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PUBLISHED DOCUMENT

Nanotechnologies

Part 3: Guide to assessing airborne exposure in occupational settings relevant to nanomaterials

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This document comprises a front cover, an inside front cover, pages i to ii, pages 1 to 28, an inside back cover and a back cover.

Foreword

Publishing information

This Published Document is published by BSI and came into effect on 30 November 2010.

The initial drafting of this Published Document was produced in association with BIS as part of their ongoing programme of support for standardization.

PD 6699, *Nanotechnologies*, now comprises the following parts:

Part 1: *Good practice guide for specifying manufactured nanomaterials*;

Part 2: *Guide to safe handling and disposal of manufactured nanomaterials*;

Part 3: *Guide to assessing airborne exposure in occupational settings relevant to nanomaterials*.

Use of this document

As a guide, this Published Document takes the form of guidance and recommendations. It should not be quoted as if it were a specification and particular care should be taken to ensure that claims of compliance are not misleading.

It has been assumed in the preparation of this Published Document that the execution of its provisions will be entrusted to appropriately qualified and experienced people, for whose use it has been produced.

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The word "should" is used to express recommendations of this Published Document. The word "may" is used in the text to express permissibility, e.g. as an alternative to the primary recommendation of the clause. The word "can" is used to express possibility, e.g. a consequence of an action or an event.

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0 Introduction

By almost any measure, the growth of nanotechnology as a scientific and technological activity over the last ten years has been enormous. Indicators include almost exponential growth in scientific papers published, patent applications lodged, investments by national authorities and private industry, number of people employed in the area and revenue generated. This has led to the development and production of many new forms of materials at the nanoscale, with a range of divergent properties when compared to the same materials at a larger scale. Well-known examples include materials like carbon nanotubes (CNT), which have greatly enhanced strength and conductivity when compared to other forms of carbon, and quantum dots, which emit light at frequencies which depend on their particle size. These new nanomaterials are synthesized in a wide range of production processes and, in turn, lead to a wide range of applications and processes in which they can be used.

Against this background, concerns have been expressed about the potential risk to the health of individuals involved in the manufacture and use of these materials and to the environment (RS/RAEng 2004 [1]). A full understanding of the potential risks of such materials when manufactured or used requires an understanding of the intrinsic toxicity of the materials and the extent to which people (or the environment) are exposed. Since publication of the Royal Society/Royal Academy of Engineering report [1] in 2004, there has been a large increase in research activity focused on identifying, categorizing and quantifying the potential risks associated with a wide range of new nanomaterials [2]. The focus has been largely on the toxicological aspects, with, to date, less effort on understanding and quantifying exposure. However, recent studies are contributing to increased understanding of the instruments used and their limitations, and how these can be used in combination to provide better quantification of exposure [3],[4]. As yet, though, there is no consensus on which methods are appropriate for each situation, how they are to be applied in detail, and what the limitations of these methods might be.

1 Scope

This Published Document gives guidance on the development and implementation of plans and strategies for the assessment of exposure by inhalation of nanomaterials, based on an understanding of the nature of the exposure and the capabilities and limitations of exposure measurement instrumentation. It is applicable to all workplace settings in which nano-objects, including nanoparticles and nanotubes, are manufactured, processed or used. Sources of other data and information are also provided.

The Published Document describes a structured, step-by-step approach to exposure assessment which takes into account the purpose, the type of information needed, and the usefulness and limitations of the various approaches for exposure assessment for different types of nanomaterials, and provides a rationale for method selection.

This Published Document is intended to compliment the development and take-up of new nanotechnology-based materials in UK industry by providing manufacturers and users of these materials with effective strategies for assessing worker exposure to airborne nanomaterials.

Given the emergent nature of the knowledge base in this area, the guide is targeted at the professional user who already has some knowledge and experience of exposure assessment and occupational hygiene practice.

2 Terms and definitions

For the purposes of this Published Document, the terms and definitions given in PAS 136 apply.

NOTE The term “nanomaterials” includes nano-objects and aggregates and agglomerates of nano-objects, including where they are embedded within a matrix.

