nm

[SOURCE: ISO 80004-1:2023, 3.1.1]

3.13
NOAA
nano-objects, and their agglomerates and aggregates
material comprising *nano-object* (3.9), and their aggregates and agglomerates

Note 1 to entry: NOAAs include structures with one, two or three external dimensions in the nanoscale, which might be spheres, fibres, tubes and others as primary structures. NOAAs can consist of individual primary structures in the nanoscale and aggregated or agglomerated structures, including those with sizes larger than 100 nm.

[SOURCE: ISO 80004-1:2023, 3.2.6]

3.14
particle
minute piece of matter with defined physical boundaries

Note 1 to entry: A physical boundary can also be described as an interface.

Note 2 to entry: A particle can move as a unit.

Note 3 to entry: This general particle definition applies to nano-objects.

[SOURCE: ISO 26824:2022, 3.1.1]

3.15
risk
combination of the probability of occurrence of harm and the severity of that harm

Note 1 to entry: The probability of occurrence includes the exposure to a hazardous situation, the occurrence of a hazardous event and the possibility to avoid or limit the harm.

[SOURCE: ISO/IEC Guide 51:2014, 3.9]

4 Abbreviated terms

CB	control banding
CIB	Current Intelligence Bulletin
CNT	carbon nanotube
COPD	chronic obstructive pulmonary disease
COSHH	Control of Substances Hazardous to Health Regulations
CPC	condensation particle counter
CPI	Consumer Products Inventory
DMAS	differential mobility analysing system
DW	double-walled
EC	elemental carbon

ECHA	European Chemicals Agency
EDX	energy dispersive X-ray
eLCOSH	Electronic Library of Construction Occupational Health and Safety
ENM	engineered nanomaterial
GHS	Globally Harmonized System
HARN	high aspect ratio nanomaterial
HEPA	high-efficiency particulate matter
ICS	International Classification for Standards
ICP-AES	inductively coupled plasma atomic emission spectroscopy
ICP-MS	inductively coupled plasma mass spectrometry
LDSA	lung deposited surface area
LEL	lower explosion limit
LEV	local exhaust ventilation
MIE	minimum ignition energy
MIT	minimum ignition temperature
MNM	manufactured nanomaterial
MWCNT	multi-walled carbon nanotube
NEAT	nanoparticles exposure assessment technique
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
NOAA	nano-objects, and their agglomerates and aggregates
OECD	Organization for Economic Cooperative Development
OEL	occupational exposure limit
OPC	optical particle counter
OSHA	Occupational Safety and Health Administration
PLGA	poly(lactic-co-glycolic) acid
PPE	personal protective equipment
R&D	research and development
REACH	Registration, Evaluation, Authorization and Restriction of Chemicals
RPE	respiratory protective equipment
SbD	safety-by-design

SDS	safety data sheet
SEM	scanning electron microscopy
SW	single-walled
SWCNT	single-walled carbon nanotube
TDS	technical data sheet
TEM	transmission electron microscopy
TEOM	tapered element oscillating microbalance
TGA	thermal gravimetric analysis
UK	United Kingdom
WHO	World Health Organization
XRF	X-ray fluorescence

5 Nanomaterial types and characteristics

5.1 General

Clause 5 describes some of the more common types of engineered nanomaterials to which this document can be applied; a few of these also have naturally occurring forms. This document is not intended to provide a full and comprehensive guide of all nanomaterial types.

5.2 Fullerenes

Fullerenes comprise one of four types of naturally-occurring forms of carbon, first discovered in the 1980s.[2],[3] 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.

5.3 Carbon nanotubes

Carbon nanotubes 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[4].The principal types are usually grouped into single-walled (SW), double-walled (DW), and multi-walled (MW) carbon nanotube (CNT). Diameters can vary from around 1 nm for SWCNT to more than 100 nm for MWCNT. Their lengths can exceed several hundred micrometres. Commercial CNT can contain a significant amount of other carbon allotropes and inorganic nanoparticle catalysts.

5.4 Graphene

Graphene is a two-dimensional carbon-based material up to 10 layers thick for electrical measurements, beyond which the electrical properties of the material are not distinct from those for the bulk (also known as graphite). Graphene nanoplates can have a high aspect ratio with lateral sizes ranging from sub-micrometre to a 100 micrometres[5].

5.5 Nanowires

Nanowires are small conducting or semi-conducting nanofibres with a single crystal structure, a typical diameter of a few tens of nanometres 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 of nanowires include inter-connectors in nano-electronic devices, photovoltaics and sensors.

5.6 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.

5.7 Metals and metal oxides, ceramics

This category includes a wide range of nanoparticles, including ultrafine titanium dioxide and fumed silica. Such nanoparticles can be formed from many materials, including metals, oxides and ceramics. 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.

5.8 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.

5.9 Organic nanoparticles

Examples of organic nanoparticles are chitosan, silk fibroin or other biodegradable polymers, including poly(lactic-co-glycolic) acid (PLGA) for biomedical applications.

5.10 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.

5.11 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 cation exchange, typically with large organic molecules, which partially or completely de-laminate the primary sheets.

6 Nanomaterial hazard, exposure and risk

6.1 General

A hazardous material can be identified as follows.

— It can be listed as a substance with an assigned an OEL in national publications.

— It can have a hazard classification in the United Nations Globally Harmonized System[6].

— It can have a hazard classification in national regulations.

— It can be identified as a hazardous material in a safety data sheet, with information about the specific hazards it represents.

— It can be identified in national or international publications which list hazardous chemicals.

Occupational exposure limits for categories of NOAA have been proposed by different organizations and are summarized in References [7] and [8]. Guidance on the categorization of NOAA have been suggested and are summarized in Annex A. However, with the limited knowledge about the toxicity of some NOAA and the concern that current safety data sheets do not adequately reflect the hazardous nature of such NOAA, nanomaterials in a particulate form, or in a form where nano-objects potentially can be released, should be considered potentially hazardous unless sufficient information to the contrary is obtained.

It is well-established that inhalation exposure to many types of particles, including nanoparticles, can negatively impact the health of individuals or exposed populations. These data are from studies of workers, animals and the general population exposed to particulate air pollution[9],[10],[11]. The lung effects depend on the particle dose, physicochemical properties and susceptibility of the individuals. Animal studies have shown that nano-objects 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[12]. Based on adverse lung effects observed with ultrafine particles of similar size, form factor and/or chemical composition as NOAA, concerns exist that lung diseases such as pneumoconiosis and chronic obstructive pulmonary disease (COPD) associated with exposure to coal dust and pulmonary fibrosis and lung cancer associated with exposure to asbestos can occur in the case of NOAA exposure[13],[14]. In fact, pleuropulmonary symptoms in young workers have potentially been associated with exposure to silica nanoparticles used in polyacrylate spray paint[15]. In a study of workers exposed to TiO_2 nanoparticles, various markers of cardiopulmonary effects were observed to be at least in part due to the nano-object exposure [16]. In another study, workers showed changes in lung function and inflammatory markers in exhaled breath condensates when machining nanomaterial composites [17].

Toxicity, specifically for relatively insoluble particles, appears to relate to the total surface area and the displaced volume of the nano-objects[18],[19],[20]. However, there are other physicochemical factors that can influence the toxicity of nanomaterials, such as shape, crystalline state, elemental composition and surface chemistry[21]. In addition to inhalation, risks to health associated with NOAA can result from dermal exposure, exposure through the eye, ingestion, and intravenous/intramuscular exposure[22]. NOAA can also generate risks to safety, in particular resulting from fire, explosion and chemical reactions[23].

6.2 Risk to health

6.2.1 Hazard information

For some nanomaterials, various health effects have been observed in animal studies. These include cardiovascular and respiratory diseases, as well as carcinogenicity[24],[25],[26],[27]. As research continues, it is understood that pulmonary exposure can lead to adverse outcomes in a number of organ systems beyond the lung and heart. For example, the silver Current Intelligence Bulletin (CIB) uses hepatic toxicity (biliary hyperplasia) as the adverse outcome for risk assessment[28]. Health effects depend on various physico-chemical properties of the material itself and other pollutants that can be absorbed in the nanomaterial. Considering the lack of information on specific materials, it has been suggested to apply read-across in order to extrapolate from known airborne particle exposures and predict potential health effects for an unknown material. Read-across is defined as the grouping of materials in categories with similar physico-chemical properties as they can have similar toxicological properties[29]. Various approach to grouping are used, some based on the chemical composition of the material, while others are based more on the physico-chemical properties (size, shape, solubility). A detailed review on approaches can be found in Reference [29].

6.2.2 Exposure

6.2.2.1 Routes of exposure

Routes of exposure for nanomaterials are similar to general chemicals: inhalation, ingestion, dermal and injection.[22] Inhalation and dermal exposure are the main routes of exposure. Oral exposure is less likely at the workplace although it can mainly occur through hand to mouth transfer after dermal exposure. At high concentrations, ocular exposure should be considered since NOAA can penetrate the cornea.

6.2.2.2 Potential risk considerations to health from inhalation of NOAA

More than 30 major reviews and position papers have discussed the potential risks to health and to the environment from exposure to NOAA.[30] The potential risks to health from inhalation of NOAA, specifically bio-persistent NOAA1), are summarized as follows.

a) 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 can be expected to be accompanied by altered biological properties, some of which can imply alterations in toxicity.

b) Due to their small size, nano-objects can reach parts of biological systems that are not normally accessible by larger particles. This includes the increased possibility of crossing cell boundaries or moving 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, from which they can then be directly transported to the brain. This process is known as translocation, which can be active or passive and, in general, nano-objects can translocate much more easily than larger structures.

c) NOAA have a much higher surface area than the same mass of larger particles to the extent that surface area is a driver for toxicity, which clearly implies potentially increased toxic effects.

d) In addition, for some NOAA, reduction in size has been shown to relate to increased solubility. This effect can lead to increased bioavailability of materials which are considered to be insoluble or poorly soluble at larger particle sizes2).

e) A specific issue relates to comparisons between biopersistent high aspect ratio (ratio of length to diameter) NOAA (e.g. some forms of carbon nanotubes or nanowires) and asbestos.[2] 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

   1) their physical dimensions mean they cannot be removed by lung clearance mechanisms, and

   2) 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 NOAA of similar morphology (shape and rigidity) and durability are therefore likely to persist in the lungs, if inhaled.

