Health-related aerosol measurement: a review of existing sampling criteria and proposals for new ones

James H. Vincent*

Department of Environmental Health Sciences, University of Michigan, Ann Arbor, MI 48109, USA. E-mail: jhv@umich.edu; Tel: (734) 936-0703

Received 6th July 2005, Accepted 8th September 2005
First published as an Advance Article on the web 29th September 2005

Interest in particle size-selective sampling for aerosols in working and ambient living environments began in the early 1900s when it became apparent that the penetration into—and deposition in—the respiratory tract of aerosol-exposed humans of inhaled particles was dependent on particle size. Coarse particles tended to be filtered out during inhalation and in the upper parts of the respiratory tract, so only progressively smaller particles penetrated down to the deep regions of the lung. Over time, following experimental studies with ‘breathing’ mannequins in wind tunnels and with human volunteer subjects in the laboratory, a clear picture has emerged of the physical, physiological and anatomical factors that control the extent to which particles may or may not reach certain parts of the respiratory tract. Such understanding has increasingly been the subject of discussions about aerosol standards, in particular the criteria by which exposure might be defined in relation to given classes of aerosol-related health effect—and in to turn aerosol monitoring. The ultimate goal has been to develop a set of criteria by which exposure standards are scientifically relevant to the health effects in question. This paper reviews the scientific basis for such criteria. It discusses the criteria that have already been widely discussed and so are either being applied or are on the threshold of practical application in standards. It also discusses how new advanced knowledge may allow us to extend the list of particle size-selective criteria to fractions that have not yet been widely discussed but which may be of importance in the future.

Introduction

Aerosols in working and living environments may pose risks to human health if they are inhaled. Environmental standards are developed in order that such risks may be regulated. These require monitoring of aerosol exposures of people in a manner that reflects the nature and magnitude of the risk, taking account of how particles enter the body through nose or mouth during breathing and where in the human respiratory tract they are deposited. This paper reviews what is known about how airborne particles are inhaled, and hence how people are exposed. It then discusses how that knowledge provides a basis for standards, including a review of particle size-selective criteria—or conventions—for the monitoring of aerosol exposures in working and living environments that are currently accepted, and the introduction of some new criteria that might be added to the list in the future.

The human respiratory tract

The route of aerosol exposure that is by far the most important takes place through either the nose or the mouth, or both. For the purpose of this discussion, the human respiratory tract comprises three regions—extrathoracic (including the nasopharynx and mouth in the head), tracheobronchial (including the trachea, main bronchi and bronchi of the conducting airways of the lung) and alveolar (including the bronchioles, alveolar ducts and alveolar sacs). Reviews of the anatomy and physiology of the human respiratory tract as they relate to aerosol inhalation are available from many sources, notably in the 1994 report of the International Commission of Radiological Protection and in the 1999 review by Phalen.

Total lung capacity depends on an individual’s sex, age, weight and height, and varies from about 4 to 6 L. The tidal air volume inspired during each breath is typically about 0.5 L and can be as high as 1 L. A typical adult breathing pattern has a breath rate of from about 7 to 30 breaths per minute, depending on the activity undertaken. It is the nasopharyngeal region that particles first encounter immediately they have been inhaled. Nasally-inhaled particles entering the complex system of nasal passages encounter highly distorted and turbulent flows. Larger particles may be deposited by inertial and gravitational forces, smaller ones mainly by diffusion. Particles deposited in the anterior part of the nasopharyngeal region may be eliminated by external nose blowing and those in the posterior part by the mechanical action of the cilia on the surfaces of the internal passages, by which means they may eventually reach the epiglottis and be swallowed, and so enter the gastrointestinal (GI) system. If they are subsequently absorbed they will remain in the body; otherwise they may be excreted. Particles entering through the mouth meet similarly distorted and turbulence air motions, and are deposited by the same mechanisms. Mouth-inhaled particles deposited in the throat and larynx may be removed directly by expectoration, or may be swallowed and enter the GI system. Particles that are not deposited in the head pass through the larynx and enter the lung. Some may be deposited in the tracheobronchial

James H. Vincent, PhD, DSc, FRSC is Professor and former Chair of Environmental Health Sciences in the School of Public Health at the University of Michigan.

This journal is © The Royal Society of Chemistry 2005

J. Environ. Monit., 2005, 7, 1037-1053 1037
region by inertial and gravitational forces, where some are cleared by the mechanical action of the cilia, by which particles are conveyed back upwards towards the larynx and are eventually swallowed into the GI system. Particles that pass through the tracheobronchial region and arrive in the alveolar region may be deposited there by the influence of gravitational forces and diffusion. Particles deposited in this region are cleared by the action of the scavenging macrophage cells that are present on the alveolar walls. In terms of the fate of deposited particles, it is an important distinction that particles deposited in the conducting airways are cleared relatively quickly and those deposited in the alveolar region relatively slowly. In order to rationalize inter-subject differences, it is useful to define a ‘reference worker’, for which the representative anatomical values shown in Table 1 define a ‘typical person’, taking into account the large amount of anatomical and physiological variability that are present among people of different sizes, genders, state of health, etc.\(^2\)\(^3\)

**Framework for health-related aerosol sampling**

**Standards and criteria.** In general, the framework for conducting practical aerosol sampling should comprise five ingredients; criteria, instrumentation, strategy, analytical methods and—finally—a limit value. A health-related aerosol standard should contain all these ingredients. The concept of exposure is central to this framework, and is defined in terms of the performance required of the sampling or monitoring instrument that will be used, the second the analytical method that will be used to analyze samples. It is the first that is the subject of this paper.

