TECHNICAL REPORT

ISO/TR 18637

First edition
2016-12-01

Nanotechnologies — Overview of available frameworks for the development of occupational exposure limits and bands for nano-objects and their aggregates and agglomerates (NOAAs)

Nanotechnologies — Vue d'ensemble des cadres disponibles pour la définition de limites et bandes d'exposition professionnelle applicables aux nano-objets, à leurs agrégats et agglomérats (NOAA)

Reference number
ISO/TR 18637:2016(E)

Contents

Page

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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 documents 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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

The committee responsible for this document is ISO/TC 229, *Nanotechnologies*.

Introduction

Nano-objects and their aggregates and agglomerates (NOAAs) represent a subset of particulate materials that can be dispersed in the air and can represent health risks via inhalation exposures. NOAAs include structures with one, two or three external dimensions in the nanoscale from approximately 1 nm to 100 nm, which may 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. An aggregate comprises strongly bonded or fused particles (structures). An agglomerate is a collection of weakly bound particles (structures)[1][2][3][4].

The purpose of this document is to describe a general framework for the development of occupational exposure limits (OELs) or occupational exposure bands (OEBs) for individual NOAAs or categories of NOAAs with different levels of available data. OELs and OEBs are important tools in the prevention of occupational illness. OELs have a long history in industrial hygiene and are based on observations of workers or studies of laboratory animals. OELs are established to minimize the likelihood of adverse effects from exposure to potentially hazardous substances in the workplace[5][6]. An OEL is generally substance-specific (although sometimes generically expressed, such as dust). Sufficient data to develop an OEL may not be available, especially for substances such as NOAAs used in emerging technologies. To aid in hazard communication and exposure control decisions for substances without OELs, hazard banding has been used for many years[7][8][9]. Substances are assigned to a hazard band based on limited toxicity data usually from animal studies. Hazard banding schemes typically consist of qualitative bands ranging from low to high severity of effects. Thus, a hazard band represents a range of potential toxicities for a particular substance or category of substances. Some hazard banding schemes include associated OEBs[10]. The term OEB is a general term for exposure concentration ranges used in some hazard banding schemes that are related to the ranges of hazard potentials. In contrast to an OEB, an exposure band is a range of potential concentrations of a substance (or category of substances) to which workers may be exposed in a defined occupational scenario and which is based on factors such as the amount of NOAA processed or used, the nature of the process, and the form of the NOAA including dustiness[3]. In control banding, the hazard band and the exposure band are combined to determine the control band for any particular occupational scenario (e.g. ISO/TS 12901-2).

OELs and OEBs are part of an overall occupational safety and health (OSH) program and are not intended to identify and address all safety and health risks associated with a specific process or task. OELs and OEBs are intended to provide occupational safety and health professionals with a health basis for assessing the effectiveness of exposure controls and other risk management practices. The exposure assessment of nanomaterials including carbon nanomaterials [such as fullerene, graphene, single-walled carbon nanotube (SWCNTs) and multi-walled carbon nanotube (MWCNTs)], metal oxides (TiO_2, SiO_2, zinc oxide, iron oxide), and metals (silver and gold nanoparticles) remains a challenge in the field of occupational hygiene, as there have been relatively few studies on the characterization of workplace exposures to NOAA. Sampling and analytical methods that have the capabilities to accurately measure nanomaterials are still under development. Most sampling devices that measure airborne particle count concentrations, such as condensation particle counters and optical particle counters, cannot differentiate ambient exposures to background nanoparticles from NOAA in the workplace environment. Airborne measurements of carbon nanotubes (CNTs) and carbon nanofibres (CNFs) using mobility particle sizers also sometimes could present a unique challenge due to the arcing caused by the charged airborne CNT and CNF agglomerates in the differential mobility analyser[11]. Although several groups have attempted to measure and count CNT structures using transmission electron microscopy or other microscopic methods[12][13], there are still no standard methods for measuring and counting CNT structures. In addition, determining the mass concentration of CNTs and CNFs based on measuring the elemental carbon (EC) remains a challenge due to other sources of elemental carbon in the workplace, such as organic composite materials and air and diesel pollution that could interfere in the determination of CNT and CNF exposures.

