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Workplace atmospheres — Ultrafine, nanoparticle and nano-structured aerosols — Inhalation exposure characterization and assessment

Air des lieux de travail — Particules ultrafines, nanoparticules et aérosols nanostructurés — Caractérisation et évaluation de l'exposition par inhalation

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Foreword

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

In exceptional circumstances, when a technical committee has collected data of a different kind from that which is normally published as an International Standard ("state of the art", for example), it may decide by a simple majority vote of its participating members to publish a Technical Report. A Technical Report is entirely informative in nature and does not have to be reviewed until the data it provides are considered to be no longer valid or useful.

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Introduction

Aerosol exposure has historically been characterized by the mass concentration of airborne material, usually associated with specific size ranges corresponding to different deposition regions within the respiratory system. However, there are indications that mass concentration alone may not provide a suitable indication of the health risks associated with some aerosols. A number of toxicology studies have indicated that, on a mass for mass basis, some very small respirable insoluble particles may be more toxic than larger respirable particles with a similar composition [4 to 11]. Ambient aerosol epidemiology studies since the early 1990s have demonstrated an increase in health impact from particles smaller than 2,5 µm compared to those smaller than 10 µm on a mass for mass basis [12 to 22]. While there is very limited health impact data specific to inhaling very fine respirable particles from the occupational environment, there is evidence to suggest that health effects associated with inhaling such particles generated in hot processes, such as metal processing and welding, are greater than mass-based exposures would indicate [23][24]. Taken together, the evidence points towards a particle size-related health risk following inhalation exposure to some occupational aerosols that is not appropriately reflected by mass concentration alone. In recognition of the potential importance of particle size, the term “ultrafine aerosol” has gradually been adopted and loosely refers to particles “smaller than 100 nm in diameter”. The term is now widely used to refer to incidental aerosols where there are potential particle size-dependent health effects. As research and development into nanotechnology has increased over recent years, concern has also been expressed over the potential health impact of purposely generated particles with nanometre diameters or nanoscale structures [25 to 28]. In this context, the terms “engineered nanoparticle” and “engineered nanoaerosol” have also been used loosely to describe particles and aerosols associated with engineered nanometre-structured materials. However, a generally accepted set of definitions for these terms is still under discussion. For clarity, in this report, the term “nanoparticle” is used to describe all aerosol particles with diameters smaller than approximately 100 nm that present a potential inhalation health hazard. Larger particles with a nanometre-scale structure that may also present a potential health hazard (such as agglomerates of nanoparticles and nanometre-diameter fibres) are referred to as “nanostructured” particles, and aerosols of nanoparticles and nanostructured particles are referred to as “nanoaerosols”.

With only limited toxicity data and negligible exposure data, it is currently unclear how exposure to nanoaerosols should be most appropriately monitored and regulated. There is strong toxicity-based evidence that aerosol surface area is an appropriate exposure metric for low solubility particles that removes the dependency on particle size [5][8][9][29]. However, there are also indications that in some instances particle number within specific particle size ranges may be important [23]. Recent studies on particle translocation within the body have further indicated a size-dependency on the likelihood of deposited particles moving from the respiratory system to other organs [30][31]. At the present time, there is insufficient information to determine which physical exposure metrics – size-selective number, surface area and mass concentration – are most relevant, or which are the most appropriate exposure characterization techniques to use. A first step to providing the necessary information is to establish the means by which exposure can be measured against different metrics. In the short term, this will provide a means to evaluate exposures where there is concern over the inadequacy of mass-based methods, particularly in emerging nanotechnologies where engineered nanoparticle exposure may be significant. It will also provide a basis for developing a deeper understanding of associations between aerosol exposure and health effects using a range of exposure metrics and will lay the foundation for future characterization standards.

In this context, the overall aim of this Technical Report is to provide generally accepted definitions and terms, as well as guidelines on measuring occupational nanoaerosol exposure against a range of metrics. By providing the means to undertake potentially more relevant exposure measurements where current methods and standards appear inadequate, it addresses an immediate need and will form a basis for extending knowledge on how occupational exposure to nanoaerosols should most appropriately be measured. The development and adoption of appropriate measurement approaches is an essential step toward developing and implementing future exposure measurement standards for nanoaerosols.