**Indices of exposure.** For the purpose of exposure assessment, and in turn aerosol standards, the intensity of exposure is expressed as the concentration—amount per unit volume of air—of the particulate matter in whatever fraction is of interest. In reality, exposure intensity takes on instantaneous values, and this may be assessed by the use of real-time, direct-reading instruments. But in practice it is usually assessed by aerosol sampling in terms of its time-averaged value, typically over a few hours of sampling duration. Concentration itself may be expressed in terms of one or more indices, including particle number, surface area, volume and mass. Nowadays most limit values that appear in aerosol standards are expressed in terms of the latter, based on the determination of the mass of particulate material collected by a sampling instrument chosen for a given aerosol fraction. However, as discussed below, this approach has shifted over the years, partly driven by the availability of instrumentation and analytical methods and partly by changing knowledge about which is the most appropriate index from a toxicological standpoint.

**The inhalable fraction**

**Experimental data.** Experimental studies to investigate the efficiency with which particles enter the human body during breathing began in Britain and Germany in the late 1970s and continued into the 1990s. They were performed in wind tunnels, generating copious data for the aspiration efficiency of the human head. Since the aerosol and fluid mechanical phenomena which govern inhalability are all external to the human body, these were reliably represented by inert experimental systems in the form of life-size mannequins with simulated breathing through the nose and/or mouth. The experiments involved measuring the concentration of particles upstream of and inhaled by the mannequins.

The earliest such experiments were reported by Ogden and colleagues,\(^4\)\(^5\) Armbruster and Breuer\(^6\) and Vincent and Mark,\(^7\) and later ones by Vincent et al.,\(^8\) and Kennedy and Hinds.\(^9\) Taken as a whole, the data sets represented particle aerodynamic diameter \((d_{\text{ae}})\) up to about 100 \(\mu\)m, windspeeds \((U)\) from about 0.5 to 9 \(\text{ms}^{-1}\), simulated conditions intended to represent the range of those corresponding to people at work, and for both nose and mouth breathing. The results are summarized here in Fig. 1, where the aspiration efficiency of the human head is represented by the shaded area reflecting the overall variability in the experimental results. The results from the individual studies were quite consistent with one another, with the main trend being the one between inhalation efficiency \((\eta_{\text{in}})\) and \(d_{\text{ae}}\). They were not strongly dependent on whether breathing was through the nose or mouth. Closer inspection of the data reveal that the trends were relatively independent of \(U\) up to about 4 \(\text{ms}^{-1}\), but that a strong dependence on \(U\) emerges for the range from about 4 to 9 \(\text{ms}^{-1}\). These trends provided the first hint that a single curve, or a simple set of curves, to represent inhalability might be achievable.

The technical difficulties associated with investigating inhalability at very low windspeeds are great, much to do with achieving uniform test aerosol concentrations over the parts of the wind tunnel test section of interest. Yet we have become increasingly aware that very low windspeeds are very relevant to many aerosol exposure situations, especially indoors in workplaces which have been shown to be characterized by windspeeds mostly lower than 0.5 \(\text{ms}^{-1}\), often much lower.\(^10\)\(^11\) Aitken et al.\(^12\) investigated this regime in ‘calm’ air chambers where the peak local air velocities were no greater than 0.2 \(\text{ms}^{-1}\). Their results, for both mouth and nasal breathing, are summarized here by the shaded area in Fig. 2. Most

---

**Table 1** Values for respiratory anatomical and physiological parameters for defining a ‘reference worker’\(^3\)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>70 kg</td>
</tr>
<tr>
<td>Height</td>
<td>175 cm</td>
</tr>
<tr>
<td>Age</td>
<td>20 to 30 years</td>
</tr>
<tr>
<td>Body surface area</td>
<td>1.8 m²</td>
</tr>
<tr>
<td>Lung weight</td>
<td>1 kg</td>
</tr>
<tr>
<td>Lung surface area</td>
<td>80 m²</td>
</tr>
<tr>
<td>Trachea weight</td>
<td>10 g</td>
</tr>
<tr>
<td>Trachea length</td>
<td>12 cm</td>
</tr>
<tr>
<td>Total lung capacity</td>
<td>5.6 L</td>
</tr>
<tr>
<td>Functional residual capacity</td>
<td>2.2 L</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>4.3 L</td>
</tr>
<tr>
<td>Residual volume</td>
<td>1.3 L</td>
</tr>
<tr>
<td>Respiratory dead space</td>
<td>160 mL</td>
</tr>
<tr>
<td>Breathing rate</td>
<td>15 breaths min(^{-1})</td>
</tr>
<tr>
<td>Tidal volume</td>
<td>1.45 L</td>
</tr>
<tr>
<td>Minute volume</td>
<td>21.75 L</td>
</tr>
<tr>
<td>Inspiratory period</td>
<td>2 s</td>
</tr>
<tr>
<td>Expiratory period</td>
<td>2 s</td>
</tr>
</tbody>
</table>

\(^1\) The diameter of a particle that has the same falling speed under gravity as the particle in question, taking into account not only particle dimensions but also shape and density.
Particle size-selective criteria for the inhalable fraction. The versions of the criteria for the inhalable fraction are shown as curves describing the efficiency of particle inhalation as functions of $d_{ae}$. Such curves are intended for use as ‘yardsticks’ against which the performances of various candidate aerosol sampling instruments may be assessed.

For some types of aerosol, inhaled particles constitute a risk to health, regardless of where they are deposited inside the respiratory tract. This is considered to be the case for all substances that may be carcinogenic, or may be soluble in body fluids so that molecules can enter the bloodstream regardless of where they are actually deposited. For other types of aerosol, inhaled particles may lead to adverse health effects if they are deposited soon after entering the body—in the mouth or nasal passages—even if they do not penetrate any further into the respiratory tract. So, in the first place, inhalable aerosol is a fraction which is an objective for measurement in itself in many occupational and environmental situations. With this in mind, the search for an inhalable aerosol criterion begins with what is known about the aspiration efficiency of the human head.