Scientific and technical methodologies used to set exposure limits may differ from one entity to another, which can lead to disparities in worker protection from country to country[14]. Therefore, harmonizing the scientific methodologies used in developing OELs, including using the best available evidence for interspecies extrapolation and specifying the type of data and uncertainties involved in the OEL determination is necessary for a robust health and safety evaluation framework for NOAAs.

This document provides a collaborative, science-based platform to describe and evaluate the state-of-the-art in such data and methods.

Current risk assessment methods are likely to apply to NOAAs[15], although the limited health hazard data for many NOAAs and the considerable variety in the types of manufactured NOAAs present a challenge to the efficient development of OELs for individual NOAAs. To date, few OELs and OEBs have been developed for specific NOAAs and none have been formally regulated by a government agency. Standard OEL and OEB methodologies for NOAAs are needed to evaluate the evidence on the hazard potential of NOAAs in the workplace to provide a health basis for risk management decisions, including selection and evaluation of engineering control options. One of the goals of this document is to identify both the similarities and differences in the methods used to develop OELs. This evaluation may lead to improvements in methods for setting exposure limits or bands.

This document presents an overview of the state-of-the-art in the development of OELs and OEBs for NOAAs. Current approaches for assigning default hazard bands in the absence of NOAA-specific toxicity data are described. These approaches build on current hazard and control banding strategies, such as those developed in ISO/TS 12901-2. The current state of the methods and data to develop OELs and OEBs for NOAAs is described in this document, along with an evaluation of those methods used in developing the current OELs for NOAAs. Categorical approaches to derive OEBs for NOAAs with limited data are also discussed, such as those based on biological mode-of-action (MOA) and physico-chemical (PC) properties. The basis for the framework described in this document is the U.S. NIOSH Current Intelligence Bulletin *Approaches to Developing Occupational Exposure Limits or Bands for Engineered Nanomaterials*[16]. This document also takes into consideration other state-of-the-science reports, including outputs of the workshop “Strategies for Setting Occupational Exposure Limits for Engineered Nanomaterials,” which was held on September 10-11, 2012 in Washington, DC, USA[6] and the OECD Working Party on Manufactured Nanomaterials Expert Meeting on Categorization of Manufactured Nanomaterials, September 17-19, 2014[17].

The primary target audience of this document is occupational safety and health professionals in government, industry, and academia, who have the expertise to develop OELs or OEBs based on the guidance in this document. In addition, the evidence-based approach described in this document may be useful in the evaluation and/or verification of current hazard and control banding schemes and for identifying the key data gaps. Control banding requires information on both the applicable hazard category and exposure category. Appropriately verified control banding tools would be broadly useful, as these tools require less specialized expertise and resources (than for a comprehensive risk assessment) and are accessible to a wider group of individuals and small businesses. Therefore, this document can be considered complementary to ISO/TS 12901-2 on control banding for nanomaterials as it describes the state-of-the-art in the process of assigning nanomaterials to hazard bands/OEBs when the scientific evidence is not sufficient to develop an individual OEL.

Some of the cited methods lead to results that are not necessarily consistent and this may be due to method selection biases of the authors. In these cases, diverse results will also make it difficult to use information to confidently establish exposure and band levels. It is beyond the scope of this document to attempt to identify the methods which lead to both correct and consistent results. In the event that methods lead to diverse results, it is hoped that this report will lead to additional methods development that will lead to improvements and that these improvements can be relied on for setting exposure and banding levels.

The objectives of this document include

a) describing an evidence-based state-of-the-art framework to develop OELs or OEBs for manufactured NOAAs, and

b) examining the currently available data and other approaches and methods used (e.g. benchmark substances and benchmark exposure levels) in the occupational risk management decision-making for NOAAs.