3 Abbreviations

APS	Aerodynamic particle sizer
CNT	Carbon nanotube
CPC	Condensation particle counter
DMA	Differential mobility analyser
EDX	Energy dispersive x-ray analysis
ELPI	Electrical low pressure impactor
FMPS	Fast mobility particle counter
HARN	High aspect ratio nano-objects
ICP-MS	Inductively coupled plasma mass spectroscopy
ICPM-OES	Inductively coupled plasma optical emission spectrometry
OPC	Optical particle counter
NEAT	Nanoparticle emission assessment technique
NIOSH	National Institute for Occupational Safety and Health
NM	Nanomaterial
NP	Nanoparticle
PCOM	Phase contrast optical microscopy
SEM	Scanning electron microscope
SMPS	Scanning mobility particle sizer
TEM	Transmission electron microscope

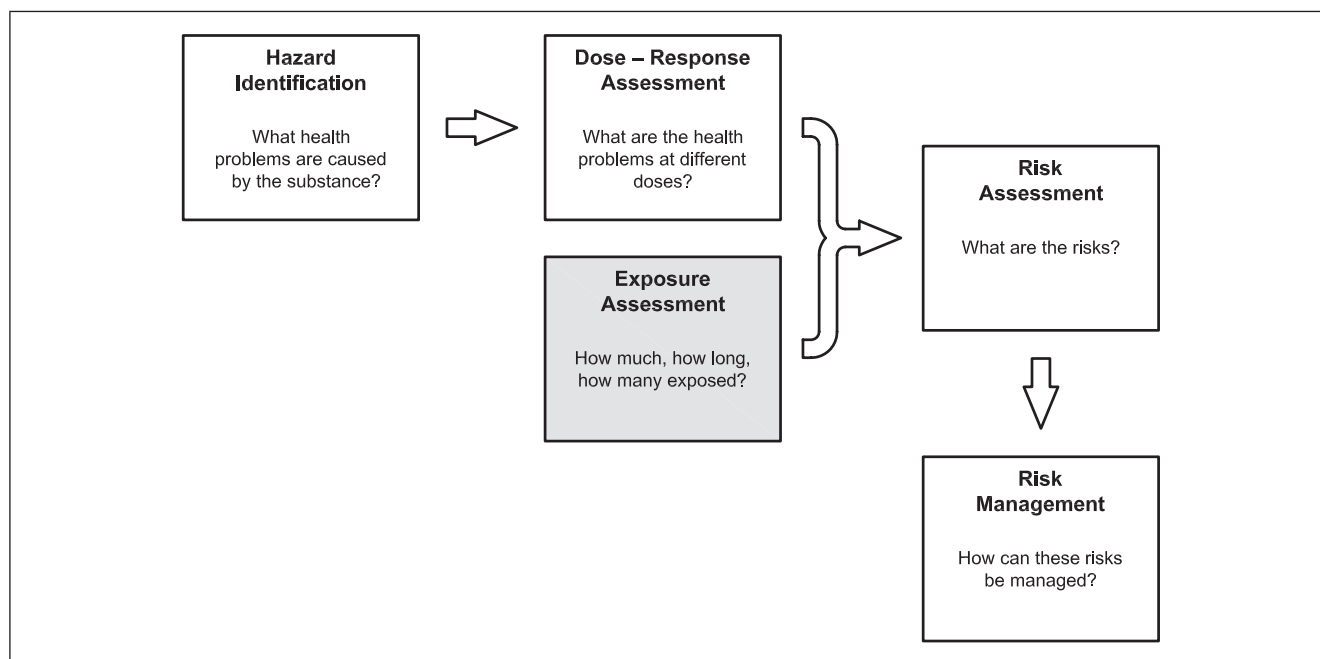
4 Exposure assessment generic

4.1 Defining exposure

The risk to the health of an individual or a population arising from exposure to a chemical agent is generally considered to be a function of the intrinsic harmfulness of the chemical (its toxicity) and the dose (amount) which accumulates in the specific biological compartment (e.g. the lungs). In an occupational context it is difficult to quantify the dose, specifically in the case of insoluble particulates. In order to quantify and manage the risks, it is usual to use exposure as a proxy for dose. Knowledge of plausible exposure levels and duration

enables realistic interpretation of dose-response relationships. Knowledge and control of exposure is critical in risk assessment and management, as indicated in Figure 1.

Figure 1 The risk assessment paradigm relating hazard, exposure and risk



Critical questions in relation to exposure are: how much, how long and how many people are exposed? Thus, exposure is usually measured (quantified or assessed) in terms of its intensity (concentration) and duration (or frequency). Control of exposure (to zero) effectively removes the risks from the toxic agent. Without exposure there is no risk.