In the past, recommendations for the health-related sampling of coarse particles in most countries have been based on the concept of ‘total’ aerosol. This concept is intended to relate to all particulate matter that might be considered airborne, and implies that all airborne particles have the same 100% efficiency of inhalation. As seen from Fig. 1 and 2, we now know that this assumption is not supported by the science. Nonetheless, practical sampling instruments for ‘total’ aerosol continue to be sold commercially to this day and are extensively deployed for health-related aerosol sampling in the occupational and environmental hygiene contexts. It follows that ‘total’ is defined in each situation by the particular sampling instrument chosen. With this in mind, the concept of inhalability emerged as a means of unifying aerosol exposure in a scientific manner which is strongly related to how aerosols enter the bodies of people during breathing (and hence to health). The first formal criterion for the inhalable fraction was proposed by the International Standards Organisation (ISO) in its 1983 technical report. However, this was based on only a small subset of the data available at the time. In the years that followed, a more representative empirical function emerged of the form

$$I(d_{ae}) = 0.5 \{1 + \exp(-0.06d_{ae}) \} + f(d_{ae}, U)$$

(1)

where $I(d_{ae})$ is inhalability, equivalent to the aspiration efficiency of the human head. The first group of terms on the right hand side represents a version first proposed in 1985 by the American Conference of Governmental Industrial Hygienists (ACGIH) which sets threshold limit values (TLVs) for a wide range of substances found in workplace environments. Although the ACGIH TLVs are not intended for use in regulatory instruments, but rather as guidelines for professional occupational hygienists in their day-to-day work in protecting workers, they are widely respected—and hence influential—around the world. The second term on the right of eqn (1) takes account of the observed effects at higher windspeeds, noting the potential importance of these to human exposure in some outdoor situations. This term was expressed as an empirical function of $d_{ae}$ and $U$, thus

$$I(d_{ae}, U) \equiv pU^r \exp(qd_{ae})$$

(2)

in which $d_{ae}$ is in μm and the windspeed $U$ is in ms$^{-1}$, with $p = 1 \times 10^{-2}$, $q = 2.75$ and $r = 0.055$ for the range $1 \leq U \leq 9$ ms$^{-1}$. For lower windspeeds ($U < 4$ ms$^{-1}$), eqn (1) reverts back to the original ACGIH curve. The generalized expression described by eqn (1) and (2) was subsequently incorporated into the final 1995 ISO standard (ISO 7708). Meanwhile, the version applying to lower windspeeds was embodied in the criteria adopted for workplaces in 1993 by the Comité Européen de Normalisation. The complete inhalability criterion is shown as a set of continuous curves in Fig. 1.

The above convention is based on the assumption that the air is moving fast enough such that particle motion is governed by the inertial forces, which are proportional to the square of the windspeed. However, with respect to terminology, the original form of expression for the aspiration of the human head was indeed the ‘inhalable’ fraction. But at the time of the publication of the 1983 ISO recommendations, the alternative term ‘inspirable’ was adopted in order to avoid confusion with the use of the term ‘inhalable’ elsewhere, notably in research publications sponsored by the United States EPA for describing the fraction of inhaled aerosol that penetrates deeper into the human respiratory tract. Later, however, after EPA had adopted other terminology in its standards documentation, the international aerosols standards community reverted back to the term ‘inhalable’, and so it remains to this day.

![Fig. 1](image1.png)

**Fig. 1** Aspiration efficiency of the human head as a function of particle aerodynamic diameter ($d_{ae}$) in moving air. The shaded area summarizes the experimental data for windspeeds ($U$) from about 0.5 to 9 ms$^{-1}$ and simulated breathing conditions intended to represent the range of those corresponding to people at work and for both nose and mouth breathing. The continuous curves represent the convention for the inhalable fraction given by eqn (1) and (2).

![Fig. 2](image2.png)

**Fig. 2** Aspiration efficiency of the human head as a function of particle aerodynamic diameter ($d_{ae}$) in nearly-calm air. The shaded area summarizes the experimental data, and the continuous curve represents a proposed convention for the inhalable fraction for calm air as given by eqn (3).
Fig. 3 Schematic diagram of the human respiratory tract, indicating the primary regions of interest, aimed at providing a basis for discussing experimental data for regional deposition of inhaled particles and particle size-selective criteria for aerosol sampling (based on ICRP, 1994).^4

entirely by inertial forces. But at very low wind speeds and in calm air, the motion of particles under the influence of gravity becomes very important. The mannequin studies in nearly calm air showed clearly that the aspiration efficiency of the human head differs markedly from eqn (1). Based on their experimental results, Aitken et al.^5 suggested an alternative convention of the form

$$d_{50} = 1 - 0.0038d_{50}$$

for the inhaleable fraction in very slowly-moving air. This is a plausible suggestion, supported by the earlier experimental study for such conditions reported by Ogden et al.^6 It is shown as a continuous curve in Fig. 2.

In the fractions defined by eqn (1) and (3) it is relevant to mention again the index of exposure. In the first report of ACGH^4 the inhaleable fraction was referred to as ‘IPM’, or the ‘inhaleable particulate mass’ fraction. However it is important to note that the inhalation fractions as defined above are completely independent of any chosen index of exposure. Rather it is expressed as a dimensionless function of particle size alone, and so may be applied to any index of exposure. The same is true for all the other fractions described below.

Regional deposition of inhaled aerosols

**Framework.** The deposition of inhaled particles in the human respiratory tract is more complex, involving successive stages where one set of physical fluid and aerosol mechanical processes gives way to another, always linked with anatomical and physiological parameters. In its 1994 report, the ICRP^7 described a morphological model in which the dose of inhaled radioactive particles to relevant regions of the respiratory tract was presented, allowing for whether breathing takes place through the nose or mouth, and for particle deposition during both the inhalation and exhalation phases of the breathing cycle. The simplified version in Fig. 3 shows that both inspiration and expiration are partitioned between nose and mouth breathing, not necessarily in the same proportions. For nose breathing, there are two nasal extrathoracic regions, the anterior and the posterior nasal passages (ET1 and ET2, respectively). Particles inhaled through the nose large enough for their motions to be dominated by inertial and gravitational forces tend to deposit primarily towards the rear of ET1. For mouth breathing, particles deposited in the extrathoracic head region (ET3) are collected primarily by impaction in the larynx. As extrathoracic deposition differs between nose and mouth breathing, in turn so too does penetration below the larynx and into the lung. Particles entering the tracheobronchial (TB) region are deposited mainly by inertial forces. The smaller ones penetrating down to the alveolar (Alv) region are deposited there mainly by gravitational forces and by diffusion. Particles not deposited during inspiration may then be deposited in the tracheobronchial and extrathoracic regions during expiration. Those not be deposited will be exhaled.