It is anticipated that this document will contribute to the development of standard hazard and risk assessment methods and facilitate the systematic evaluation of the potential health risk of occupational exposure to NOAAs.

Nanotechnologies — Overview of available frameworks for the development of occupational exposure limits and bands for nano-objects and their aggregates and agglomerates (NOAAs)

1 Scope

This document provides an overview of available methods and procedures for the development of occupational exposure limits (OELs) and occupational exposure bands (OEBs) for manufactured nano-objects and their aggregates and agglomerates (NOAAs) for use in occupational health risk management decision-making.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/TS 80004-2 and the following apply.

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

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

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

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 agglomerates 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 26824:2013, 1.2]

3.2
aggregate
particle comprising 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/TS 80004-2:2015, 3.5]

3.3
bulk material
material of the same chemical composition as the NOAA, at a scale greater than the nanoscale

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).

3.5
health hazard
potential source of harm to health

[SOURCE: ISO 10993-17:2002, 3.7]

3.6
health risk
combination of the likelihood of occurrence of harm to health and the severity of that harm

[SOURCE: ISO 10993-17:2002, 3.8]

3.7
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.

Note 2 to entry: The terms nanofibril and nanofilament can also be used.

Note 3 to entry: See 3.9 Note 1 to entry.

[SOURCE: ISO/TS 80004-2:2015, 4.5]

3.8
nano-object
discrete piece of material with one, two or three external dimensions in the nanoscale

Note 1 to entry: The second and third external dimensions are orthogonal to the first dimension and to each other.

[SOURCE: ISO/TS 80004-1:2010, 2.2]

3.9
nanoparticle
nano-object with all external dimensions in the nanoscale where the lengths of the longest and the shortest axes of the nano-object do not differ significantly

Note 1 to entry: If the dimensions differ significantly (typically by more than 3 times), terms such as nanofibre or nanoplate may be preferred to the term nanoparticle.

[SOURCE: ISO/TS 80004-2:2015, 4.4]

3.10
nanoscale
length range approximately from 1 nm to 100 nm

Note 1 to entry: Properties that are not extrapolations from a larger size are predominantly exhibited in this length range.

[SOURCE: ISO/TS 80004-1:2010, 2.1]

3.11
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 26824:2013, 1.1]

3.12
solubility
maximum mass of a nanomaterial that is soluble in a given volume of a particular solvent under specified conditions

Note 1 to entry: Solubility is expressed in grams per litre of solvent.

[SOURCE: ISO/TR 13014:2012, 2.27]

3.13
occupational exposure limit
maximum concentration of airborne contaminants deemed to be acceptable, as defined by the authority having jurisdiction

[SOURCE: ISO 16972:2010, 3.133]

3.14
occupational exposure band
quantitative representation of hazard band which describes hazard potential of a particular material or class of materials in workplace air

3.15
breathing zone
space around the face of a worker from where he or she takes his or her breath

[SOURCE: ISO 24095:2009, 3.1.2.1]

4 Symbols and abbreviated terms

ACGIH	American Conference of Governmental Industrial Hygienists
AGS	Ausschuss für Gefahrstoffe (German Committee on Hazardous Substances)
AGW	Arbeitsplatzgrenzwert (occupational exposure limit)
AIST	Japanese National Institute of Advanced Industrial Science and Technology
BALF	bronchoalveolar lavage fluid
BAuA	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (German Federal Institute for Occupational Safety and Health)
BEI	biological exposure index
BEL	benchmark exposure level
BMD	benchmark dose
BMDL	benchmark dose estimate, 95 % lower confidence limit