Along with increasing production volumes 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 NOAA and that a suitably cautious approach should be taken in their handling and disposal.

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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.

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.

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. The 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 internal dose will accumulate and, despite the potential toxicity of the particles, there will be no risk to health. Various factors can influence exposure and health effects including environmental/workplace factors such as ventilation, workload (breathing rate) and worker factors such as age, gender, weight and pre-existing health conditions[31].

An appropriate response to the potential risks from NOAA, particularly when hazard information is unavailable, is to understand the potential exposures which can 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. In addition, read-across can be used to estimate potential risk associated with exposure[29].

6.2.2.3 Potential risk considerations to health from dermal exposure

Concerns have also been raised about the potential risks to health arising from dermal exposure to some types of NOAA, particularly nano-objects[32]. Indeed, transcellular and intercellular routes can explain the passage of NOAA from the stratum corneum to the epidermis and dermis and entering the bloodstream[33],[34],[35]. NOAA can then reach internal organs (kidneys, ovaries, etc.)[36],[37],[38]. If the major part of these studies have been conducted with intact human or porcine skin, other researchers have considered the effect of skin damages, e.g. through flexion or abrasion, and shown that it can increase the passage of NOAA through the skin[39],[40]. Additional information is provided in Annex B. Similarly, to what is recommended for exposure by inhalation, appropriate protective measures (engineering controls, administrative controls and personal protective equipment) should be considered to limit skin exposure when handling NOAA[31],[41],[42].

There are also concerns of skin allergy and dermatitis especially when handling NOAA made of metals or made with metal catalyst residues[43].

6.2.2.4 Potential risk considerations from other potential routes of exposure

6.2.2.4.1 Oral or ingestion exposure

Potential health effects associated with NOAA ingestion have also been pointed out based on the possibility of nanoparticle transfer across the gastro-intestinal wall.[44],[45] A recent study, based on the measurement of the concentration of titanium dioxide nanoparticles in internal organs after chronic exposure using a kinetic model in order to account for accumulation over time, has shown that a risk for liver, ovaries and testes exists[38].

6.2.2.4.2 Ocular or eye exposure

The ocular route is another possible port of entry in the human body. Even if the use of NOAA as an ocular drug delivery presents some real benefits,[46],[47] the penetration of NOAA through ocular tissues can also lead to harmful effects. Several factors such as the chemical composition, size, dose and time after exposure, and the potential of biodistribution pattern, can affect the toxicity of nanomaterials in ocular tissues[46],[48]. Additional information is provided in Annex B.

6.2.2.4.3 Accidental injection

Although it is poorly documented, accidental injection is another potential route of exposure in occupational conditions. Voluntary injections of NOAA used as therapeutics or diagnostics are common in nanomedicine or biomedical settings as parenteral injections (intravenous/intramuscular).[22] During these medical operations, accidental injections on health workers can occur but their frequency and their consequences have not been documented.

6.3 Risks to safety

6.3.1 Hazard information

Safety risks associated with NOAA can be linked to three phenomena: fire, explosions and chemical reactions.[23] The phenomena of fire and explosion are associated with the rapid oxidation of a combustible material. In the case of chemical reactions, risks relevant to NOAA include the NOAA acting as a catalyst for chemical reactions, reacting during accidental contact between incompatible materials, or becoming instable, leading to unexpected decomposition/degradation, polymerization, or photoactivity. As particle size/surface area is one of the main factors that control chemical reactivity, an increase in the risks associated with safety is expected for NOAA compared to larger scale particles, both in terms of probability and consequences. Yet, there is still very few data about safety risks associated with NOAA.

For instance, a strong decrease in the minimum ignition energy has been observed with aluminium nanoparticles compared to their microscale counterparts, with a transition from a diffusion-controlled mechanism for large particles to a kinetically-controlled process for nanoparticles[49]. Nanoscale powders are thus more susceptible to electrostatic ignition. At the very low size range, a small increase in the minimum explosible concentrations is detected[50]. It can be attributed to the tendency of very small particles to agglomerate. For aluminium and magnesium powders, the size range with the highest risks of explosion is 100 nm and 300 nm.

6.3.2 Risk of fire and explosion from NOAA

Explosive dust clouds can be generated from most organic materials, many metals and even some non-metallic inorganic materials. Whether a hazardous explosive atmosphere is present is determined with the aid of the safety characteristic lower explosion limit (LEL).

It is well known, that dust explosions occurring at workplaces are mainly caused by ignition sources like open flames, hot surfaces, friction, mechanical and electric sparks and electrostatic discharges as well. The ignition sensitivity of combustible dusts in air is characterized by the minimum ignition energy (MIE) and minimum ignition temperature (MIT) cloud, whereas the explosion severity is characterized by maximum explosion pressure (p_{max}), maximum rate of pressure rise[$(\mathrm{d}p/\mathrm{d}t)_{max}$] and explosion index ($K_{St}$). The values of these characteristics depend on several influencing parameters such as instance particle size and shape, moisture, dust concentration, combustible and inert agents.

In general, the sensitivity and severity of dust explosions are influenced by the dust concentration, amount of oxygen, and combustible agents, and increase with decreasing dust particle size, moisture and inert agents.

For NOAA dust clouds, due to the agglomeration, the values of the explosion severity are generally comparable to the values of very fine micrometer range powders, while the ignition sensitivity can further increase with decreasing particle size of primary particles (due to higher specific surface area of the NOAA dust)[51],[52]. For example, experiments with carbonaceous NOAA in dust clouds demonstrate very similar explosion severities to those of powders in micrometer range[52],[53].

However, for some metallic powders from nano to microscale, investigations confirmed a higher explosion severity with decreasing the particle size until a critical diameter. Below this critical diameter the explosion severity (p_{max}, $\mathrm{d}p/\mathrm{d}t_{max}$) decreases for all the considered powders[54]. Investigations in the ignition behaviour of metal NOAA powders like iron, aluminium and titanium resulted in MIE-values lower than 1 mJ[55],[56]. Depending on the test procedures, experimental evidence of pyrophoric behaviour has been observed for NOAA in dust clouds of iron and titanium[57].

When correlating various ignition and explosion characteristics of aluminium NOAA, magnesium NOAA and carbon nanotubes with the particle size, it becomes clear that the dependence on particle size cannot be the only key factor for understanding explosion severity. So other factors have to be considered as well (e.g. concentration, dispersion and turbulence)[50], and NOAA specific properties (e.g. low sedimentation rate, agglomeration, high surface area, high sensitivity to ignition)[58],[59]. Other physico-chemical parameters related to the heat transfer by conduction or radiation during the flame propagation should also be taken into account. When Vignes et al. neglected agglomeration, the specific pattern observed for metal nanopowders can be attributed to the characteristics of a dust flame propagation driven by conduction[54].

Several standards assessing the flammability and explosibility of micrometer powders. At the nanoscale, CEN/TS 17274 provides protocols for the assessment of the explosible and flammable properties of powders containing nano-objects[60]. This document does not include changes in equipment or procedures compared with the testing of microscale powders. Only special care in testing is recommended due to the possibly high sensitivity of nanomaterials.

7 General approach to managing risks from NOAA

In most countries, the law relating to the use of chemicals or other hazardous substances at work requires employers to control exposure to hazardous substances to prevent ill health to both employees and others who can be exposed. For example, in the United Kingdom (UK), the Control of Substances Hazardous to Health Regulations (COSHH) 2002[61], which is based on a risk assessment approach, provides a framework for assessing and managing the potential risks from NOAA. This framework comprises eight main steps:

a) identify the hazards and assess the risks;

b) decide what precautions are needed;

c) prevent or adequately control exposure;

d) ensure that control measures are used and maintained;

e) monitor the exposure;

f) carry out appropriate health surveillance;

g) prepare plans and procedures to deal with accidents, incidents and emergencies;

h) ensure employees are properly informed, trained and supervised.

The approach proposed in this document closely follows this framework.

This approach generally relies on having good information about the hazardous nature of materials, the effectiveness of control approaches and convenient and accessible ways to monitor exposure. One of the difficulties in applying this approach to new nanomaterials is that the information available can be incomplete.

Knowledge on the health hazards of nanomaterials has increased and grouping and read across approaches are being developed. However, the knowledge gaps concerning the health hazards of new nanomaterials can introduce significant uncertainty into any risk assessment. It is inappropriate in the absence of knowledge to assume that a nano-object form of a material has the same hazard potential as it has in a larger particulate form. In general, the greater the gaps in knowledge are, the more cautious the control strategy should be.

The general approach adopted in this document to managing risks from NOAA is illustrated in Figure 1, which is also a guide to the rest of this document. Figure 1 provides a step-by-step approach to managing the risks from NOAA, recognizing the associated uncertainties and developing and implementing an effective strategy to control exposure and manage the risks.

Employers shall provide whatever information, instruction, training and supervision as is necessary to ensure the health and safety at work of their employees. Participation of workers in health and safety leads to healthier and safer workplaces and produces a range of benefits for workers and managers.