In the simplified ICRP system (see Fig. 3), we first note that the aspiration efficiency of the human head is given by

$$I = \frac{N_{in}}{N_0}$$

where $N_{in}$ represents particle flux that is inhaled and $N_0$ is that initially in the volume of air inhaled. For inhaled particles, the efficiency with which particles are deposited in the extrathoracic (including both nasopharyngeal and mouth) region during inspiration is given by

$$D_{ETin} = \frac{N_{ETin}}{N_{in}} = E_{ETin}$$

where $D_{ETin}$ is the flux of particles to nasal and mouth surfaces inside the extrathoracic region and $N_{ETin}$ is the flux of particles that progress further and so enter the lung below the larynx, both during the inspiration part of the breathing cycle. The local efficiency with which these particles are deposited in the tracheobronchial region is

$$D_{TBin} = \frac{N_{TBin}}{N_{ETin}} = E_{TBin}$$

where $D_{TBin}$ is the flux of particles to the surfaces of the tracheobronchial region and $N_{TBin}$ is the flux of particles that progress further and so enter the alveolar region. The efficiency of deposition for the tracheobronchial region as a fraction of what was inhaled initially is

$$D_{TBin} = \frac{N_{TBin}}{N_{in}} = \frac{N_{TBin} - N_{alvin}}{N_{in}} = (1 - E_{ETin})E_{TBin}$$

using eqn (5) and (6), where the star in the last term indicates that this deposition efficiency is now given with respect to the aerosol that is inhaled initially. This now involves the effective filtration efficiencies of both the extrathoracic and the tracheobronchial regions.

Next, if $D_{alv}$ is the flux of particles to the surfaces of the alveolar region, the local efficiency of deposition there is

$$D_{alv} = \frac{N_{alv}}{N_{alvin}} = E_{alv}$$

where $N_{alv}$ is the flux of particles that have reached the alveolar region, remain airborne and so leave during the exhalation part of the breathing cycle. In turn, alveolar region deposition as a fraction of the inhaled aerosol is

$$D_{alv} = \frac{(1 - E_{ETin})(1 - E_{TBin})E_{alv}}{N_{in}}$$
using eqn (5)–(8). Now we must consider the deposition of still-airborne particles during exhalation. Based on Fig. 3, the regions encountered by the particles still airborne are considered to be additional segments in the sequence of filters already considered. It follows therefore that

\[
{\frac{D_{T_{\text{Bout}}}}{N_{\text{inh}}} = (1 - E_{ET_{\text{in}}})(1 - E_{TB_{\text{in}}})(1 - E_{d_{\text{alv}}}E_{T_{\text{Bout}}})}
\]  

(10)

and

\[
{\frac{D_{ET_{\text{out}}}}{N_{\text{inh}}} = (1 - E_{ET_{\text{in}}})(1 - E_{TB_{\text{in}}})(1 - E_{TB_{\text{out}}}E_{ET_{\text{out}}})}
\]  

(11)

In these, it is a fair approximation that \(E_{ET_{\text{in}}} = E_{ET_{\text{out}}}\) and \(E_{TB_{\text{in}}} = E_{TB_{\text{out}}}\). However, when these equations are folded into numerical calculations of regional deposition efficiency (see below), it is found that the contributions due to particle deposition during expiration are relatively small and so may be neglected for present purposes. With this in mind, the efficiency of total respiratory tract deposition is given by

\[
E_{\text{total}} = \frac{D_{ET} + D_{TB} + D_{d_{\text{alv}}}}{N_{\text{inh}}} = E_{ET} + (1 - E_{ET})E_{TB} + (1 - E_{ET})(1 - E_{TB})E_{d_{\text{alv}}}
\]  

(12)

The preceding equations provide a set of relationships that connect the fluxes of particles penetrating to and depositing in the various parts of the respiratory tract. They provide a basis for designing experiments to investigate regional lung deposition as well as for defining criteria for aerosol fractions that might relate to specific types of health effect.

In much of what follows, attention will be focused on the range of conditions for which particle motion is governed primarily by aerodynamic effects, and hence depends of aerodynamic diameter. This features in most criteria for the aerosol fractions of health-related interest (see below). The behavior of smaller particles where their motion is dominated by diffusion, and hence where the more relevant metric of particle size is the equivalent volume diameter \(d_{\text{eq}}\), will be treated separately.

In its earlier report in 1966, the Task Group on Lung Dynamics of ICRP used the (then) available experimental data on aerosol inhalation and regional deposition to create a set of physiologically-based empirical models, providing a framework for calculating deposition, and in turn dose, of radioactive aerosols to all parts of the human respiratory tract.\(^{19}\) This was revised in the later ICRP report in 1994, taking into account the large body of new research that had been conducted during the intervening years. The James et al.\(^{17}\) paper in the 1994 report describes the development of a comprehensive system of models for regional aerosol deposition. This provides an important contemporary basis for discussing the experimental data from regional deposition studies and, in turn, for extending the current framework of particle size-selective aerosol exposure criteria.