BSI	British Standards Institution
CMAR	carcinogenic, mutagenic, asthmagenic, or reproductive toxicant
CNF	carbon nanofibre
CNT	carbon nanotube
DFG	Deutsche Forschungsgemeinschaft (German Research Foundation)
DMEL	derived minimum exposure level
DNEL	derived no-effect level
EPA	United States Environmental Protection Agency
EU	European Union
EU-OSHA	European Agency for Safety and Health at Work
GBP	granular biopersistent particle
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
IARC	International Agency for Research on Cancer
IFA	Institut für Arbeitsschutz (German Institute for Occupational Safety and Health)
ILV	indicative limit value
JSOH	Japan Society for Occupational Health
LC50	concentration associated with 50 % lethality
LOAEL	lowest observed adverse effect level
MAK	Maximale Arbeitsplatzkonzentration (maximum workplace concentration)
MOA	biological mode of action
MOEL	Korean Ministry of Employment and Labour
MSHA	United States Mine Safety and Health Administration
MWCNT	multi-walled carbon nanotube
NIOSH	United States National Institute for Occupational Safety and Health
NOAAs	nano-objects, and their aggregates and agglomerates including those larger than 100 nm
NOAEL	no observed adverse effect level
NRV	nano-reference value
OECD	Organization for Economic Cooperation and Development
OEB	occupational exposure band
OEL	occupational exposure limit
OEL (PL)	period-limited occupational exposure limit

OELV	occupational exposure limit value
OSH	occupational safety and health
OSHA	United States Occupational Safety and Health Administration
PC	physico-chemical
PCM	phase contrast microscopy
PEL	permissible exposure limit
QRA	quantitative risk assessment
REACH	Regulation, Evaluation, Authorization and Restriction of Chemicals
REL	recommended exposure limit
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SCOEL	Scientific Committee on Occupational Exposure Limits
STEL	short-term exposure limit
STOT-SE	Specific target organ toxicity — single exposure
STOT-RE	Specific target organ toxicity — repeated exposure
SWCNT	single-walled carbon nanotube
TLV	threshold limit value
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UF	ultrafine
VLEP	Valeur Limite d'Exposition Professionnelle (occupational exposure limit)
WHO	World Health Organization
WHS	Work Health and Safety

5 Description of available processes for setting OELs and OEBs

5.1 General considerations

Exposure to substances or mixtures in the workplace can occur through inhalation, absorption through the skin or ingestion. Most exposure occurs through the inhalation of vapours, dusts, fumes or gases. For some chemicals, absorption through the skin may also be a significant source of exposure.

The response of the body to exposure from substances and mixtures depends on the nature of the substance, the health effects it can cause and the amount of the substance or mixture absorbed by the body. Individuals also have differing abilities to metabolize chemicals which can cause considerable variation in the toxic effects between people. The extent to which a person is exposed mainly depends on the concentration of the substance or mixture in the air and the amount of time exposed and, of course, on the effectiveness of controls. Substances and mixtures may cause immediate acute health effects or it may be decades before effects on the body become evident.

Occupational exposure limits are intended to prevent adverse health effects in "nearly all workers"[18] even with repeated or daily exposures over a working lifetime. Some OELs are based on health effects data only (e.g. ACGIH TLV), and other OELs also include consideration of the technological feasibility (e.g. NIOSH RELs) or economic feasibility (e.g. OSHA PEL) of measuring and controlling exposures.

For a few substances, usually the more potent probable and established human carcinogens, it is not currently possible to assign an appropriate exposure limit. For these substances, exposure should be controlled to the lowest practicable level. Biological monitoring may provide a more reliable indication of workplace exposure for these substances.

The evaluation of hazards posed by atmospheric contaminants in the working environment is often a complex task, taking into account the potentially large variability of exposure at the workplace requiring sound occupational hygiene exposure assessment strategies. For this reason, it is essential that those persons responsible for such assessments are knowledgeable and experienced professionals, who are fully aware of all issues canvassed in this document and have appropriate qualifications and experience in occupational hygiene.

NOTE A knowledgeable and experienced professional is an individual who will properly perform a specific job. This person utilizes a combination of knowledge, skills and behaviour to improve performance. More generally, competence is the state or quality of being adequately or well qualified, having the ability to perform a specific role[3].

The relationship between various exposure limits should not be used as a general measure of their relative toxicity. This is because, among other things, the values for different substances are often established with regard to different biological effects, such as irritation or systemic toxicity. Similarly, the exposure limits should not be used as a basis for the evaluation of community air quality, or for long term, non-occupational exposures.