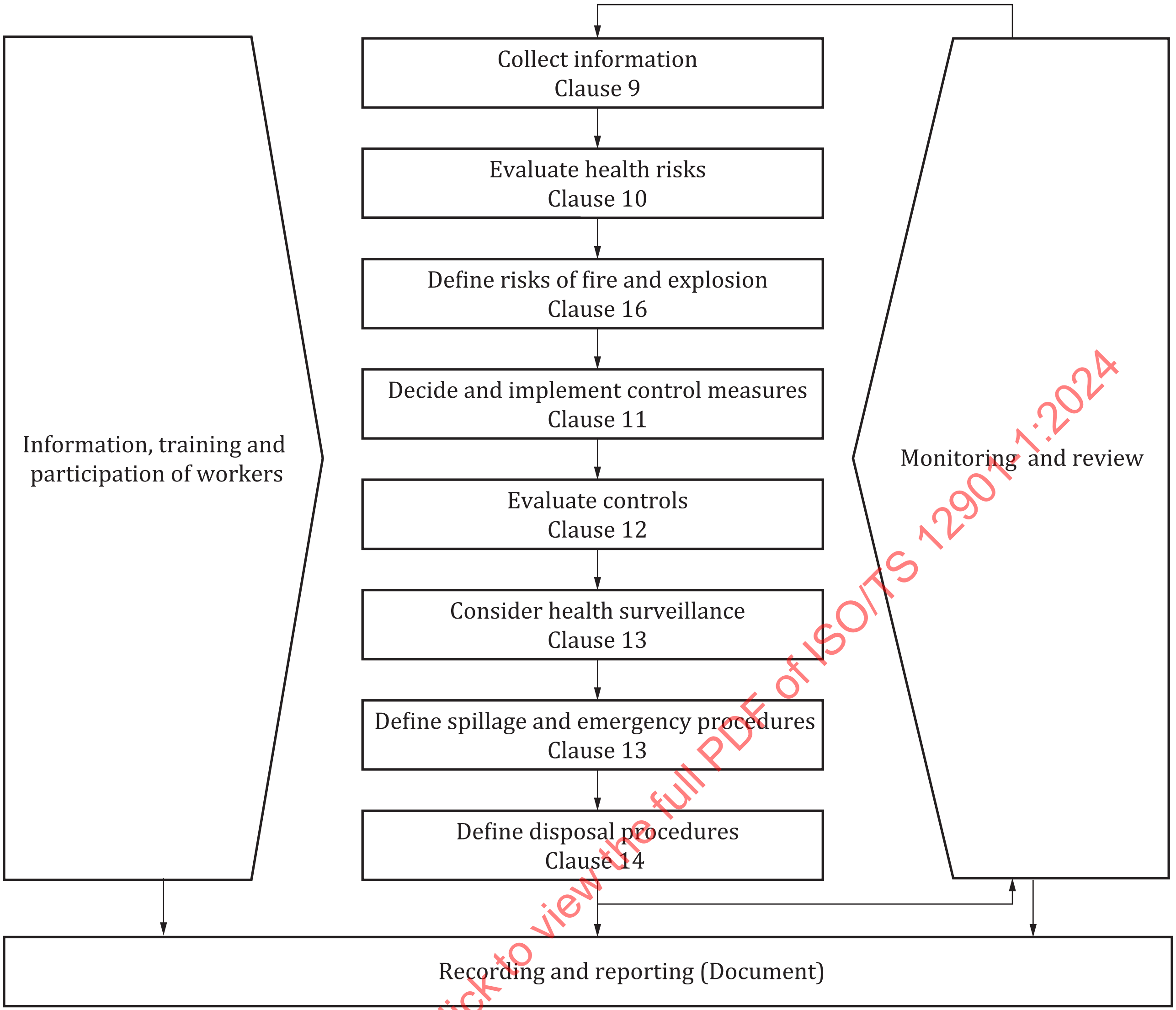

Figure 1 — Approach to managing risks from NOAA

8 Identification and competence of person conducting risk assessment

An initial decision relates to who will carry out the risk assessment. As in general chemical risk assessments processes, several people can be involved, such as those involved in the development or implementation of a process, managers or occupational hygienists. The current state of knowledge concerning NOAA suggests that it will be difficult for an individual with no background knowledge of nanoparticle risk issues to make effective judgments about the appropriate steps to take. While this document helps address this situation, it is strongly recommended that those involved in developing risk assessments for NOAA seek information more widely on these issues or undertake some external training. For further information on risk assessment, see ISO/TR 13121[30].

9 Information collection

This is a key step in the risk assessment. If little is known about the material, it will be necessary to treat it as hazardous and apply tighter exposure controls. Therefore, it is necessary to begin by collecting information about the nanomaterial, what goes into producing the material, and the manufacturing or handling process. Also, it is essential to collect information about the workplaces where the materials are developed, manufactured and included in the manufacturing of other products. When researching workplace environments, information should include industrial hygiene practices of the company, engineering controls, personal protective equipment (PPE) procedures, housekeeping standards and company incentives for encouraging a healthy work environment.

The focus of the information collection step should provide guidance for conducting a comprehensive risk assessment. Sources such as the PubChem database [hosted by the National Library of Medicine (NLM)] and the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) registered substance database [hosted by the European Chemicals Agency (ECHA)] provides data on chemicals and compounds. PubMed (also hosted by NLM) is a good source for scientific articles and studies about health effects, routes of exposure and the groups of people and ecosystems that can potentially come in contact with specific nanomaterials or substances.

In addition, some institutions have databases useful in identifying nanomaterials on the market such as Consumer Products Inventory (CPI) and Electronic Library of Construction Occupational Health and Safety (eLCOSH)[62],[63],[64].

While conducting research and gathering information, the following list has examples of the types of questions to ask.

a) What are the commercial (or common) and technical names for the material?

b) Is there a safety datasheet (SDS)[3] or a technical datasheet (TDS)?

c) What is the chemical composition?

d) What is the form of the nanomaterial (e.g. powder, pellets, NOAA in liquid solution, composite materials)?

e) Is nanomaterial present? In what proportions?

f) Are the particles long and thin?

g) What is the particle size distribution?

h) How dusty is the material? How easily are particles released into the air?

i) Is the material water soluble?

j) How hazardous or toxic is the material?

k) Are there materials which can be used instead of the nanomaterial that are potentially less hazardous, but still achieve the required end properties?

During the research process, it is important to document both the information that is available and the information gaps. For commercial NOAA, some of the information will be available on product SDS or TDS. In using these sheets, however, it is necessary to evaluate the extent to which suppliers have accounted for the nanoscale nature of the substance.

The information collection should identify all those who can be exposed to the material, such as production employees and ancillary or support-services employees (i.e. cleaners or maintenance workers, onsite contractors, visitors, supervisors and managers, students, office workers, and anyone outside the production facility or passing by it). Potential exposure routes (inhalation, dermal, oral, etc.) should also be noted for each of the aforementioned demographics.

10 Health risk evaluation

10.1 General

Risks are associated with the toxicity of material and the exposures that people have to that material. Information shall be collected that helps assess what the risks can be.

3) Guidance on the preparation of SDS for manufactured nanomaterials is given in ISO/TR 13329[65].

10.2 Hazard assessment

For most particulate materials, including soluble NOAA, that can become airborne and be inhaled, the primary health concern is for effects resulting from respiratory exposure. Particulate effect can be independent of whether the material is a nanomaterial or not. This should be the first consideration for any nanomaterial that is being manufactured or used. However, consideration should also be given to other means of exposure, such as skin contact, ocular or eye exposure or ingestion, and other potential hazards related to the properties of those materials, such as fire and explosion (see Clause 16).

An assessment of hazard, coupled with an assessment of the likelihood of exposure, can be used to decide on a control strategy. Clearly, the more information is available, the better this categorization will be. Information on the hazardous nature of some NOAA continues to increase and a number of sources are now available which can provide input for decision making[66],[67]. Frameworks, including those based on grouping, read-across and adverse outcome pathways, that supports the assessment of risk for new nanomaterials are being developed[68],[69],[70],[71]. The information needs to be evaluated critically in terms of quantity and quality. Gaps in the information regarding hazard shall also be identified. Decisions can be informed by peer-reviewed science, anecdotal evidence or professional judgment. Emerging scientific evidence should be appropriately considered and efforts made to keep up to date with the latest information. In principle, all relevant information should be available on safety data sheets, but it has been indicated that at the current time many of these do not adequately represent the nanoforms of the material[65].

For all of the categories of NOAA identified, these materials can be reasonably assumed to have a hazardous potential equal to or greater than that of the larger, non-nanoscale forms of the material, if existing.

10.3 Exposure assessment

The key deliverable from this step is an exposure characterization; a summary and synthesis of the gathered exposure information. The exposure characterization should include:

a) a statement of purpose, scope, level of detail, and the approach used in the assessment;

b) estimates of exposure for each relevant pathway, both for individuals and populations (e.g. groups of workers);

c) an evaluation of the overall quality of the assessment and the degree of confidence in the exposure estimates and conclusions drawn, including sources and the extent of uncertainty.

Questions to consider for supporting the information gathering include the following.

— What are the processes which can lead to the release of NOAA into the air or onto a surface?

— What are the tasks along the life cycle of the material where people are potentially exposed to NOAA (e.g. production, cleaning, accidental releases, maintenance, transport, storage and disposal)?

— Who can potentially be exposed during each task? The individual undertaking the task, adjacent workers, visitors, contractors, managers and others can be exposed.

— What are the potential routes of human exposure (e.g. inhalation, ingestion, dermal penetration, ocular exposure and accidental injection)?

— What is the chance of the exposure occurring? Consider operational work, accidental releases and maintenance (including non-scheduled maintenance).

— How often is exposure likely to occur (e.g. continuous over a working shift, intermittently or rarely)?

— What concentrations are people exposed to and for how long? This can require collection and assessment of existing data or collection of new data (see Clause 12).

— Which control measures can be applied for each task? These can include segregation of personnel from the source by enclosing them or the process, or by using engineering controls such as local exhaust ventilation (LEV), supplying PPE, and education and training of workers.

In addition, any relevant existing measurement data should be collected.

In some cases, information collected can be insufficient. As uncertainty about the levels of exposure increases, the need for caution in the assessment increases. It is therefore necessary to be cautious and determine where significant doubt exists. Based on this assessment, a prioritized plan should be developed to collect additional exposure information. This can include an exposure assessment programme, methods for which are summarized in Clause 12.

10.4 Health risk assessment and prioritization

At this stage, potential hazards should have been identified and an assessment made of the likely exposures. Consideration of hazard and exposure leads to an assessment of the risks. The next stage is to decide how to manage those risks. If the risks are significant or can become so, or if there is uncertainty about the level of risk, then precautions are required.

Not all risks can be addressed immediately and prioritization is required based on the assessments of:

— the most severe risks to health;

— the number of workers potentially exposed;

— the earliest risks likely to occur;

— the potential for chronic disease due to repeated exposure (e.g. in workers);

— the risks that need to be addressed first.

The most important of these is the severity of the risks. If a risk is severe it should be dealt with immediately. Less severe risks should not assume greater priority merely because they can be dealt with more easily or occur more frequently.

10.5 Document and review

The findings of the risk assessment should be recorded when the assessment is made or as soon as is practicable afterwards. In some circumstances, not all the findings will occur at the same time. Some can require further information before they can be resolved, e.g. where there is a pilot operation which runs for a period before being assessed completely or where exposure monitoring results are awaited. In these circumstances, the record of the significant findings should be completed or updated as information becomes available.