Workplace atmospheres — Ultrafine, nanoparticle and nano-structured aerosols — Inhalation exposure characterization and assessment

1 Scope

This Technical Report has been prepared in response to

— increasing concern over the potential health risks associated with occupational exposure to nanometre-diameter and nanometre-structured aerosol particles (collectively referred to as nanoaerosols, including the subset of particles produced as a by-product of industrial processes and generally referred to as ultrafine aerosols),

— the lack of current guidelines and standards applicable to minimizing the health risks, and

— the need to establish valid sampling methodologies as part of the process of formulating appropriate exposure and exposure monitoring standards.

The principle aim is to provide the necessary background information and sampling guidelines to enable occupational hygienists and researchers to effectively characterize and monitor nanoaerosol exposures in the workplace in advance of specific exposure limits and standards being developed and implemented. Occupational nanoaerosols represent a class of airborne material dominated by particles smaller than typically 100 nm in diameter (either as discrete particles or as agglomerates).

This Technical Report contains guidelines on characterizing occupational nanoaerosol exposures and represents the current state-of-the-art, with an emphasis on nanometre-diameter particles. Background information is provided on the mechanisms of nanoaerosol formation and transportation within an occupational setting and on industrial processes associated with nanoaerosol exposure. Exposure metrics appropriate to nanoaerosols are discussed, and specific methods of characterizing exposures with reference to these metrics are covered. Specific information is provided on methods for bulk aerosol characterization and single particle analysis.

2 Terms and definitions

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

2.1
accumulation aerosol
aerosol associated with particle growth from the nucleation range through coalescence, coagulation and/or condensation

NOTE Distribution modes typically extend from 50 nm to 1 µm, but are not confined to these limits.

2.2
aerodynamic diameter
diameter of a spherical particle with a density of 1 000 kg/m^3, that has the same settling velocity as the particle under consideration

NOTE Aerodynamic diameter is related to the inertial properties of aerosol particles and is generally used to describe particles larger than approximately 100 nm.

2.3
aerosol
metastable suspension of solid or liquid particles in a gas

2.4
agglomerate
〈aerosols〉 group of particles held together by relatively weak forces, including van der Waals forces, electrostatic forces and surface tension

NOTE The term is frequently used interchangeably with “aggregate”.

2.5
aggregate
〈aerosols〉 heterogeneous particle in which the various components are held together by relatively strong forces and thus not easily broken apart

NOTE The term is frequently used interchangeably with “agglomerate”.

2.6
coagulation
formation of larger particles through the collision and subsequent adhesion of smaller particles

2.7
coalescence
formation of homogeneous particles through the collision of smaller particles and subsequent merging or mixing of constituent material

2.8
engineered nanoparticle
nanoparticle intentionally engineered and produced with specific properties

2.9
mobility
〈aerosols〉 propensity for an aerosol particle to move in response to an external influence, such as an electrostatic field, thermal field or by diffusion

2.10
mobility diameter
diameter of a spherical particle that has the same mobility as the particle under consideration

NOTE Mobility diameter is generally used to describe particles smaller than approximately 500 nm, and is independent of the density of the particle.

2.11
nanoaerosol
aerosol comprised of, or consisting of, nanoparticles and nanostructured particles

2.12
nanoparticle
particle with a nominal diameter (such as geometric, aerodynamic, mobility, projected-area or otherwise) smaller than about 100 nm

2.13
nanostructured particle
particle with structural features smaller than 100 nm, which may influence its physical, chemical and/or biological properties

NOTE A nanostructured particle may have a maximum dimension substantially larger than 100 nm.

EXAMPLE A 500 nm diameter agglomerate of nanoparticles would be considered a nanostructured particle.

2.14
nucleation aerosol
aerosol dominated by particle formation from the gas phase, such as through nucleation from a supersaturated vapour

NOTE Aerosol distributions typically extend from less than 1 nm to 50 nm, but are not confined to these limits.

2.15
particle
small discrete mass of solid or liquid matter

NOTE See Reference [32].

2.16
primary particle
particle not formed from a collection of smaller particles

NOTE The term typically refers to particles formed through nucleation from the vapour phase before coagulation occurs.