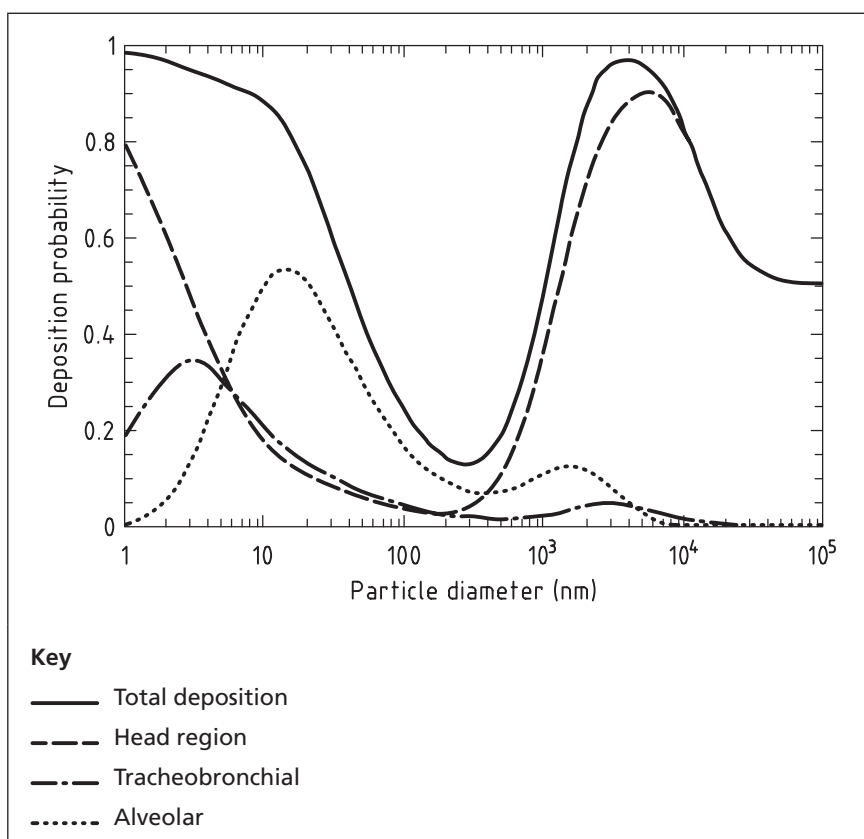
4.2 Routes of exposure

The main routes by which workers can be exposed to particles are inhalation, ingestion and dermal penetration.

- a) Inhalation is considered to be the primary route by which particles suspended in air can enter the bodies of workers. Once inhaled, particles deposit in all regions of the respiratory tract. The site and extent to which particles deposit in the respiratory tract are dependent on particle size, expressed in terms of aerodynamic diameter (for particles greater than approximately 300 nm) or thermodynamic diameter for particles less than 300 nm¹⁾. Figure 2 shows the fractional deposition of inhaled particles in the nasopharyngeal, tracheo-bronchial and alveolar regions of the human respiratory tract for nasal breathing at rest, using the predictive mathematical model of the International Commission for Radiation Protection [5]. There is an increasing total deposition as particle size decreases below around 300 nm.

¹⁾ The "aerodynamic particle diameter" is the diameter of a sphere with a density of $10^3 \text{ kg}\cdot\text{m}^{-3}$ and the same terminal settling velocity in air as the particle of interest. The "thermodynamic particle diameter" is the diameter of a spherical particle that has the same diffusion coefficient in air as the particle of interest.

Figure 2 Predicted total and regional deposition of particles in the human respiratory tract related to particle size, using ICRP 66 model



- b) Ingestion exposure to particles in general can arise from hand-to-mouth contact by sucking or licking a contaminated surface, or by eating contaminated food. It might also be caused by swallowing mucus containing deposited particles which has been cleared from the lung. Occupational ingestion exposure to nanomaterials has not yet been studied to any extent.
- c) Dermal exposure is of increasing concern in workplaces [6]. Workers can be exposed via the skin by handling or touching materials or surfaces coated with nanomaterials. One of the challenges in managing the risks arising from dermal exposure is that protective equipment designed to prevent exposure, such as gloves, can in itself act as a reservoir of contaminant, potentially exacerbating the exposure. Currently, there is little evidence that insoluble NP depositing on the skin can penetrate the epidermis [7],[8]. However, only a few studies have been published thus far. Local effects, such as sensitization and dermatitis, have not been investigated for NP and so cannot be ruled out.

This Published Document focuses on exposure by inhalation.

