



BSI Standards Publication

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

**National foreword**

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## **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)*

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# Contents

	Page
Foreword.....	iv
Introduction.....	v
<b>1 Scope.....</b>	<b>1</b>
<b>2 Normative references.....</b>	<b>1</b>
<b>3 Terms and definitions.....</b>	<b>1</b>
<b>4 Symbols and abbreviated terms.....</b>	<b>3</b>
<b>5 Description of available processes for setting OELs and OEBs.....</b>	<b>5</b>
5.1 General considerations.....	5
5.2 Description of evidence-based process.....	6
5.3 Substance-specific OELs.....	8
5.4 Categorical OELs.....	8
5.5 Initial or default occupational exposure bands.....	9
<b>6 Substance-specific OELs for nanomaterials.....</b>	<b>10</b>
6.1 General overview.....	10
6.2 Available substance-specific OELs.....	10
6.2.1 Carbon nanotubes.....	10
6.2.2 Nanoscale TiO <sub>2</sub> .....	11
6.2.3 Fullerenes.....	12
6.3 Evaluation of OEL methods.....	12
6.3.1 Similarities and differences.....	12
6.3.2 Influence of methods on derived OEL values for nanomaterials.....	13
6.3.3 State of the science in support of risk assessment methods for nanomaterials OELs.....	14
<b>7 Categorical OELs for nanomaterials.....</b>	<b>15</b>
7.1 Summary of options proposed.....	15
7.1.1 United Kingdom.....	15
7.1.2 Germany.....	15
7.1.3 NIOSH.....	17
7.1.4 Japan's (AETL) approaches.....	17
7.1.5 OECD.....	18
7.2 Evaluation of categorical OEL.....	19
7.2.1 Similarities and differences.....	19
7.2.2 State of the science supporting categorical OELs.....	20
<b>8 OEBs and control banding for nanomaterials.....</b>	<b>21</b>
8.1 Overview of current hazard and control banding schemes.....	21
8.1.1 Comparison of hazard bands and OEBs as applied to inhaled NOAAs.....	22
8.1.2 ISO hazard banding scheme for NOAAs.....	25
8.2 Case studies on banding NOAAs.....	26
8.3 Evaluation of the evidence for initial (default) OEBs for categories of NOAAs.....	28
8.3.1 Categorical analyses and read-across.....	28
8.3.2 Utility of <i>in vitro</i> data in OEL/OEB development for NOAAs.....	29
8.3.3 Options for deriving an OEL or OEB for NOAAs.....	30
<b>9 Feasibility considerations in the OEL and OEB setting process.....</b>	<b>30</b>
<b>Annex A (informative) Standard processes for OEL setting.....</b>	<b>32</b>
<b>Bibliography.....</b>	<b>62</b>

## 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](http://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](http://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](http://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)<sup>[1][2][3][4]</sup>.

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<sup>[5][6]</sup>. 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<sup>[7][8][9]</sup>. 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<sup>[10]</sup>. 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<sup>[3]</sup>. 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<sub>2</sub>, SiO<sub>2</sub>, 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<sup>[11]</sup>. Although several groups have attempted to measure and count CNT structures using transmission electron microscopy or other microscopic methods<sup>[12][13]</sup>, 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<sup>[14]</sup>. 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<sup>[15]</sup>, 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*<sup>[16]</sup>. 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<sup>[6]</sup> and the OECD Working Party on Manufactured Nanomaterials Expert Meeting on Categorization of Manufactured Nanomaterials, September 17-19, 2014<sup>[17]</sup>.

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 21824:2013, 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]