Given the emerging state of knowledge concerning the risks of NOAA, it is probable that important new knowledge will become available at some time. It is critical therefore that the assessment is reviewed at least annually and that those involved in the process take steps to ensure that their knowledge is kept up-to-date.

11 Control of risk

11.1 Hierarchy of control

Exposure should be prevented preferably by avoiding, so far as is reasonably practicable, the use of a hazardous substance by substituting it or changing the process to a safer alternative. If, this is not possible, then exposure should be controlled by applying protection measures appropriate to the activity and consistent with the priority order given in Figure 2, which describes the hierarchy of control.

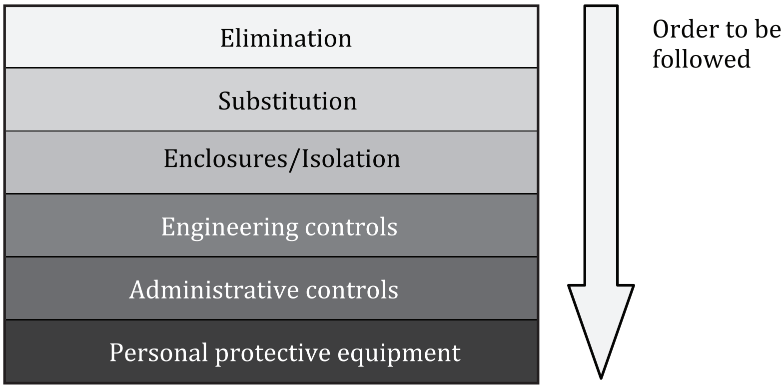

Figure 2 — Hierarchy of control

11.2 Control measures

11.2.1 General

If exposure cannot be prevented, it should be adequately controlled. The hierarchy of control measures as applied to inhalation, dermal and ocular risks comprises the following.

11.2.2 Elimination

Avoid using the hazardous substance or the process which causes exposure. This is unlikely to be an option if the nanomaterial has been selected for its specific properties. However, consideration should be given as to whether the improved properties of the nanomaterial justify any enhanced risks associated with its use, including to the environment.

11.2.3 Substitution/modification

Change the nanomaterial or process to one which has less risk to human health, safety and the environment. If a less risky material is available, it can be possible to modify it without impacting on desired end properties especially for fibres to design them short or non-rigid. It can also be possible to reduce the likelihood of exposure by, for example, binding powder nanomaterials in liquid or solid media. Dispersions, pastes or pelletized forms should be used instead of powder substances wherever this is technically feasible. The process or task can also be substituted for example, use of a vacuum cleaner fitted with a high-efficiency particulate matter (HEPA) filter instead of a brush when cleaning up dust.

11.2.4 Enclosures/isolation

Operations where deliberate release of NOAA into the air occur, should, if possible, be performed in contained installations, or where personnel are otherwise isolated from the process (e.g. in a cabin). This includes gas phase nanomaterial production and spray drying. All other processes involving the use of dry nanomaterials should be performed in enclosed installations where possible. More information about process enclosure is available in References [72] and [73].

11.2.5 Engineering controls

All processes where there is a likelihood of dust formation should be carried out with extraction ventilation. Many types of extraction ventilation systems are available, including fume cabinets, fume hoods and dust extractors/vacuum cleaners.[74] Selection of appropriate controls will depend on the level of risk. More information about engineering control approaches is available.[72],[73] Regular maintenance and performance testing of extraction facilities should be carried out. Extracted air should not be re-circulated without exhaust air purification. General dilution ventilation can also be appropriate to reduce background exposure, although it has no immediate effect on the worker's exposure if the source of exposure is located close to the worker. Dermal exposure can be reduced by re-engineering the work process to avoid splashing or immersion and deposition on surfaces.

11.2.6 Administrative controls

Procedural controls should accompany engineering controls, though the risk assessment can indicate that procedural controls alone are sufficient in some circumstances. Procedural controls include reducing the number of personnel exposed or the time spent by personnel on the process, limiting the process to specified areas and denying unauthorized persons access to these areas. The personnel involved should be informed of the specific hazards of the nanoparticles handled or released through the process, the need for special measures, and the potential health effects of exposure to aerosols. Relevant information in the operating instructions can be included. Routine monitoring should be carried out as needed. The use of medical surveillance should be considered (see Clause 13).

Work wear should be cleaned by the employer and stored separately from private clothing. Cleaning of workplaces should be carried out regularly, in line with risk control plans.

11.2.7 Personal protective equipment

11.2.7.1 General

In the hierarchy of control, PPE is a last option or a supplemental option to help support all the other methods of exposure control.

11.2.7.2 Protection from inhalation exposure

Certified respirators have been shown to provide stated level of protection for NOAA[75],[76],[77],[78],[31] and so are likely to form an important element of a control strategy where control of emissions at source is not practical. Information on the selection and use of respirators can be found in various guidance documents, for example the International Classification for Standards (ICS) 13.340.[79] Appropriate types of respiratory protective equipment (RPE) include disposable filtering face-pieces, half and full facemasks, and a range of powered (air supplied) hoods. Helmeted powered air-purifying respirators can be used to prevent exposure to welding fumes. Note that face covering are not RPE and surgical masks do not protect against inhalation from against nano-objects.[31] Face covering and surgical masks should not be worn to protect against dust. All wearers of tight-fitting respirators (half-mask and full facemasks) should undergo face-piece fit testing to ensure correct fitting and proper wearing[80],[78],[31].

PPE, especially respiratory protection, needs a significant investment in training, supervision and maintenance if it is to provide the intended level of protection. Incorrect selection or fitting or insufficient use can render it ineffective. Information on the establishment and implementation of a respiratory protective device programme is available in ISO/TS 16975-1[81]. In addition, ISO/TR 12885 provides specific guidelines on the selection and use of RPE in occupational settings when nano-objects or nanomaterials are produced or handled.

11.2.7.3 Protection from dermal exposure

It is to be noted that organizations such as NIOSH and AIHA recommend the double-gloving, especially when using thinner gloves, or to replace them frequently.[41],[42] It is recommended to replace disposable gloves more frequently than once a day, especially when handling liquid solutions containing NOAAs. Nevertheless, research is still needed to better understand the effect of certain parameters such as the shape, charge and functionalization of the nanomaterials.

Appropriate protection from dermal exposure by NOAA such as disposable protective gloves and chemical protective clothing should be worn when handling nanomaterials.

A few studies have evaluated the effectiveness of protective gloves against NOAA but the quality of evidence in terms of performance is limited. In a study, two models of disposable nitrile gloves were tested and rated poor in terms of effectiveness and the researchers even warned against the use of one of them for handling nano-objects in aqueous solution[82],[83]. Polychloroprene, butyl rubber and latex gloves can be suitable but the thickness also plays a role in the barrier efficiency.

To limit dermal exposure to airborne nanomaterials and personal clothing contamination, good practice guides published by some health and safety agencies recommend wearing chemical protective clothing[31],[72], for instance type 5 nonwoven chemical protective clothing. Even if type 5 chemical protective clothing are designed to provide full body protection against airborne solid particulates[84],[85], some studies have reported poor performance against airborne nanomaterials for some models of type 5 chemical protective clothing when tested in conditions simulating use in the workplace[86],[87],[88],[89]. The efficiency of type 5 chemical protective clothing can even be as low as 10 % depending on the seam design or the presence of a zipper[90].

Care should be taken when selecting gloves and protective clothing as manufacturers' published data does not always provide enough information to ensure adequate protection against NOAA, especially when considering the effect of the type and chemical state of the NOAA. In addition, there are four basic criteria for the selection of dermal protective equipment, assuming that the PPE is worn and maintained correctly:

— they should be appropriate for the risk(s) and conditions where they are to be used,

— they should be suitable for the ergonomic requirements and state of health of the intended wearer,

— they should fit the intended wearer correctly,

— they should prevent exposure without increasing the overall risk.

11.2.7.4 Protection from ocular exposure

The ocular route is another possible port of entry in the human body. Due to limited knowledge on NOAA, a precautionary principle for ocular exposure should be considered especially when there is a significant risk for inhalation exposure. In circumstances when exposure to airborne NOAA is relatively high and other control measures cannot be applied, inhalation and ocular protections should be implemented such as powered air purifying respirator or full face RPE.

11.3 Selection of controls

11.3.1 General

The selection of controls should be based on the risk assessment. In general, the purpose of applying controls is to ensure that exposure of the workforce is as low as reasonably practicable. In general, it is advisable to adopt a control as high in the control hierarchy as is technically and economically feasible. However, this needs to be balanced against the level of control required to provide a safe working environment and the efficacy of the control measures. The risk assessment should help to decide the appropriate control, taking account of necessity, practicability and cost. In all cases, selection of controls should, as a minimum, be based on national standards and supplemented with additional controls, as appropriate.

Beyond this, guidelines concerning the control approaches to be used in specific exposure situations have been published elsewhere[72],[91],[92],[93],[73]. In addition, several generic approaches can be applied which can be helpful.

When little information on the nanomaterial is available, the precautionary principle should be applied and the highest level of control measures should be considered.

11.3.2 Hazard-based control

The basis of the hazard-based control approach is to allocate control methods based on knowledge of or assumptions about the hazardous nature of the materials being used. It is particularly recommended when there is a gap of knowledge about the concerned nanomaterials. This approach can be applied to nanofibres or nanotubes of toxicological concern. If their use cannot be avoided, it is expected that a high level of control is used (e.g. to control exposure at source by carrying out all tasks, including packaging for disposal, in a ducted fume cupboard, or by using other suitable effective LEV). When using other types of LEV, try to enclose the process as much as possible. A similar approach is taken in the United States which is described in Reference [94].

11.3.3 Control banding and other qualitative approaches

Control banding (CB) is an approach by which control methods are selected based on knowledge or assumptions about the hazardous nature of the materials being used and the exposure potential of the situation. CB has frequently been used in risk management guidance for other particles and chemicals and is usually based on a matrix having the axes exposure and hazard into which various control approaches are placed. CB therefore requires the user to have knowledge of, or make judgments concerning, the relative hazard of the materials being used and/or the relative exposure potential of the material and situation.