Most substances used in industry have not been assigned exposure limits. This does not imply that these substances are safe or non-hazardous. In many cases there is insufficient information on the health effects of these unlisted substances to allow national regulatory bodies to assign an exposure limit, even on a tentative basis. In other instances, the use of the substance does not lead to significant airborne levels of contaminant, or its use is so restricted that an exposure limit is not warranted.

It is a good general policy to keep the exposure to any substance as low as is practicable, irrespective of whether present information indicates it is hazardous or not. Some substances previously thought to be comparatively safe have subsequently been found to pose serious long term health risks.

There are three types of exposure limits:

— time-weighted average (TWA) limit;

— short term exposure limit (STEL);

— peak or ceiling limit.

These limits and other technical aspects of setting OELs are further described in A.1.2.

5.2 Description of evidence-based process

The methods for developing OELs depend on the available data. Schulte, et al.[5] describe three general scenarios for varying amounts of toxicological data. This framework was refined to describe linkages between the evidence basis for these general categories through benchmark substances. Benchmark substances are well-characterized materials (e.g. airborne particles or fibres) with sufficient dose-response data from animal and/or human studies to develop quantitative risk estimates and health-based OELs (Figure 1)[19][20]. Benchmark materials also provide a reference (e.g. as a positive or negative control) in comparative toxicity assays with new NOAAs that have limited toxicological data but similar physico-chemical properties and inferred biological mode-of-action (MOA)[19][20][21]. The focus of this document is on occupational airborne exposures to nanomaterials since inhalation is the major route of exposure to potentially hazardous substances, including NOAAs, in the workplace.

As shown in Figure 1, in the first case, if dose-response data are sufficient, an OEL for an individual NOAA can be developed using quantitative risk assessment (QRA). The definition of sufficient will ultimately be based on a judgment about the available data, and may include weight of evidence evaluations, including the availability of adequate data for benchmark dose modelling[22] or no observed adverse effect levels (NOAELs) or lowest observed adverse effect levels (LOAEL) from well-conducted studies. Second, if data are insufficient for QRA for a specific substance, but adequate information is available on a similar substance in the same mode-of-action category, then a categorical OEL may be assigned by qualitative or quantitative methods including read-across and structure-bioactivity modelling, with comparisons between NOAAs and benchmark substances. Third, if data are insufficient to develop a substance-specific or categorical OEL, then initial (default) hazard and control bands may be derived by comparing NOAA properties to that of similar materials in broad categories. The objective of this evidence-based approach is to facilitate decision-making about exposure control strategies for NOAAs in the workplace based on best available evidence. The framework allows for iteration and revision of an OEB or OEL as new data become available based on standard criteria for data and methods. At this time, more examples of OELs developed for NOAAs are available than of categorical OELs or OEBs for NOAAs.

The data available for developing OELs or OEBs for NOAAs may include

a) data from *in vivo* and *in vitro* testing of specific NOAAs (e.g. from the OECD testing program, manufacturers of NOAAs, and non-regulatory government agencies such as the NIOSH and the NTP in the US), and

b) existing toxicology or epidemiology studies of lung effects from inhaled particles and fibres for comparative toxicity analyses.

General chemical hazard databases (e.g. as used in GHS[23] hazard classification) are also available for some of the parent or bulk materials with similar chemical composition to the NOAA for use in hazard band/OEB allocation and control banding (e.g. see ISO/TS 12901-2). Table 1 summarizes the type of data and methods needed to develop OELs or OEBs.