2.17
secondary particle
particle formed through chemical reactions in the gas phase (gas to particle conversion)

2.18
surface area, active
surface area of a particle that is directly involved in interactions with surrounding gas molecules

NOTE Active surface area varies with the square of particle diameter when particles are smaller than the gas mean free path, and is proportional to particle diameter for particles very much larger than the gas mean free path.

2.19
surface area, specific
surface area per unit mass of a particle or material

2.20
ultrafine aerosol
aerosol consisting predominantly of ultrafine particles

NOTE The term is often used in the context of particles produced as a by-product of a process (incidental particles), such as welding fume and combustion fume.

2.21
ultrafine particle
particle with a nominal diameter (such as geometric, aerodynamic, mobility, projected-area or otherwise) of 100 nm or less

NOTE The term is often used in the context of particles produced as a by-product of a process (incidental particles), such as welding fume and combustion fume.

3 Symbols and abbreviated terms

AFM	Atomic Force Microscopy
BET	Brunauer, Emmett and Teller method of measuring surface area [33]
CPC	Condensation Particle Counter
DMA	Differential Mobility Analyser
EDX	Energy Dispersive X-ray analysis
EELS	Electron Energy Loss Spectroscopy
ELPI	Electrical Low-Pressure Impactor
ESEM	Environmental Scanning Electron Microscope
FEG-SEM	Field Emission Gun Scanning Electron Microscope
GSD	Geometric Standard Deviation
HEPA	High-Efficiency Particulate Air filter
ICRP	International Commission on Radiological Protection
MMAD	Mass Median Aerodynamic Diameter
NSOM	Near-field Scanning Optical Microscopy
OPC	Optical Particle Counter
SEM	Scanning Electron Microscope
SMPS	Scanning Mobility Particle Sizer, Stepped Mobility Particle Sizer
SPM	Scanning Probe Microscopy
STEM	Scanning Transmission Electron Microscope
STM	Scanning Tunnelling Microscopy
TEM	Transmission Electron Microscope
TEOM®	Tapered Element Oscillating Microbalance[1)]
A_d	minimum acceptable fractional projected area of a particle with diameter d in a microscope field of view (see Annex A)
A_f	area of the field of view in a microscope, in square metres (m^2) (see Annex A)
A_s	effective area of a collection substrate, in square metres (m^2) (see Annex A)

1) TEOM® is an example of a suitable product available commercially. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of this product.

C_d particle number concentration as a function of particle diameter, in number of particles per cubic metre (particles/m^3) (see Annex A)

d particle diameter, in metres (m)

E_d sampling efficiency as a function of particle diameter (see Annex A)

N_d minimum acceptable number of particles with diameter d per field of view in a microscope (see Annex A)

n_s minimum acceptable particle density on a microscope sample, in number of particles per square metre (particles/m^2) (see Annex A)

q sampling flow rate, in cubic metres per second (m^3/s) (see Annex A)

t sampling time, in seconds (s) (see Annex A)

λ wavelength of illuminating light, in metres (m)

4 Background

4.1 Nanoaerosols (including ultrafine aerosols) and potential health effects

Since the late 1980s, toxicological evidence has been emerging indicating that the health effects associated with inhaling nanoaerosols may not be closely associated with particle mass. Early studies with polytetrafluoroethene (PTFE) particles around 20 nm in diameter showed that airborne concentrations of a supposedly inert insoluble material lower than 50 µg/m^3 could be fatal to rats [4][5][34]. Since then, a number of studies have indicated that the toxicity of insoluble materials increases with decreasing particle size on a mass for mass basis. The precise mechanisms by which these materials exhibit higher levels of toxicity at smaller particle sizes have yet to be elucidated, although there are many hypotheses. A number of studies indicate that biological response depends on the surface area of particles deposited in the lungs [8][9][35 to 37]. It has also been suggested that due to their small diameter, nanoparticles are capable of penetrating epithelial cells, entering the bloodstream from the lungs [31][38 to 41], and even translocating to the brain via the olfactory nerves [30]. Health effects associated with such particle activity would be closely associated with particle size, and also possibly particle number. Particles in the nanometre size range have a high percentage of surface atoms, and are known to show unique physico-chemical properties. One would expect particles within this size range to demonstrate biological behaviour closely associated with particle diameter, surface area and surface activity.