Several nano-specific types of control-banding/risk prioritization tools have been developed and validated in the last years and can be used as a support to help in selection of controls and risk prioritization.[95],[96] Although Liguori et al. stated that the available tools are developed for different purposes and are leading to different results, most of the tools give important guidance on nano workplace risk assessment.[97] ISO/TS 12901-2 describes a specific tool based on control banding to further support the implementation of good practice in this area[1].

In ISO/TR 12885:2018, 8.2.2 other possible qualitative approaches are mentioned and whenever necessary they should be used as recommended.

11.3.4 Safety-by-design approach

In the nanotechnology field, safety-by-design (SbD) is considered an important approach to achieve safer nanomaterials, products and their production processes[98],[99]. Thus, safe-by-design solutions should be considered prior to remediation ones. Whenever possible, risks should be assessed during the research and development (R&D) and/or project phase and necessary risk treatment measures considered, according to the practices of safe innovation[99].

The SbD concept addresses the safety of nanomaterials and nano-enabled products and associated processes through the whole life-cycle: from the R&D phase to production, use, recycling and disposal[100].

Thus, producers should consider safety when developing new nanomaterials or modifying existing ones and designing inherently safe production processes. Downstream users of nanomaterials should consider the use of those materials that show lower EHS hazards, resulting from their physicochemical properties such as size or shape, from surface functionalisation or from other characteristics. Concomitantly, the process operations, considering facilities, equipment and performed tasks should be designed to reduce risks to workers.

The design of safer production processes focuses in reducing the emission of NOAA from the main operations and should also consider the transport of raw materials and products, cleaning and maintenance of equipment, and waste disposal among others.

This approach will allow the selection of control measures at the highest levels of the hierarchy mentioned in 11.1.

11.3.5 "State of the art" approaches

During the last few years, organisations have published guides recommending control measures for activities involving the production and handling of nanomaterials. The number of peer-reviewed scientific publications dedicated to the investigation of these measures is lower compared to publications dedicated to risk assessment.[101] ISO/TR 12885 offers guidelines on control measures and Annex C provides a list of guidance and articles including different approaches to risk management[72].

11.4 Evaluation of the effectiveness of control measures

The effectiveness of control approaches should be assessed. Measurement methods which can be used to carry out this assessment are provided in Clause 12. The purpose of applying controls as part of a precautionary approach, when hazard information is unavailable or when there is limited hazard information, is to ensure that exposure of the workforce is as low as practical. Collection of exposure information associated with the implementation of controls enables demonstration and documentation that effective control has been achieved. Methods for health surveillance are given in Clause 13. Judgements considering whether effective control has been achieved can be made by comparison of measured levels with:

— the prevailing national OEL;

— the proposed national or international benchmark levels specifically for types of NOAA;

— other self-imposed (in-house) exposure limit values, considering any proposed margin of safety to take account of known or assumed differences in the toxicity of NOAA when compared to larger versions of the same material;

— the workers disease prevalence compared with previous years to evaluate the effectiveness of control measurements; this is a growing area.

NOTE Currently, specific biomarkers for inflammation or elements traces are the most assessed alternatives. However, since there is no defined biomarker for nanomaterials, it will depend on occupational health department to consider this strategy as complementary evaluation or when decisive results are incomplete.[102],[103] For further information, see Clause 13.

There are already specific NOAA OELs for TiO_2[104] and CNT[105]and several other specific or general OELs have been proposed[8],[7],[106]). Some nanomaterials which only exist in the form of agglomerated and aggregated nanoparticles, such as carbon black and fumed silica, also have specific OELs.

11.5 Information, instruction and training

Arrangements should be put in place to ensure that all control measures are properly and fully applied. Clear allocation of managerial responsibilities and accountabilities is particularly important in this respect. The arrangements should include training/refresher training of those individuals who use the control measures and procedures for ensuring measures are working as they should.

The training methods can include:

— giving information or instruction;

— coaching or on-the-job training; training in the 'classroom';

— open and distance learning; in groups or individually; and

— computer-based or interactive learning.

It should meet the training needs of the whole workforce, including migrant workers who might not have good native language speaking, also people with poor literacy skills or those with disabilities, such as of sight or hearing [107].

Everyone who is involved or can be affected should be provided with the information, instruction and training required to ensure their safety. It is necessary to inform and involve the employees in the risk assessment process. Without the informed and competent participation of employees, any risk management measures identified as necessary in the risk assessment are unlikely to be fully effective. It is therefore necessary that the employees know at least:

— the names of the substances to which they are liable to be exposed and the risks to health created by exposure;

— any relevant OEL or similar self-imposed (in-house) exposure limit value that applies to the substances;

— the information on any safety data sheet that relates to the substances;

— the significant findings of the risk assessment;

— the precautions they should take to protect themselves and their fellow employees;

— the results of any monitoring of exposure, especially if these exceed any OEL; and

— the collective results of any health surveillance (see Clause 13).

12 Measurement methods

12.1 Need for measurement

Clause 12 focuses on measurement of NOAA. Particle sampling and measurement is often needed to understand exposure and risk in workplace scenarios. Measurement can be used to support the following objectives, including:

a) identification of sources of nanomaterial emissions;

b) assessment of the effectiveness of any control measure implemented;

c) ensuring compliance with any OEL or self-imposed (in-house) limit value;

d) identifying any failures or deterioration of the control measures which can result in a serious health effect.

Each of these tasks requires specific and often different types of instrumentation. A range of instrumentation is available (see 12.2). In the workplace, airborne primary nano-objects, NOAA or composite particles are emitted from processes and tasks. The need to detect and measure all these forms is a significant factor in determining an appropriate sampling strategy (see 12.3). More information about these instruments and particle measurement generally is provided in ISO/TR 27628[108].

12.2 Selection of instruments

Many instruments are available which can be used to measure NOAA. New instruments are also being developed. A summary of currently available samplers for gravimetric or chemical analysis and instruments for time-resolved measurement of number, mass and surface area concentration are provided in Table 1, Table 2 and Table 3. EN 16966 can also be referred to for the different metrics in use and applicable instrumentation [109].

In the workplace, airborne primary nano-objects, NOAA and composite particles can be collected onto filters for off-line gravimetric or chemical analysis and the time weighted average mass concentration (mg/m^3) calculated[110]. For metals, chemical analysis is preferred to gravimetric analysis. The choice of collection medium (e.g. filter or impaction plate) will be dictated by the type of analysis, the type of sampler, the sampler flow rate and the collection efficiency requirement [111],[112],[113],[114].

Table 1 lists some of the most established measurement devices. The cascade impactors listed in Table 1 also gives information about mass-based particle sizes.

Table 2 and Table 3 list some of the most established measurement devices. New devices are continually being developed and other novel measurement approaches are described in References [117] and [108].

Table 1 — Samplers to collect airborne particles and NOAA on filters for off-line gravimetric or chemical analysis

Metrics	Devices	Remarks
Mass	Respirable sampler and filter	Gravimetric analysis and elemental analysis for metal-based NOAA [e.g. inductively coupled plasma mass spectrometry (ICP-MS), inductively coupled plasma atomic emission spectroscopy (ICP-AES), X-ray fluorescence (XRF)].
	Inhalable sampler or total sampler and filter	Gravimetric analysis and elemental analysis for metal-based NOAA (e.g. ICP-MS, ICP-AES, XRF). Some countries have limit values or OELs relating to the inhalable fraction of metal particles / dust.
	Open face sampler and filter	Gravimetric analysis and elemental carbon (EC) by thermal gravimetric analysis (TGA) for CNTs and graphene.
	Cascade impactors and filters	Gravimetric analysis and elemental analysis for metal-based NOAA (e.g. ICP-MS, ICP-AES, XRF) or EC by TGA for CNTs and graphene.
	Sampler mimicking the deposition of nanoparticles and NOAA of less than 300 nm in the human respiratory system[115],[116]	Gravimetric analysis and elemental analysis for metal-based NOAA (e.g. ICP-MS, ICP-AES, XRF).
Number, size and morphology	Respirable, inhalable or open face sampler and filter and other NOAA samplers	Qualitative analysis (size and morphology, type of particles, such as primary, agglomerated, aggregated, composite particles) by electron microscopy. Semi-quantitative / quantitative, mainly for nanotubes and nanofibres.

Table 2 — Devices for time-resolved measurement of number, mass and surface area concentration — Hand-held and personal instruments

Metrics	Devices / techniques	Remarks
Particle number concentration (and particle number-based size distribution)	Hand-held condensation particle counter (CPC)	CPCs provide real-time particle number concentration measurements between their particle diameter detection limits. They operate by condensing vapour onto sampled particles and detecting / counting the droplet formed. Can be used with an upper size selective inlet and able to detect down to around 10 nm. Without a nanoparticle pre-separator, they are not specific to the nanometre size range.
	Optical particle counter (OPC)	OPCs provide real-time size distribution and particle number concentrations. They typically measure agglomerates and particles of optical diameter between 0,3 µm and 10 µm to 15 µm. Some OPCs are not suitable for use in environment with medium / high concentrations. Low cost sensors, which have an output in particle number concentration. Their performance requires assessment and their use can be limited to the environment of low concentrations.
Particle mass concentration (and particle mass-based size distribution)	Personal tapered element oscillating microbalance (TEOM)	Real-time monitors, such as the TEOM, can be used to measure nano-aerosol mass concentration online, with a suitable size-selective inlet.
	Personal and hand-held photometer	Photometers provide real-time mass concentrations. They typically measure agglomerates and particles of optical diameter between 0,1 µm and 10 µm. Some real-time photometers can be fitted with a respirable size-selector at the inlet. They need to be calibrated for the dust of interest in the workplace and can be used in circumstances when the size distribution of airborne particles, refractive index and shape do not change with time[118].
Particle surface area concentration	Personal and hand-held diffusion charger	Personal and hand-held lung deposited surface area (LDSA) devices typically measure LDSA concentrations in the particle size range between 10 nm to about a few hundred nanometres. Surface area is a better metric for agglomerates but their measurement can be limited due to instrument availability and size range limitations.