**Experimental data and models.** Inhalation experiments with human volunteer subjects began in the 1950s with the pioneering work of Hatch and Gross\(^ {20}\) and was continued by many others. In all of them, human subjects were asked to inhale monodisperse spherical test aerosols of a non-toxic material (e.g., polystyrene latex) and known particle size under controlled breathing conditions. In most of them, inhalation was achieved through a tube inserted into the mouth of the subject, whose nose was clamped in order to avoid additional air entering or leaving through that portal. Some experiments were designed specifically to investigate inhalation through the nose.

In one experimental design, the concentration of aerosols delivered from a continuous, well-defined source and entering during the inspiration part of the breathing cycle was measured, along with the concentration of particles exiting during exhalation. This was often achieved by using light scattering apparatus to count individual particles in the air close to the mouth during each part of the breathing cycle. In this way, the efficiency of total aerosol deposition \(E_{\text{total}}\) was obtained in real-time for each particle size tested. In an extension of this approach, the aerosol supply was delivered to the inspired air as a bolus, in the form of a short pulse of test aerosol injected at a specific, pre-determined part of the breathing cycle. The concentration of particles in the exhaled air now took the form of a time-varying trace of concentration as a function of time that reflected the fate of the particles in the original bolus. By interpretation of the bolus, it was possible to obtain the efficiency of aerosol deposition in various regions of the respiratory tract. Another experimental approach that has been widely applied involves the use of radioactive labeled test aerosols that could be detected in the respiratory tract using the methods derived from applied nuclear physics. For example, if the label was a gamma emitter, the particles deposited in the respiratory tract could be measured non-invasively by means of gamma camera techniques. By observing the clearance of particles from the respiratory tract over time, the results could be partitioned in order to obtain the deposition in the various parts of the respiratory tract characterized by faster or slower clearance mechanisms. An important feature of the results of such experiments was that, because they involved studies with real people, they reflected the large biological variability between individuals.

**Extrathoracic deposition:** Experimental results for deposition in the head \(E_{ET}\) have been published by Hounam et al.\(^ {21}\), Lippmann\(^ {22}\) and Heyder and Rudolph\(^ {23}\) and others for nasal deposition in ET1 and ET2 following nasal breathing, and Lippmann,\(^ {24}\) Stahlhofen et al.\(^ {26}\) and Chan and Lippman\(^ {25}\) for mouth deposition in ET3 following mouth breathing. James et al.\(^ {27}\) used these data to model extrathoracic deposition in terms of \(d_{\text{eq}}\), the tidal volume \(V_T\), and the breathing flowrate \(Q\) (the tidal volume divided by the inspiratory period, with the latter approximately equal—depending on breathing pattern—to half the time period of a complete breathing cycle). As mentioned earlier, deposition of larger particles during nasal breathing takes place mainly towards the rear of the anterior part (ET1). During mouth breathing it takes place mainly in the larynx part of ET3. James et al. proposed (after Rudolph et al., Stahlhofen et al. and Rudolph et al.\(^ {26–28}\)) that

\[
E_{ET} \approx E_{ET1} = 1 - \left( \frac{1}{1 + 0.005d_{eq}^2/Q} \right)
\]  

(13)

for nose breathing and deposition primarily in ET1, together with

\[
E_{ET} = E_{ET1} = 1 - \left( \frac{1}{1 + 0.00017(d_{eq}^2Q^{0.6}V_T^{0.2})^{1.4}} \right)
\]  

(14)

for mouth breathing and deposition in ET3.\(^ {8}\) In these expressions and all the others that follow, \(d_{eq}\) is given in \(\mu\text{m}\), \(Q\) in \(\text{L min}^{-1}\) and \(V_T\) in \(\text{L}\). Guided by eqn (13) and (14), the experimental data for \(E_{ET1}\) and \(E_{ET3}\), respectively are summarized as shaded areas in Fig. 4a as a function of \(d_{eq}^2Q\) and in

\(\text{Fig. Environ. Monit., 2005, 7, 1037–1053}\)
Fig. 4 Efficiency of extrathoracic deposition (ET_{ET}): (a) for nasal deposition (mainly in the anterior region) following nose breathing, and (b) head deposition (mainly in the larynx) following mouth breathing. The data are plotted as functions of combinations of variables suggested by James et al. The shaded areas represent the experimental data and the continuous curves are calculated from the models proposed by James et al.

Fig. 5 Efficiency of tracheobronchial deposition: (a) shown as intrinsic efficiency (ET_{TB}); and (b) efficiency relative to what was inhaled (ET*). The shaded area in (a) summarizes the experimental data, and the continuous lines in both (a) and (b) are calculated from the models of James et al.

The model for ET_{TB} may be combined with those for ET_{ET} to calculate the efficiency of the deposition in the conducting airways region as a proportion of what was inhaled, ET_{TB}*. This was achieved using eqn (7) along with eqn (15) and eqn (13) or (14). The results are shown for both nose and mouth deposition in Fig. 5b. Here because the models for ET_{ET} for nose and mouth breathing take different functional forms, the results are expressed in the form of ET_{TB}* versus d_{ae} for a ‘reference worker’ for which Q = 43.5 L min^{-1} and V_T = 1.5 L (see Table 1). The difference in deposition for nose and mouth breathing is now clearly seen, most notably the much higher deposition for mouth breathing. Also shown is the peak in tracheobronchial deposition for d_{ae} between 5 and 10 µm.