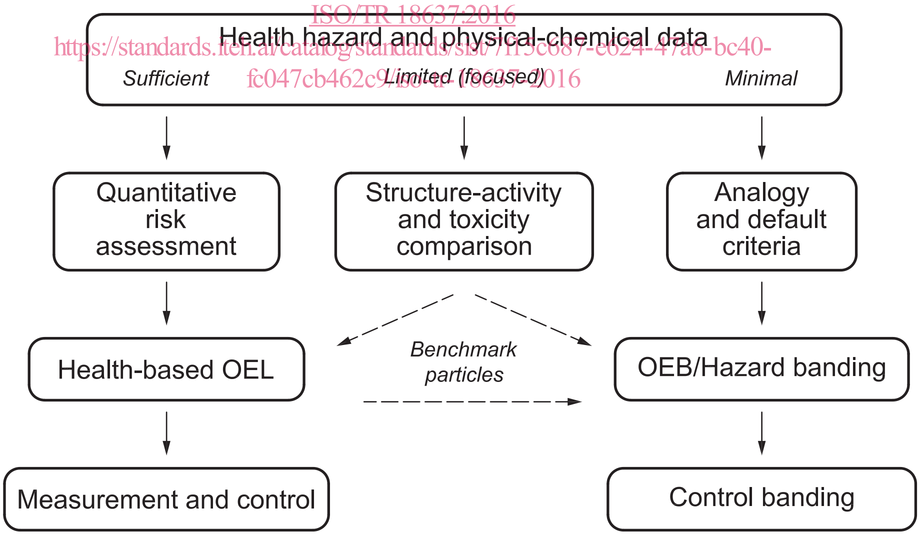

Figure 1 — Evidence-based strategy to develop exposure control limits and bands for NOAAs, based on level of evidence

Table 1 — Data and methods needed to develop exposure limits or bands

Guidance value	Level of evidence	Data, analysis tools and methods
Substance-specific OEL	Sufficient	Substance-specific dose-response data for quantitative risk assessment; availability of substance-specific sampling and analytical method
Categorical OEL	Limited (focused)	Comparative toxicity, clustering and categorization to estimate hazard or risk based on physico-chemical properties and biological mode-of-action data
OEB	Minimal or inadequate	Analogy; default hazard categories and exposure control options are applied.

5.3 Substance-specific OELs

The substance-specific OELs typically do not take separate account of the nanoparticle size, although some of these OELs do specify the particle size sampling criteria associated with regional respiratory tract deposition. These sampling criteria include inhalable (total), thoracic (airways), and respirable (pulmonary) size fractions. Nanoparticles are capable of depositing anywhere in the respiratory tract region, including the pulmonary region where gas exchange takes place. Some of the individual OELs are specific to the dust and/or fume forms, and fumes by nature consist of nanostructured particles. The OELs for fumes may be lower mass concentrations than the OELs for dust of the same chemical substance (e.g. the NIOSH REL and OSHA PEL for copper is 1 mg/m^3 for the dust and 0,1 mg/m^3 for the fume)[24]. In other cases the OEL applies to both the dust and fume (e.g. iron oxide, NIOSH REL is 5 mg/m^3 and OSHA PEL is 10 mg/m^3; cobalt metal dust and fume, NIOSH REL is 0,05 mg/m^3 and the OSHA PEL is 0,1 mg/m^3). It is relevant to note that those OELs vary at least as much by chemical composition as by descriptors of particle size (dust, solid particles generated by any mechanical processing of materials such as crushing, grinding, and handling or fume, airborne dispersion consisting of small solid particles created by condensation from the gaseous state).

Clause 6 and Table 2 provide a description and list of the OELs that have been developed for specific nanomaterials by non-regulatory government agencies, companies, and nongovernmental organizations. To date, no regulatory standards have been circulated for NOAAs.

5.4 Categorical OELs

Historically, many airborne particulate materials were regarded as a “nuisance” or as “low toxicity” dusts and categorical OELs, such as a generic inhalable OEL of 10 mg/m^3 and a respirable OEL of 4 mg/m^3 were set for many low-toxicity poorly-soluble dusts including aluminium oxides, graphite, titanium dioxide and others[25]. In Germany, the DFG MAK commission recently reduced the OEL for biopersistent granular particles from 3 mg/m^3 to 0,3 mg/m^3 (respirable fraction), reflecting concerns about a possible carcinogenic potential for this category of substances[26]. All these values, however, were not intended for particulate materials with specific known inhalation or systemic toxicity (e.g. asbestos and lead, respectively) for which substance-specific OELs were also determined.