Table 3 — Devices for time-resolved measurement of number, mass and surface area concentration — Research and benchtop instruments

Metrics	Devices / techniques	Remarks
Number concentration	Research grade CPC	Some CPC can measure particles down to 1 nm.
Number concentration and particle number-based size distribution	Low pressure cascade impactor combined with electrical detection Number by calculation	Real-time size-selective (aerodynamic diameter) detection of active surface area concentration, giving aerosol size distribution. Active surface area does not scale directly with geometric surface area for particles larger than 100 nm. Data can be interpreted in terms of particle number concentration. Can detect airborne particles between 6 nm and 10 µm. Size-selected samples can be further analysed off-line.
	Differential mobility analysing system (DMAS)	Real-time size-selective (electrical mobility diameter) detection of particle number concentration, giving aerosol number-based size distribution.
	Wide-range hybrid aerosol spectrometer	Real-time device measuring particles from approximately 10 nm to 35 µm and providing particle number concentrations and number-based size distribution. Two analyzers in one device: an optical aerosol spectrometer and an electrical particle detector.
	Aerodynamic particle sizer	Real-time device (aerodynamic diameter) measuring particle number concentration and number-based size distribution of agglomerates (from 0,5 µm to 20 µm).
Mass concentration and mass-based size distribution	Low pressure impactors	— Gravimetric low pressure impactors. — Real-time low pressure impactor device. — The only devices offering a cut point around 100 nm are Berner-type low pressure impactors or micro-orifice impactors. — They allow gravimetric and chemical analysis of samples on stages below 100 nm.
Mass concentration by calculation	Low pressure cascade impactor combined with electrical detection	Real-time size-selective (aerodynamic diameter) detection of active surface area concentration giving aerosol size distribution. Mass concentration of aerosols can be calculated, only if particle charge and density are assumed or known. Can detect airborne particles between 6 nm to 10 µm. Size-selected samples can be further analysed off-line.
	DMAS	Real-time size-selective (mobility diameter) detection of number concentration, giving aerosol size distribution. Mass concentration of aerosols can be calculated only if particle shape and density are known or assumed.
Surface area concentration	Diffusion charger	— Benchtop or research grade LDSA real-time monitors. — Unipolar corona diffusion charger for aerosols.
	Low pressure cascade impactor combined with electrical detection	Real-time size-selective (aerodynamic diameter) detection of the active surface area concentration. Note that the active surface area does not scale directly with the geometric surface area above 100 nm.
	Electron microscopy	Electron microscopy: scanning electron microscopy (SEM), transmission electron microscopy (TEM). Off-line analysis of electron microscope samples can provide information on particle surface area with respect to size. TEM analysis provides direct information on the projected area of collected particles, which can be related to geometric area for some particle shapes.
Surface area concentration by calculation	DMAS	Real-time size-selective (mobility diameter) detection of number concentration, giving aerosol size distribution. Data can be interpreted in terms of aerosol surface area under certain circumstances. For instance, the mobility diameter of open agglomerates has been shown to correlate well with projected surface area[119],[108].
	DMAS and low pressure cascade impactor combined with electrical detection used in parallel	Differences in measured aerodynamic diameter and mobility can be used to infer particle fractal dimension, which can be further used to estimate surface area.

Specific samplers to collect airborne NOAA on substrate other than membrane filters are also available[120],[121].

12.3 Sampling strategy

12.3.1 Air sampling

12.3.1.1 General

Currently, there is no single sampling method that can be recommended to be used to characterize exposure to all particulate forms of nanomaterials. Therefore, attempts to characterize workplace exposure to NOAA usually involve a multifaceted approach incorporating more than one of the sampling techniques mentioned in the previous subclause[122]. However, sampling strategies for measuring emissions in workplaces relevant to NOAA have emerged [123],[124],[125],[126]. This is typically a stepwise process which involves an initial assessment of particle number concentration using a simple device such as CPC (together with an OPC where larger agglomerated forms of NOAA can be present) and/or respirable mass concentration. Identification of this release (or sources of emissions and leaks) in itself can be sufficient to reconsider the control systems and to adapt better engineering control measures to more effectively control the release.

If a possible release (or source of emission and leak) is identified, this can be followed by a more extensive characterization of that release.

The tiered approach for exposure assessment is a formal methodology for conducting workplace exposure assessments and measurements of aerosols containing NOAA. The tiered approach commonly contains three hierarchical tiers, detailed in 12.3.1.2 to 12.3.1.4.

12.3.1.2 Tier 1

Tier 1 focuses on data gathering prior to workplace assessment to identify possible sources of exposure. Exposure evaluation as part of the control banding approach can be used in Tier 1[1].

12.3.1.3 Tier 2

Tier 2 includes practical measurements and assessment of the workstation and workers' breathing zone air. An example of tier 2 is the nanoparticle emission assessment technique (NEAT). It emphasizes identifying potential emission source(s) and includes measurement in the workers' breathing zone. Upon determining the extent of emissions in the workplace, a control strategy (which can include the use of a control banding model) can be developed and implemented to minimize occupational exposures to NOAA.

In Tier 2, mass concentrations (respirable fraction) and particle number concentrations have been commonly measured in combination with some analytical characterization of the airborne dust by using time resolved instruments such as hand-held condensation particle counters and optical particle counters or sizers and samplers (respirable and inhalable).

Sampling strategies such as NEAT 1.0[123],[124]and NEAT 2.0[126] have made provisions for sampling (as collected on a filter), and for the subsequent off-line TEM and energy dispersive X-ray (EDX) qualitative or semiquantitative analysis of the size and chemical characterization of the NOAA collected. SEM with EDX analysis can also be utilized.

ICP-MS or ICP-AES or XRF are useful at quantifying the mass concentrations of metal-based airborne NOAA. Other chemical analyses may be utilized provided they have adequate sensitivity to ensure reliable exposure measurements. Elemental carbon analysis by TGA can be used to evaluate the mass concentration of CNTs and graphene in the workplace.

The information obtained from chemical analysis (as described in this clause above) can inform what percentage and in what size ranges the NOAA of concern can contribute to the real-time measurement of particles. The accuracy of this approach will depend upon the NOAA having at least one detectable element that is not present in outdoor aerosols.

12.3.1.4 Tier 3

Tier 3 is a comprehensive (multi-metric) measurement strategy of mass, number and surface area concentrations including the use of research grade real-time instruments.

Tiered approaches have been developed in References [127], [72], [128] and [129]. In general, they differ in their methodologies for Tier 2, and in their criteria and justification for a Tier 3 approach.

Tier 3 can be used for a more in-depth assessment of exposure to hazardous substances especially for new chemical substances or materials, for research purposes or for the set-up of new processes (prevention through design).

Regardless of the approach used, when assessing mass, number or surface area concentrations with a real-time device, measuring and characterizing background levels is critical. For the interpretation of peak exposures or increased concentrations from real-time data, the recording of contextual information (e.g. task related activities, other relevant work conditions) is important.

If measuring workers' exposures to specific NOAA is of interest, personal sampling using filters or grids suitable for analysis by electron microscopy or chemical identification should be employed. Electron microscopy with EDX analysis can be used to identify the particles, and can provide an estimate of the size distribution of the particles of interest. Care should be taken to prevent overloading the filters or grids. The use of a respirable sampler with a filter, combined with gravimetric and chemical analysis (e.g. ICP-MS, ICP-AES, XRF for metal NOAA) will provide a measurement of the larger particles e.g. agglomerates. Personal cascade impactors can be useful tools to obtain complementary information on size and mass concentrations of smaller agglomerates. Open face samplers are used to sample nanotubes or platelets for subsequent elemental carbon analysis (e.g. CNTs and graphene) or analytical electron microscopy analysis and counting. Analysis of these filters for air contaminants of interest can help identify the source of the respirable particles. Standard analytical chemical methodologies, including gravimetric analysis, should be employed.

The above approaches can be combined with an occupational hygiene assessment of engineering controls especially LEV. This involves the measurements of flow rates, smoke visualization and expert opinion.

12.3.2 Surface sampling

Using surface sampling to detect the presence of nanomaterials is not routinely part of the initial assessment, but can be conducted to determine if surface contamination is suspected. Surface sampling does not provide size-specific information but can be useful for determining whether NOAA have migrated away from active work processes or other handling areas in the workplace, and have contaminated nonproduction work areas. The decision to collect surface samples should be made by qualified persons (e.g. occupational hygienists) and is also dependent on the NOAA or nanomaterial of interest.

The sampling area, sampling substrate, and sampling technique should all be consistent with recognized consensus standards[94],[130], many of which give the following requirements, recommendations and practices.

— When collecting wipe samples, wear a pair of nitrile disposable gloves.

— The wipe material should consider the work surface to be sampled:

  — The wipe material should also not have detectable amounts of the contaminant being measured.

  — Recommended wipe materials include ghost wipes, smear tabs, Whatman filter paper and other pre-packaged moist disposable towelettes.

— When wiping a workplace surface, use a sampling area of 100 cm^2 (i.e. 10 cm by 10 cm). Adjustments can be needed based on the amount of nanomaterials or NOAA that is on a workplace surface:

  — Reference [134] suggests a surface sampling area of 100 cm^2 since it is about the size of a worker's palm.

  — An "S" or "Z" pattern is commonly used to ensure that the entire work surface is adequately wiped and sampled.

  - Wipe the surface within a disposable 10 cm × 10 cm template using horizontal “S”- or “Z”-shaped stroke patterns.
  - Fold the exposed side of the wipe in and then wipe the same area with vertical “S”- or “Z”-shaped stroke patterns. Folding the wipe is critical to prevent sample loss.
- Gloves and template are discarded after each sample collection (to eliminate the potential cross-contamination during subsequent surface sampling).
- Wipe samples can be collected from various workplace surfaces that are suspected to be contaminated, as well as in areas expected to be free of nanomaterials or NOAA.
- Wipe samples can subsequently be analysed in accordance with the appropriate consensus standards and/or validated analytical methods for the chemical substance of interest.
- Consensus wipe sampling methods that should be considered for the surface sampling of nanomaterials include, but are not limited to:
  - ASTM D6966;[131]
  - ASTM E1728/E1728M;[132]
  - NIOSH Method 9102”[133]; and
  - OSHA ID-125G[134].

Additional methods for the assessment of dermal exposure can be found in ISO/TS 21623[135] and ISO/TR 14294[136].