Alveolar deposition: Experiment results for aerosol deposition in the alveolar region have been reported by Altshuler, et al., George and Breslin, Lippmann, Lippmann, Chan and Lippmann, Stahlhoven et al. and others, all for mouth breathing. This time the efficiency of deposition in the alveolar region was presented directly as a fraction of the aerosol originally inhaled, E_{alv}*. The results are summarized as the shaded area in Fig. 6, with E_{alv}* shown as a function of d_{ae} down to about 1 µm. As particle size increases, E_{alv}* rises, reaching a peak at around 0.5 for d_{ae} around 3 µm. But then, for large particles still, E_{alv}* falls back down again, reaching zero at around d_{ae} = 10 µm. This reflects the fact that all particles larger than this were deposited in the higher regions of the respiratory tract and so were not available to the alveolar region. Again, James et al. inspected the available experimental data and developed the expression

\[ E_{alv} = 1 - \exp(-0.146 (d_{ae}^{0.65})) \]  

for the intrinsic deposition efficiency of the alveolar region, where t_{alv} is the residence time for particles in the alveolar region, estimated as

\[ t_{alv} \approx \frac{60 VT}{Q} \]
where $t_{inh}$ is expressed in s and—as before—$V_T$ and $Q$ are expressed in L and L min$^{-1}$ respectively. In the complete version of the model as described by James et al., $t_{inh}$ contains terms that account for dead spaces in different parts of the lung during the breathing cycle. But, for present purposes, these are neglected. Eqn (16) may be combined with eqn (9), involving the individual modeled filtration efficiencies of the extrathoracic and tracheobronchial regions ($E_{ET}$ and $E_{TB}$, respectively), in order to calculate $E_{total}$. This was carried out for mouth breathing by for the ‘reference worker’, and the results are shown as the smooth curve in Fig. 6.

Deposition of very fine aerosols: Specific concerns about very fine aerosol fractions are more recent that those about the other fractions that are discussed above. Part of the concern stems from the fact that particles in the size range well below 0.1 μm (100 nm) may penetrate readily into the body beyond the initial site of deposition, even if they are of intrinsically insoluble material. Studies of the total deposition of inhaled particles in this size range have been reported by Tu and Knutson, Heyder et al., and Schiller et al., for particles with equivalent volume diameter ($d_v$) down to as low as 5 nm, for nose and mouth breathing and a range of breathing conditions. The results for $E_{total}$ as a function of $d_v$ are summarized as the shaded area in Fig. 7a for the range of $d_v$ above 0.01 μm. The results show that $E_{total}$ rises steeply as the particles decrease in size, reaching close to unity for $d_v = 0.01$ μm. There are only slight differences between nasal and mouth breathing and for the different breathing flowrates investigated.

In view of the current elevated interest in possible health effects associated with inhaling ultrafine particles, the studies cited take on special importance. In the first instance, the high efficiency of total respiratory tract deposition is important. But regional deposition is especially important, and James et al. also developed a set of corresponding equations for fine particles whose motions are governed by diffusion, thus

$$E_{ET} = 1 - \exp[-1270 \, (D_b Q^{-0.25} t_{inh}^{0.500})]$$
for nasal deposition, region ET

$$E_{ET} = 1 - \exp[-1460 \, (D_b Q^{-0.25} t_{inh}^{0.535})]$$
for nasal deposition, region ET

$$E_{ET} = 1 - (1 - E_{alv})(1 - E_{ET})$$
for nasal deposition, regions ET, ET and ET

for head deposition, region ET

$$E_{TB} = 1 - \exp[-7930 \, (D_b t_{inh}^{0.639})]$$
for tracheobronchial deposition

$$D_v = 1 - \exp[-75260 \, (D_b t_{inh}^{0.610})]$$
for alveolar region deposition

In these equations, $D_b$ is the coefficient of Brownian diffusion in m$^2$ s$^{-1}$, given by

$$D_b = \frac{k_b T}{5 \pi \eta V} C(d_v)$$

where $T$ is the air temperature (in K), $k_b$ is Boltzmann’s constant (=1.23 \times 10^{10}$ J K$^{-1}$), and $C(d_v)$ is the Cunningham slip correction factor that allows for particle motion as it moves between discrete collisions with gas molecules. In the above equations, $t_{inh}$ is the residence time of particles in the tracheobronchial region, estimated to be about 20 ms, and $t_{inh}$ is the residence time of particles in the alveolar region given by eqn (17).

Using the set of eqn (18) together with the earlier eqn (12), $E_{total}$ may be calculated for both nose and mouth breathing. The results are shown in Fig. 7a alongside the experimental data, presented as continuous and dashed curves for nose and mouth respectively. It is seen that the $E_{total}$ for nose breathing is slightly greater than for mouth breathing. But the difference is very small. The various regional deposition efficiencies for ultrafine particles calculated from the James et al. models are plotted in Fig. 7b. They are broadly consistent with the available experimental data. They show some important trends. Firstly, the deposition of ultrafine particles in all regions increases as the particles become smaller. The efficiency of deposition in the nasal passages during nose breathing is greater than in the head during mouth breathing. For the
tracheobronchial region, it is generally very small. The efficiency of deposition in the alveolar region is the greatest.

Deposition of fibres: Interest in fibres as a subject for aerosol sampling began many years ago with the emergence of awareness about asbestos exposure as a significant risk to health. However there appear to be no direct experimental data on regional deposition of fibrous particles in the human respiratory tract for fibres. But this is not surprising since the geometry and dimensions of fibres—asbestos or otherwise—raise serious concerns about the risk associated with any exposure, no matter how small, even under controlled clinical research conditions. Although experimental data do exist for deposition in the alveolar regions of rat lungs, the link with human exposure is tenuous without human data. The best approach for discussing the regional discussion of fibres lies in the availability of large amounts of human data for non-fibrous particles. One of the links is the set of equations for the particle aerodynamic diameter of fibres developed by Cox and Stöber. For fibres in the range where the equivalent value of \( d_{eq} \) is greater than about 0.5 \( \mu \text{m} \), it may be assumed that inertia and/or gravity are predominant influences on deposition in the confined spaces of the respiratory tract. Here, therefore, the available experimental data for deposition in the extrathoracic, conducting airways and alveolar regions can be reasonably translated to fibres from the results for non-fibrous aerosols. However, for fibres where the calculated \( d_{eq} \) is less than 0.1 \( \mu \text{m} \), where it must be assumed that diffusion becomes the primary mechanism for deposition, the most appropriate metric for particle diameter for the purpose of translating the experimental data for non-fibrous particles to fibrous ones will be a function of fibre length and width, \( l_f \) and \( d_f \), respectively. Gentry and coworkers showed the relationship between diffusion coefficient (\( D_p \)) and fibre dimensions to be a complex one. But their results suggested that a fair, appropriate metric for translating regional respiratory tract deposition from the results for spherical particles to fibres in the diffusion regime is the fibre width (\( d_f \)).