Advantages of categorical approaches include:

— more efficient use of data;

— reduced costs;

— reduced animal use;

— increased sample size;

— greater robustness of results;

— increased biological plausibility for other materials in the same mode of action category[27].

Categorical approaches are compatible with hazard and risk assessment frameworks proposed for NOAAs (e.g. References [5], [20] and [28]) and with a standard risk assessment paradigm[29]. Methods to derive OELs for NOAAs using categorical approaches may include quantitative or qualitative read-across[27]; comparative potency analyses of NOAAs to benchmark (reference) particles in the same mode-of-action (MOA) category[19][20], e.g. using a “parallelogram” approach[19][30][31][32]; and assigning an untested substance to the low end of the distribution of OELs for materials in the same hazard class[33].

Other risk analysis and categorization approaches include both occupational and environmental components, such as screening tools of potential risks over the NOAA lifecycle[34][35]. The multi-criteria decision analysis (MCDA) approach includes evaluation of the risks and benefits with weightings obtained through expert elicitation[28]. This process has been used to assign NOAAs to qualitative risk categories (low, medium, high)[36].

Clause 7 summarizes the categorical OELs that have been proposed by governmental and nongovernmental organizations. These categories are based on broad groups of physico-chemical properties that influence toxicity (soluble, biopersistent low toxicity, biopersistent high toxicity, and fibres). The BSI and IFA categories are provisional exposure limits based on existing OELs for particles and fibres in these categories, which includes in some cases a precautionary downward adjustment for the nanoscale form. The extent to which chemical substance-specific data are available would allow refinement of the categorical OELs to an individual OEL that may be more applicable to an individual substance.

5.5 Initial or default occupational exposure bands

When data are not sufficient to develop an individual OEL, hazard banding approaches are often used to facilitate decision-making among engineering control options[5]. Control banding typically utilizes a matrix approach to categorize substances according to their hazard and exposure potential[37][38][39][40][41][42] to determine an appropriate control technology (such as general ventilation, local exhaust, or containment)[39][41][42][43]. The combination of the selected hazard and exposure bands determines the control band and associated engineering control options. However, the utility of such an approach is frequently limited by the availability of adequate toxicological data for use in hazard assessment. The absence of such data makes workplace risk characterization and the subsequent selection of appropriate control measures problematic. Another suggested approach is the utilization of initial default hazard categories or OEBs for NOAAs based on the physico-chemical properties associated with point-of-entry or systemic toxicity, including particle surface chemistry and area, shape, diameter, and solubility, as well as any evidence on the mutagenicity, carcinogenicity, or reproductive toxicity of the nanomaterial or parent material[20][42][44][45][46].

ISO/TS 12901-2 also incorporates available toxicological information and physico-chemical properties to designate nanomaterials into hazard bands. In this method, nanomaterials are grouped into one of five inhalation hazard groups (A to E) according to increasing severity described in GHS hazard classification applicable to chemicals[23].

— Category A (no significant risk to health) corresponds to an OEB of 1 mg/m^3 to 10 mg/m^3 (as 8 h time-weighted average)

— Category B (slight hazard; slightly toxic) — 0,1 mg/m^3 to 1 mg/m^3

— Category C (moderate hazard) — 0,01 mg/m^3 to 0,1 mg/m^3

— Category D (serious hazard) — <0,01 mg/m^3

— Category E (severe hazard) has no concentration ranges provided in ISO/TS 12901-2 and other hazard allocation schemes (8.1)

The decision logic for assigning NOAAs into these hazard bands includes considerations of solubility, fibrous nature and hazardous properties of bulk and analogous materials[3].

Hazard and control banding approaches were developed to facilitate risk management decision-making in small business. A key research need for hazard and control banding strategies in general, and those specific to NOAAs, is evaluation and validation of the utility of these strategies to provide adequate