12.4 Limitations

Measuring particle number concentration in isolation can be misleading. In all particle number concentration measurements, the integration limits over which a particular instrument operates are critical in understanding the reported results. CPC instruments become increasingly insensitive to particles smaller than 20 nm. Concentrations measured with instruments with different sensitivities can therefore differ substantially, particularly if the particle count median diameter is close to or in this range. In this case, instruments will significantly underestimate the nanomaterial aerosol number concentration. Real-time instruments such as CPCs do not provide physico-chemical discriminations and will count water droplets as particles. They require maintenance and calibration as specified by the manufacturers[137].

A further complication relates to the ambient airborne particles and the difficulties for the real time instruments discussed have to distinguish between task / process related emissions and background. Unless the workplace is operating under clean room conditions, airborne particles from external sources will enter the workplace and contribute to the levels of NOAA in the area of the process under investigation. Unless this is considered for real-time data, it can lead to an overestimation of the NOAA levels emitted from the process under investigation. Ultrafine particles, which can be produced in the vicinity of the task or process that is monitored, e.g. from heaters or from electric motors, can also contribute towards overestimation. The process itself can also produce particles. One way to overcome this problem is to determine ambient or background particle counts prior to the commencement of manufacturing or processing of the NOAA. Another method is to carry out simultaneous measurement in the “near field” (close to the task / process) and the “far field” (away from the task or process). The far-field should be representative of the background particle count levels close to the near-field. In some cases, the far-field measurement is outside the workplace. The far field measurement is subtracted from the near-field to provide an estimate of the contribution of the task. This approach assumes that the far-field particles are present in the same size and concentration in the near field (which is not always the case)[138].

Criteria have been established to consider the measured emission or exposure concentration using CPCs significantly above the background. One suggestion is the difference between the NOAA emission or exposure concentration and the mean background concentration needs to be greater than three times the standard deviation of the background concentration[139], while Reference [140] has suggested a NOAA particle count level of 10 % above the background level. Other decision rules for background level are described in EN

17058. Further information on identifying and quantifying background levels are found in References [117], [141] and [142].

A further approach is to utilize differences in composition between NOAA generated in the workplace and the ambient aerosol for discrimination purposes.

Numerous errors are associated with gravimetric analysis of low-mass samples (less than 0,1 mg). Errors caused by static electricity, vibration and particle contamination should be eliminated, and filters should be conditioned and weighed under strict protocols designed to control the effects of humidity and air temperature[143]. For very lightly loaded filters (e.g. particle mass less than 0,05 mg), corrections for changes in air density (known as buoyancy corrections) are recommended[144].

In the case of lightly loaded filters, the greater sensitivity of inductively-coupled plasma mass spectrometry (compared to optical emission spectroscopy) can be required to ensure that limits of quantification are exceeded. Note that precautions should be taken to avoid contaminating the filter sample with particles or metals while loading and unloading the filter cassette, and throughout all stages of handling and analysis. In the case of lightly loaded filters, the contribution of metals from inadvertent contamination can be greater than the contribution from the particles being sampled[144]. Examples of precautions include appropriate the use of nitrile gloves while handling filters and loading/unloading cassettes in a clean laminar flow hood[145],[146].

13 Health surveillance

In most jurisdictions, the primary criterion for health surveillance is a reasonable likelihood that an identifiable disease or adverse health effect associated with exposure to a particular substance will occur in the workplace concerned. It is also necessary that there are technically feasible, available and medically accepted techniques for detecting the disease or adverse-health effect.

There can be a long latency in the development of disease associated with exposure to some NOAA. This suggests the need to consider whether medical screening tests such as those used to detect occupational respiratory diseases can be appropriate for workers exposed to NOAA[147]. If NOAA are composed of chemical substances (or from bulk materials) for which validated screening approaches exist, these same screening recommendations would be applicable to NOAA in workers[148].

In any case, a prudent approach is to collect information about the materials being used and the duration of use. Such information will help to build up a profile of potential exposures which can be important for future epidemiological studies, should any health effects emerge in the exposed population at a later date. This information can also be used in the interim to support risk management decision-making to protect workers who are potentially exposed to hazardous materials.

14 Spillages and accidental releases

Due to the potential for spillages and accidental releases of NOAA, it is essential that employers have documented policies and procedures in place that are based on adequate pre-planning activities. This documentation should include incidental (small) and emergency (uncontrolled) spills or releases.

It is vital that suitable and sufficient risk assessments are completed to determine the exact course of action to be taken in the event of a nanomaterial spillage or accidental release. The methods used should be consistent with the level of hazard and the quantity of nanomaterial involved in the spill. All clean-ups should be carried out in such a way as to ensure that exposure to personnel is as low as practical. Personnel who can be required to deal with such events should receive adequate information, instruction and training on assessing the extent of any spill or accidental release, the clean-up measures to be taken, and the PPE which should be worn (appropriate RPE, disposable coverall of low dust retention and appropriate gloves (see 11.1), as well as guidance on the safe disposal of any waste collected during the clean-up.

In the event of a spillage or accidental release, on-site personnel should determine the extent of the area potentially affected and demarcate it to restrict access by non-essential personnel. If there is a risk of fire or explosion from handling nano-structured materials, ignition sources should be eliminated including electrostatic discharges. Measures should also be put in place to reduce the likelihood of spreading NOAA from the affected areas, for example the use of adhesive walk-off mats at the affected area's exit points.

In situations where on-site personnel can reasonably be expected to deal with a spillage or accidental release of NOAA, consideration can be given to the use of wet wiping cleaning methods, barriers to minimize air currents across areas affected by a spillage and tested and certified H-class vacuum cleaner fitted with a HEPA filter for dealing with dry materials or residues from dried liquid spill areas. When using HEPA type filters it is recommended that the effectiveness of these should be verified at a frequency consistent with manufacturers' recommendations and, where possible, dedicated vacuum cleaners should be used for clean-up operations. It is also good practice to record the type of material collected and avoid mixing potentially incompatible materials in the vacuum cleaner or filters. The vacuum cleaner for the removal of combustible dust should be an explosion proof vacuum cleaner. Dry sweeping should be avoided and surfaces should be decontaminated.

Employers need to consider and document which, if any, situations should trigger an evacuation of personnel from an affected area. Personnel can need to go through a decontamination procedure. Consideration should also be given to the severity of spillages and accidental releases which on-site personnel can be expected to deal with and when other agencies, such as the emergency services and environmental protection agencies, need to become involved.

All debris resulting from the clean-up of a spillage or accidental release (including any filters, wipes, absorbent mats and materials) should be considered as nanomaterial-bearing waste. They should be reclaimed in the most convenient and safe manner in sealed containers. Guidance on the disposal of collected debris and waste is provided in Clause 15.

15 Disposal procedures

15.1 General

The waste management guidance, given in this clause, applies to nanomaterial-bearing waste streams (solid and liquid waste), including:

— powders containing nano-objects or NOAA;

— liquid suspensions containing NOAA;

— solid matrices with nano-objects or NOAA; and

— items contaminated with NOAA, such as containers, wipes and disposable PPE; any material that has come into contact with dispersible engineered NOAA (that has not been decontaminated) should be considered as belonging to a nanomaterial-bearing waste stream; this includes PPE, wipes, blotters and other disposable laboratory materials used during research activities.

15.2 Planification of storage and disposal of nanomaterials

Waste should be treated according to the waste management hierarchy.[149] The most preferred option is waste prevention and reduction. If waste is created, waste should be reused, then recycled, then recovered, and as the least preferred option, disposed (see Figure 3).

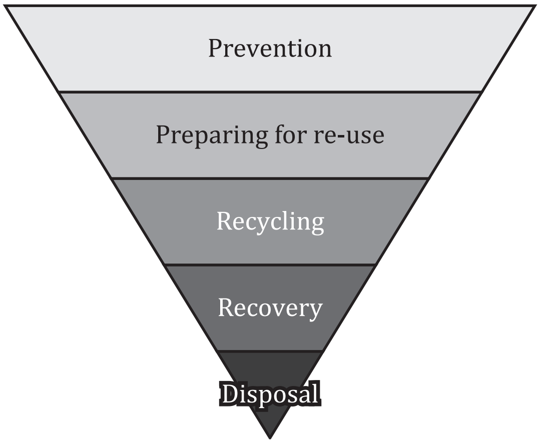

Figure 3 — Waste management hierarchy

A plan for storage and disposal of nanomaterials or contaminated waste should be developed, taking account of the hazard profile of the materials and the quantities involved. Considerations should be given to the following points.

— The physical and chemical properties of the NOAA can be different from those of the non-nanoscale form of that substance leading to potential increased physical, health and environmental hazards.

— Some high aspect ratio nano-objects (HARNs) can have similar adverse health effects in the lungs to asbestos fibres.

— NOAA can penetrate biological barriers through the disposal life cycle and can have increased bioavailability compared to the non-nanoscale form of that substance.

— NOAA disposed as waste can change from those of the pristine NOAA due to physical and chemical reactions. This can alter their toxicological, eco-toxicological, physico-chemical properties and mobility.

— Some NOAA can be associated with a risk of dust explosions.

When the nanomaterial has a known hazard profile, disposal should be planned according to this profile. The properties of the nanomaterial disposed as waste (e.g. in landfill or incineration) can change from those of the pristine material due to physical, chemical and/or biological reactions. This can alter the waste toxicological, eco-toxicological, physico-chemical properties and mobility (e.g. in landfill).

Any material that has come into contact with dispersible engineered NOAA (that has not been decontaminated) should be considered as belonging to a nanomaterial-bearing waste stream. This includes PPE, wipes, blotters and other disposable laboratory materials used during research activities. Substances from hazardous or potentially hazardous nanomaterial containing waste streams should not be put into the regular waste or flush down the drain. Work surfaces should be evaluated for surface contaminants and accordingly be decontaminated using safe work procedures. Equipment used to manufacture or handle hazardous or potentially hazardous nanomaterials should be decontaminated before it is disposed of or reused. Waste (e.g. cleaning solutions, rinse waters, rags, disposable PPE) resulting from decontamination activities should also be treated as nanomaterial-bearing waste.

NOTE The Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal is an international treaty which restricts the movements of hazardous waste between countries. In particular, it prohibits the exports of hazardous waste from developed to less developed countries[150].

15.3 Storage of nanomaterial waste prior to disposal

15.3.1 General

Best practices should be applied during the pre-disposal of nanomaterials, which include:

— waste segregation; under various national or international legislation, it is illegal to mix a hazardous waste with either non-hazardous or another hazardous waste;

— safe handling and preparation of waste to minimize exposure of the workers, the public and the environment;

— a duty of care.