Criteria for particle size-selective sampling for inhaled aerosol subfractions

Data and models for the regional penetration of inhaled particles into and deposition in the regions of the respiratory tract provide a basis for criteria for health-related particle size fractions that can be used in aerosol standards and provide guidelines for scientifically-rational, health-related aerosol sampling. Most of the criteria that will be presented later are shown as curves describing the probability of particle penetration or deposition as functions of particle size. Such curves become the ‘yardsticks’ against which the performances of aerosol sampling instruments must be compared when used in the context of health-related standards.

Historical overview. As early as 1913, McCrea noted from his microscope studies of the lungs post-mortem of South African minersworkers that particles in the alveoli of the deep lung did not exceed about 7 \( \mu \text{m} \) in physical diameter, and so identified the need to selectively measure fine particles as an appropriate index of exposure for coalworkers’ pneumoconiosis. This appears to be the first reference to what is now referred to as a ‘particle size-selective’ sampling criterion. Later this was confirmed by the earliest inhalation experiments with human volunteer subjects. The idea of the criteria based on the visual discrimination of particles by virtue of their physical dimensions was used for many years as the basis of standards. For example, in the extraction industries of Canada, Australia and South Africa, a criterion was applied that required the counting of particles which, when viewed under the microscope at appropriate magnification, were less than 5 \( \mu \text{m} \) in diameter. This approach was accompanied by occupational exposure limits that expressed aerosol concentrations in terms of particle number per unit volume of air sampled. It persisted in some areas until as late as the 1980s.

However, from the late 1950s onwards, the concept of aerodynamic particle size selection emerged. A number of quantitative definitions for the aerodynamically-defined fine ‘respirable’ fraction followed. In 1952, the British Medical Research Council (BMRC) recommended definition of airborne dust relevant to pneumoconiosis in terms of a curve describing the penetration of particles to the alveolar region as a function of \( d_{eq} \) and the use of particulate mass as the most appropriate index of aerosol concentration. Later, during the 1959 International Pneumoconiosis Conference in Johannes-Burg, this was endorsed by the international occupational hygiene community and thereafter became widely known as the ‘Johannesburg curve’. At about the same time, in the United States, the Atomic Energy Commission (AEC) proposed its own definition for respirable aerosol. Then the ICRP Task Group on Lung Dynamics proposed a model for alveolar deposition in typical subjects under typical breathing conditions, from which ACGIH defined its first version of respirable aerosol, very similar to the AEC version. In the years that followed, all three definitions for respirable aerosol were cornerstones of aerosol health related research and standards setting throughout the world.

The form of these definitions for respirable aerosol embodied an important philosophy that has persisted today in the development of aerosol sampling criteria. It was acknowledged early on that any such criterion did not provide a direct measure of actual deposited dose, but that it represented a possible worst-case exposure scenario, so that its application in standards would be conservative in the protection of workers. As will be seen below, criteria for other aerosol fractions have also subsequently been developed with this same philosophy in mind. In the modern era, however, attention is beginning to be drawn towards possible criteria that are based on actual deposition and hence are more directly relevant to dose, and these two will be discussed later.

In the early 1980s, a new approach emerged in which three aerosol fractions were defined, reflecting coarse particles (the inhalable fraction, representing aerosol that passes through the nose and/or mouth during breathing), intermediate-sized particles (the thoracic fraction, representing inhalation of the dust that penetrates past the larynx and into the lung) and fine particles (the respirable fraction, representing inhaled aerosol that penetrates down to the alveolar region of the lung). It was felt that defining these fractions would provide opportunities to sample particles relevant to the majority of aerosol-related health effects. The International Standards Organisation and ACGIH initially led the way in this effort, and represented a substantial widening of the scope of particle size-selective criteria for aerosol sampling in relation to health. Many other standards-setting bodies have since followed their lead. In this emerging new framework, the new ingredients were the coarser inhalable and intermediate thoracic fractions. Development of the inhalable fraction represented a rationalization of the old ‘total’ aerosol approach, as discussed earlier. Prior to the 1980s there was little discussion about an intermediate fraction. There was just one notable exception. In the 1970s, the US National Institute for Occupational Safety and Health proposed a criterion for the sampling of cotton dust in relation to the occupational disease of byssinosis, an airways disease prevalent among cotton mill workers. It is noted that, reflecting the discussion in the previous paragraph, these criteria are expressed in terms of aerosol penetration.

In the late 1970s interest was stirring in a standard that reflected concerns about particles in the ambient atmospheric environment associated with a wide range of respiratory tract illnesses in the general population. So in 1984 the US Environmental Protection Agency (EPA) proposed a definition for...
thoracic aerosol that subsequently became widely known as the ‘PM$_{10}$’ standard. In its 1983 report, ISO adopted a similar philosophy. In the ISO definition, however, unlike for PM$_{10}$, it was explicitly stated that the thoracic fraction was a sub-fraction of the inhalable fraction. In addition, for the finer respirable fraction, ISO recommended the optional use of the BMRC or ACGIH criteria for the respirable fraction like those already described, providing continuity between the new and the older criteria, and hence (hopefully) smoothing the path towards their implementation in actual standards.