Although further research is needed on the physical attributes of nanoaerosols which are most closely associated with potential health risk, it is apparent that measuring exposures against mass alone is not sufficient. Of the three primary physical exposure metrics (mass, surface area and number), there is strong evidence to suggest that occupational nanoaerosols should be monitored with respect to surface area. In this context, aerosol surface area is not well defined. Surface area is dependent on the characterization approach used. Geometric surface area refers to the physical surface of an object, and is dependent on the length scale used in the measurement. Measurement length scale determines the upper size of features that are not detected by the measurement method. For example, methods utilizing molecular surface adsorption have a length scale that approximates to the diameter of the adsorbed molecules [33]. Similarly, biologically relevant surface area will most likely be determined by the smallest biological molecule that interacts with particles within the body.

While a strong case may be made for using aerosol surface area as an exposure metric, it is also necessary to consider characterizing exposures against aerosol mass and number concentration until further information is available. In addition, some studies have shown there may be critical particle sizes influencing the fate and toxicity of respirable particles in the lungs [41][42]. For each of these exposure metrics, but particularly in the case of mass concentration, size-selective sampling will need to be employed to ensure that only particles within the relevant size range are sampled [43].

4.2 Lung deposition of nanoparticles

Lung deposition probability refers to the mean probability for an inhaled particle with a specific diameter to deposit somewhere in respiratory system. Total deposition probability is composed of the sum of probabilities within distinct regions of the respiratory tract. Three major anatomical regions are usually considered:

— the extra-thoracic region, which refers to deposition in the nasal passages, mouth, larynx and pharynx;

— the tracheo-bronchiolar region, consisting of the trachea and bronchi from which deposited particles are cleared by ciliary action;

— the alveolar region, consisting of the respiratory bronchioles, alveolar ducts and alveoli.

These regions have been adopted by the International Commission on Radiological Protection (ICRP) [1] and the UK National Council on Radiation Protection and Measurements (NCRP) [44] in human respiratory tract models used to calculate radiation doses to the respiratory tract of workers resulting from the intake of radionuclides.

The ICRP deposition model [1] characterizes the distribution of inhaled particulate material within the different anatomical regions specific to the age and gender of the subject and various physiological parameters. The deposition model is one of the six elements of the overall human respiratory tract model for radiological protection, together with morphometry, respiratory physiology, radiation biology, clearance and dosimetry.

The sites and magnitude of particle deposition in the human respiratory tract are determined by physical mechanisms, together with respiratory tract morphological and physiological parameters of the subject inhaling the particles.

The five main distinct mechanisms of deposition of inhaled particles are

a) sedimentation, which is due to gravitational force acting on particles,

b) inertial impaction, which characterizes the airborne behaviour of massive particles,

c) interception, which occurs when the edges of a particle contact the surface of the respiratory tract, leading to deposition,