Subclauses 15.3.2 and 15.3.3 give the appropriate approaches for collection and storage of hazardous or potentially hazardous nanomaterial waste prior to disposal.

15.3.2 Storage in waste containers

Nanomaterial-bearing waste should be packaged in compatible containers that are in good condition and afford adequate containment to prevent the escape of the NOAA. Drumming and double contained storage provisions, especially if the waste is hazardous, should be considered. Waste should not react with and degrade the containers. When combustible powders or liquids are stored, it is recommended to observe specific requirements for fire and explosion protection; in their dry state, certain NOAA can constitute a fire or explosion risk that is far greater than the same microscale materials. Cleaning up spills can be very difficult if a large container fails. Containers should be properly labelled and sealed. Label the waste container with a description of the waste and include available information characterizing known and suspected properties. Other chemicals or solvents should be added to the label.

15.3.3 Storage in plastic bags

Paper, wipes, PPE and other items with loose contamination should be collected in a plastic bag or other sealable container. When plastic bags are used to contain large quantities of waste, heavy duty plastic bags should be used. When the bag is full but not overfilled, it should be closed and carefully placed into a second plastic bag or other sealing container, avoiding outside contamination. The outer bag should be labelled with an appropriate waste label.

Waste materials should be handled carefully to avoid damage to their integrity. The outer container should not be contaminated or should be cleaned (e.g. using a H-class vacuum cleaner fitted with a HEPA filter or a dampened cloth) before removal from the work area.

Waste should also be transported and stored safely and securely. Additional considerations should be given to the safe storage and transport of flammable, combustible and explosive nanomaterials.

15.4 Disposal of nanomaterial waste

There are two main streams of disposal: incineration and landfill.

The disposal process should depend on an assessment of:

— the type of waste and its volume;

— the hazard(s) and physicochemical characteristics (including hazard classes and categories) and other material associated with the nanomaterial waste;

— if the nanomaterial waste is landfilled, leachate and landfill characteristics;

— if the waste is incinerated, the incineration parameters (e.g. temperature, oxygen content), the type and amount of chemical and airborne pollutants emitted, the combustion by-products and the residues formed as well as the solid residue treatment stage.

Under certain national and international legislation, it can be illegal to landfill liquid waste. For liquid dispersion containing nano-objects or NOAA, which cannot be incinerated, the liquid phase and the solid phase containing the nanomaterials including NOAA should be separated.

Other disposal procedures and best practices include the following.

— Material from nanomaterial-bearing waste streams should not be put into the household waste, or flushed down the drain.

— Equipment used during nanomaterial handling should be decontaminated before it is disposed of or reused.

— Waste resulting from decontamination should be treated as nanomaterial-bearing waste.

— Nanomaterials for disposal should be collected within a labelled, closed container, for instance a drum with a standard lid and clamping ring. If the hazardous properties of the newly synthesized nanomaterial are partially unknown, it is recommended to highlight this on the container with, for instance, the sentence: "Attention – contains waste of a substance not yet tested completely".

While landfill is still the main disposal method for waste worldwide, it is generally accepted to be the least sustainable. The disposal of waste to landfill implies a residual risk due to a potential loss of containment of the waste from that landfill. Landfill sites are usually classified according to whether they can accept hazardous, non-hazardous or inert waste. Engineering standards vary for different classes of landfill site and also for the age of the site itself.

Additional guidelines can be found in CEN/TS 17275.[151] CEN/TS 17275[151] provides an informative annex on the indication of applicability of 850 °C and 1 100 °C incineration processes for manufactured nano-objects.

16 Prevention of fire and explosion

Prevention of fire and explosion is governed by national and international regulations. Deposited NOAA products can be dispersed and become airborne more easily than coarser products, and NOAA can then possibly remain suspended in air for a long time. The fire and explosion properties of dusts depend on a variety of influencing factors (e.g. particle morphology, degree of agglomeration, moisture content, concentration, turbulence). During manufacture, handling and use, etc., changing these factors can also have an influence on the fire and explosion properties. The same principles applying to the management of fine powders, dusts or dusty materials should be considered for NOAA, with particular care taken in the case of easily oxidizable metallic dust.

Explosion protection measures have been described for dust dispersions and for hazardous quantities of larger sized materials,[152] and these can be applied to the handling of potentially explosive NOAA. For reactive or catalytically active nanoparticles, contact with incompatible substances should be prevented. Due to the possibly low ignition energies and ignition temperatures some NOAA can become pyrophoric or can be easily ignited on hot surfaces (deposited or dispersed), see ISO/IEC 80079-20-2[153]. Furthermore, for such ignition-sensitive NOAA, the low ignition energies of electrostatic discharges can also have an ignition effect. In this case, measures to avoid electrostatic discharges should be considered. For instance, appropriate clothes should be selected to reduce the risk of electrostatic discharge.

Furthermore, clothes should not be changed since there is a danger for electrostatic discharge. Equipment, electrical systems and transport devices should be explosion proofed. The vacuum cleaner for the removal of combustible dust should be an explosion proof HEPA filtered vacuum cleaner. The area or zone should be labelled with a warning signage (explosive atmosphere hazard warning label).

Fire prevention has to take into account electrical requirements among others. The design of electrical equipment protection should take account of the fine granulometry and very long settling time of NOAA, which necessitate dust protection[154].

The selection of an extinguishing agent should take account of the compatibility or incompatibility of the NOAA with water. Some metallic dusts react with water to form, among other things, hydrogen, which ignites very easily. Chemical powders are available to extinguish burning metallic dust powders, when using a fire extinguisher or similar, however, dispersion of the combustible dust must be avoided. Otherwise, this can result in the formation of an explosive atmosphere. To reduce the risks of fire and deflagration, it can prove necessary to use controlled-atmosphere production and storage processes, using carbon dioxide, nitrogen or another inert gas (e.g. argon when using metallic materials). This can introduce further hazards into the system, notably the risk of asphyxiation.

Annex A
(informative)

NOAA categories

World Health Organization (WHO) guidelines (2017)[7] recommend classifying manufactured nanomaterials (MNMs) into the following groups and subgroups:

— MNMs with specific toxicity:

  — MNMs with high dissolution rates through the release of ions or amenable to biodegradation and,

  — MNMs with low dissolution rates but with high specific toxicity. These are MNMs with specific toxicity, which is mediated by the specific chemical properties of their components. The respirable fibres group consists of MNMs that are rigid, biopersistent or biodurable and respirable, which have dimensions for man-made mineral fibres in the past.

— MNMs that are respirable fibres, and

— MNMs that are granular biopersistent particles.

In Reference [155], a panel of experts distinguished six possible categories of health-based nanomaterial reference values:

a) WHO fibre-like high aspect ratio engineered nanomaterials (HARNs),

b) non-WHO fibre-like HARNs and other non-spheroidal engineered nanomaterials (ENMs),

c) readily soluble spheroidal ENMs,

d) biopersistent spheroidal ENMs with unknown toxicity,

e) biopersistent spheroidal ENMs with substance-specific toxicity, and

f) biopersistent spheroidal ENMs with relatively low substance-specific toxicity.

Annex B
(informative)

Additional information on dermal and ocular exposure

B.1 Dermal exposure

The possibility of adverse effects of nanomaterials on human health cannot be ruled out[156]. Moreover, some types of nanomaterials penetrate the different layers of the skin and can end up in the bloodstream and other vital organs[157].

A few studies have evaluated the effectiveness of protective gloves against NOAA. Reusable butyl rubber and polychloroprene gloves as well as disposable nitrile rubber and latex gloves were tested with different types of NOAA in different physical forms (powder, aerosol and in solution)[158],[159],[82],[160],[86],[83]. Different levels of performance were measured depending on the glove material, the thickness, the presence of a liquid environment (liquid carrier and physiological solution simulating human sweat) and the type of NOAA. Tests were also performed in conditions simulating occupational use, e.g. by submitting specimens to static[158],[160] and dynamic deformations[159],[82],[86],[83]. With dynamic deformations, different mechanical and physicochemical phenomena were identified as facilitating the nano-objects penetration through the glove thickness[161]. The two models of disposable nitrile gloves tested were rated poor in terms of effectiveness and the researchers even warned against the use of one of them for handling nano-objects in aqueous solution[82],[83]. On the other hand, polychloroprene, butyl rubber and latex gloves seemed to be efficient. In the case of tests without mechanical deformation and with a static mechanical deformation, the results reported in terms of effectiveness were not consistent[158],[162].

B.2 Ocular exposure

If some studies have shown some benefits of nanotechnology approaches for ocular drug delivery[46], [47], the ease of penetration of NOAA through ocular tissues can also lead to harmful effects. Many factors can affect the toxicity of nanomaterials in ocular tissues: the chemical composition, size, dose and time after exposure, and the potential of a biodistribution pattern[46].

The effect of titanium dioxide (TiO_2) nanoparticle exposure was also evaluated on the ocular surface of 80 eyes of 40 rabbits in a study detailed in Reference [48]. The authors concluded that TiO_2 nanoparticle exposure induces ocular surface damage. Other researchers report no significant toxic effects of other nanomaterials (magnetic nanoparticle, compacted DNA nanoparticle, etc.)[163],[164].

Annex C
(informative)

Guidance and articles on “State of the art” approaches to control measures

Guidance and articles on “State of the art” approaches to control measures including risk management approaches are given below:

— ISO/TR 12885, *Nanotechnologies — Health and safety practices in occupational settings*[72];

— NIOSH, General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories[165];

— Ostiguy C, Debia M, Roberge B and Dufresne A. Best Practices Guidance for Nanomaterial Risk Management in the Workplace[31];

— EC, Guidance on the protection of the health and safety of workers from the potential risks related to nanomaterials at work - Guidance for employers and health and safety[166];

— EC, Working Safely with Manufactured Nanomaterials - Guidance for Workers[167];

— NIOSH, Current Strategies for Engineering Controls in Nanomaterial Production and Downstream Handling Processes[73];

— Working Safely with Nanomaterials in Research and Development[168];

— NIOSH, Nanotechnology Guidance and Publications CDC[67];

— OECD Environment Directorate, Physical-chemical decision framework to inform decisions for risk assessment of manufactured nanomaterials[169].

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