4.3 Exposure metrics

In early studies which considered the health effects of inhaled particles, dust (particle) samples were collected by drawing air through a filter or other medium and subsequently analysed off-line to estimate exposure, expressed as a concentration in air. For example, in the coal industry the samples were analysed by counting particles collected on the filter under a light microscope [9]. This resulted in an estimate of exposure

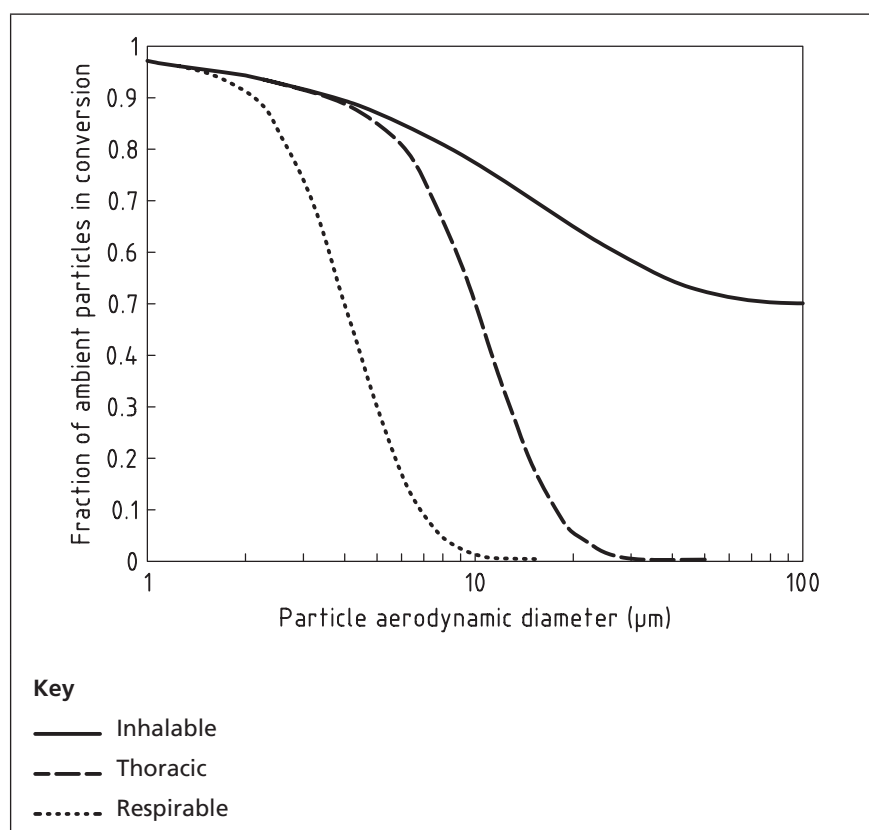
in terms of particle number concentration, expressed as number of particles per cc or per m^3 of air. Epidemiological studies in that industry later demonstrated a strong correlation between pneumoconiosis and mass concentration, typically expressed as $\text{mg}\cdot\text{m}^{-3}$. Assessment in terms of mass was less demanding and more accurate than manual counting under a microscope and so was the preferred choice. The use of workplace exposure limits (WEL), based on mass concentrations, has become the norm for measuring or regulating exposure for most hazardous chemicals and particles [10].

A further refinement of this approach involves sampling of particles based on collection of a biologically relevant aerosol fraction. In this context, biological relevance is characterized by the region of the respiratory tract to which a particle can potentially penetrate and determined as a function of particle size, measured in terms of aerodynamic diameter. Such fractions are defined as follows (ISO 7708).

- The inhalable convention: the mass fraction of total airborne particles that enters the nose or mouth during breathing.
- The thoracic convention: the mass fraction of inhaled particles that penetrate the larynx, with 50% penetration at $11.64\text{ }\mu\text{m}$ (equivalent to $10\text{ }\mu\text{m}$ when expressed as a fraction of total aerosol).
- The respirable convention: the fraction of inhaled particles that penetrate to the alveolar region of the lung, with 50% penetration at $4.25\text{ }\mu\text{m}$ (equivalent to $4\text{ }\mu\text{m}$ when expressed as a fraction of total aerosol).

The conventions are shown in Figure 3.