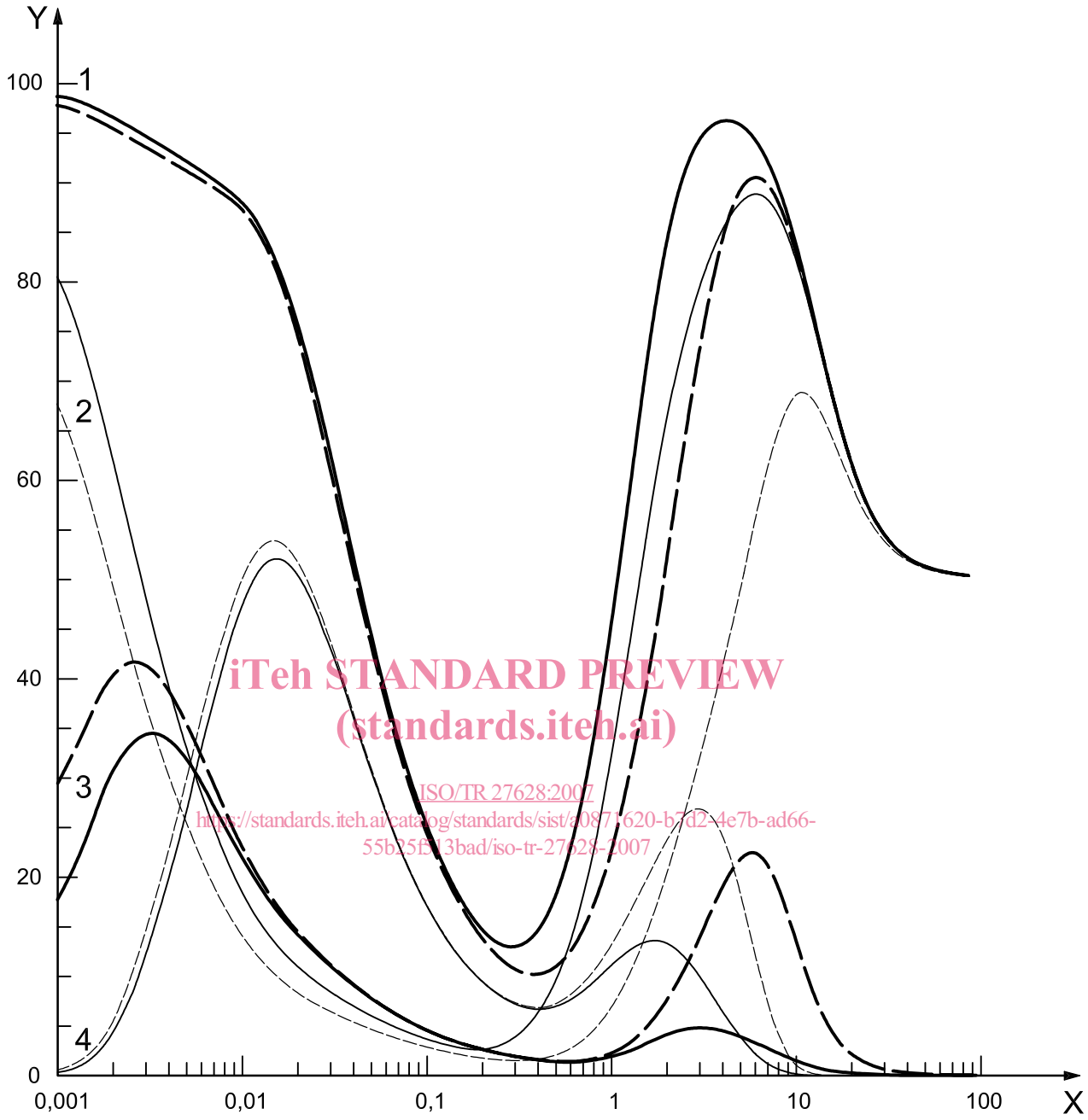
d) diffusion, due to the random (Brownian) motion of small particles, and

e) electrostatic attraction (when particles carry a charge).

In most studies, this last mechanism is neglected, although it could influence deposition if a subject is exposed to highly charged particles. Particle hygroscopicity may also affect deposition through enhancing deposition by impaction and sedimentation.

Respiratory tract morphology and other physiological parameters can vary greatly, depending on the individual as well as on the type of activity undertaken. Several factors may alter the normal structure and function of the respiratory tract, including age, respiratory illness and gender. Predictions of lung deposition probability are generally based on average parameters, and thus may not represent the range of aerosol doses that occur in a diverse population. However, lung dosimetry models do account for some factors contributing to group differences in particle deposition and clearance (e.g. age- and gender-specific anatomical and physiological parameters for particle deposition and modifying factors for conditions, such as pre-existing disease or a smoking habit, that influence particle clearance from the respiratory tract) [1].

Figure 1 shows the total and regional aerosol deposition as a function of particle size between 1 nm and 100 µm using the ICRP model. The curves are for a “reference person” either breathing through the nose or mouth, with 1/3 of the time spent sitting and 2/3 of the time spent undertaking light exercise (a standard workload [1]).



Key

X particle diameter, in micrometres (μm)

Y deposition fraction relative to ambient aerosol concentration, in percent (%)

1 total

2 extra-thoracic

3 tracheo-bronchiolar

4 alveolar

Deposition fraction includes the probability of particles being inhaled (inhalability). The subject is considered to be either a nose breather (solid lines) or a mouth breather (dotted lines) and to be performing standard work [1]. Calculations were made using the LUDEP program [2].

Figure 1 — Predicted total and regional deposition of particles in the human respiratory tract related to particle size