Figure 3 **Health-related sampling conventions for workplace aerosols (ISO 7708:1995)**



The one class of aerosols that are treated differently are fibres. Fibres have an extreme shape (aspect ratio). Their behaviour in the lungs differs substantially from many, more compact particles, and they can persist for long periods in the lungs following deposition. Exposure to fibres is not characterized in terms of averaged mass and composition, but by the number (concentration) of fibres in the air with a specific shape and composition. To assess exposure, fibres are collected on a filter and are counted by phase contrast light microscopy [11]. Only visible fibres with widths greater than 0.2 μm and less than 3 μm , a length greater than 5 μm and an aspect ratio of at least 3:1 are counted, and these are used to give an "index" of the fibre exposure. These are sometimes referred to as "regulatory" or "respirable" fibres. To count the fibres (such as asbestos) where there are also many fibres present that are not visible by light microscopy (i.e. <200 nm width), electron microscopy has been widely used, and international standards for both scanning and transmission electron microscopy are available, e.g. ISO 10312, ISO 13794.

4.4 Measurement of exposure

Particle sampling and measurement is extremely helpful in assessing exposure and risk in workplace scenarios. Measurement can be used to support various activities, including:

- assessment of personal exposure for ensuring compliance with any WEL or self-imposed (in-house) exposure standard;
- assessment of personal exposure for linking with potential adverse health effects in epidemiological studies;
- identification of emission sources;
- assessment of the effectiveness of any control measure implemented.

Each of these issues could imply different constraints on the selection of measurement approaches. For example, for epidemiological studies the currently held view is that samples collected ought to be based on personal exposure²⁾. This implies that the sampling instruments used are to be of such a size that they can be worn by the individuals (workers) participating in the study without any changes in their normal work activities and behaviour. To facilitate such a study, it is necessary for relatively large numbers of sampling instruments to be available such that estimates from large populations can be obtained.

In contrast, compliance with air quality standards for environmental pollution is based on assessments made using fixed point (static) monitors placed in predetermined positions. Here it is assumed that the concentration of pollution is largely homogenous, so exposure can be adequately assessed from measurements made with a fixed point monitor, based at some distance from the individual. The requirement for relatively few instruments, located at the fixed points, means that the constraints on size and mobility of these devices, as well as the costs, are very different from personal sampling.

²⁾ Large spatial differences in aerosol concentration can occur around industrial processes and around the human body. Placing an aerosol sampler on the body, within a few cm of the mouth and nose (personal sampling), reduces errors in estimating an individual's exposure.

Often, the quantity of interest relating to exposure cannot be measured directly (or completely) due to limitations in the analytical method, or as a result of the study design. In these cases, it is necessary to adopt a measurement strategy in which the required metric is estimated, based on what can actually be measured in practice. The early particle number-based measurements of coal dust or the measurement of fibres (see 4.3) provide good examples of this.

5 Measurement in occupational settings relevant to nanotechnologies

5.1 Relevant sizes of particles to measure

According to the current definition of the inhalable fraction, the upper value of the aerodynamic diameter of a particle that, by convention, can be inhaled into the body is 100 μm (100 000 nm). The majority of the individual nanoparticles (between 1 nm and 100 nm) released into the air will usually be present as agglomerates. It is likely that nanoparticles will be present as agglomerates which could represent structures, such as chains, several times larger than this, as found for ultrafine particles produced from welding fume. Many nanomaterials are supplied as powders which are highly agglomerated, but even during the manufacture of the primary nanoparticles they quickly agglomerate with each other and any other particles present in the air.

This means that if a 20 nm primary particle size nanomaterial is being produced or supplied, attempting to monitor only particles below 100 nm is likely to give only a very limited assessment of the actual exposure to that nanomaterial. Therefore, the challenge for any exposure measurement is to measure all the nanomaterial that could be inhaled or at least that which can reach the deep lung (respirable fraction) where it might be more difficult to clear.

5.2 Identification of nanomaterials

Unless released into a clean room, the background of particles already present in the air could be substantial (background particle counts of 10 nm to 1 000 nm sized particles are often as high as several thousand, sometimes tens of thousand, particles per mL or higher). Therefore, there are considerable peak:background challenges in detecting the release of nanomaterials into room air. This means that particle number and particles size distribution information is not specific to the nanomaterials of interest, so that further identification of the types of particles being measured might be necessary to ensure that the source and level of the nanomaterial emission are properly identified. Other common sources of ultrafine particle emission include electric motors, combustion sources, fumes and sprays.

5.3 Activities and scenarios

Exposure to airborne particles of nanomaterials can potentially occur for workers at all phases of the material life cycle. During the development of a new material, the material will probably be produced under tightly controlled conditions, typically in very small quantities. Accidental releases due to spills and accidents are possible. Once the material moves into commercial production, exposures can potentially