In the late 1990s it emerged that most of the health effects attributable to aerosols in the ambient atmospheric environment were more closely associated with a fine particle fraction within PM$_{10}$, more specifically the accumulation mode comprising particles that have origins which are very distinctive from those of the coarse mode that make up the bulk of aerosol concentrations usually contained in the PM$_{10}$ fraction. In particular, particles in the range of $d_{ae}$ below about 2.5 $\mu$m are derived in large measure from combustion processes. Out of this EPA proposed a new, fine-aerosol fraction that became known as the ‘PM$_{2.5}$’ fraction. It is important to note that unlike the other criteria described in this paper, PM$_{2.5}$ is unique in that it does not relate to the particle size dependency of how particles are deposited within the respiratory tract. Rather it relates to the source-related properties of atmospheric aerosol, notably in terms of composition.

**Existing penetration-based criteria for the thoracic, respirable and fine aerosol fractions.** The criteria for the inhalable, thoracic and respirable fractions continued to evolve during the 1980s and 1990s, and important milestones were the 1993 EH481 standard of the Comité Européen de Normalisation (CEN) and the 1995 ISO 7708 standard of the International Standards Organisation (ISO). In 1999 the ACGIH Air Sampling Procedures Committee carried out a full review and summarized the recommendations as well as identifying measurement options. From these bodies, a unified definition emerged for the thoracic fraction, $T(d_{ae})$, in the form of a curve that follows

$$T(d_{ae}) = R(d_{ae})(1 - F(x))$$

where $R(d_{ae})$ is as defined in the inhalation convention expressed in eqn (1), and $F(x)$, is the cumulative probability function of a standardized normal variable ($x$) given by

$$x = \frac{\ln(\frac{d_{ae}}{\mu m})}{\Sigma_x}$$

in which $\Gamma_x = 11.64$ $\mu$m and $\Sigma_x = 1.50$. The result is that the function $T(d_{ae})$ reaches 0.5 at $d_{ae} = 10$ $\mu$m. The application of eqn (20) and (21) in practical situations, and others like it for other particle size fractions (e.g., in assessing the dose associated with inhaling aerosols of a given particle size distribution), involves integrations of an unwieldy mathematical expression. With this in mind, a simpler mathematical relationship is available that provides almost identical results. This is described in the Appendix.

The finer respirable fraction, $R(d_{ae})$ is now defined by a curve that follows

$$R(d_{ae}) = R(d_{ae})(1 - F(x))$$

where $F(x)$ is again the cumulative probability function of a standardized normal variable ($x$) but now with $\Gamma_x = 4.25$ $\mu$m and $\Sigma_x = 1.50$. The net result is that $R(d_{ae})$ reaches 0.5 at $d_{ae} = 4.0$ $\mu$m. A significant difference from the equivalent definition in the original 1985 ACGIH report is the increase in the value of $d_{ae}$ for $R(d_{ae}) = 0.5$ from 3.5 $\mu$m to 4.0 $\mu$m. It differs from the old BMRC (or ‘Johannesburg’) definition not only in that there is now, theoretically, no particle size where penetration falls to zero, but that the value of $d_{ae}$ for $R(d_{ae}) = 0.5$ has fallen from 5.0 $\mu$m to 4.0 $\mu$m.

By now the ACGIH criteria have become conceptually and mathematically consistent with the latest ones proposed by the International Standards Organisation, but with two important exceptions. Firstly, ISO explicitly retained the windspeed dependency for the inhalable fraction, as given earlier in eqn (1), in recognition of its possible application in outdoor aerosol exposure situations. Secondly, ISO proposed an alternative definition for the respirable fraction, acknowledging the importance of a vulnerable target population, including children sick and infirm people. Again, this reflects the scope of the ISO criteria beyond occupational exposures and to the population at large. For this target population, ISO defined the respirable fraction as in eqn (25) but with $\Gamma_x = 2.5$ $\mu$m and $\Sigma_x = 1.50$. As already mentioned, the criteria as stated in the above equations are also consistent with those proposed earlier by the CEN. During their evolution over many years, a considerable—and highly welcome—degree of international harmonization has therefore been achieved. The harmonized thoracic and respirable fractions, as defined according to the primary criteria described above, are shown as continuous curves in Fig. 8. In the figure, the thoracic and respirable fractions are shown as sub-fractions of the inhalable fraction. So, for the purpose of a sampling instrument, they represent the full performance that is required from the inlet down, hence including both aspiration efficiency and subsequent particle selection inside the instrument.

In the United States, EPA has continued to promulgate its PM$_{10}$ criterion for particulate matter in the ambient atmospheric environment within its National Ambient Air Quality Standards (NAAQS), based on a similar rationale to that for the ISO thoracic convention. In the 1996 EPA criteria document it was stated that, considering—among other things—the similar convention on particles penetrating the thoracic region adopted by ISO, ‘... EPA staff recommended that the size-specific indicate include particles of diameter less or equal to a nominal 10 $\mu$m ‘cut point’ generally referred to as ‘PM$_{10}$’. In terms of collection efficiency, this represents a 50% cut point, the aerodynamic particle diameter for which particle collection is 50%. With such a cut point, larger particles are not excluded entirely but are collected with substantially decreasing efficiency, and smaller particles are collected with increasing (up to 100%) efficiency.’ In a subsequent EPA staff paper it was noted more explicitly that PM$_{10}$ ‘...is an indicator for thoracic particles (i.e., particles that penetrate to the tracheobronchial and the gas-exchange regions of the lung)’. The curve defined by EPA for PM$_{10}$ appears in the 1996 criteria document and is shown here alongside the other fractions in Fig. 8.
When it emerged during the 1990s that some health effects associated with exposure to atmospheric aerosols were markedly linked with a fraction finer than PM10, more specifically the accumulation mode, a new fine-aerosol fraction was proposed for use in extended EPA NAAQS. With this in mind, and cognizant of the nature of the particle distribution properties of atmospheric aerosol, EPA recommended a PM2.5 criterion in which

\[ PM_{2.5}(d_{ae}) = 1 - F(x) \]  

(23)

where \( F(x) \) is same cumulative probability function of a standardized normal variable \( x \) as defined earlier in which \( \Gamma_x = 2.5 \mu m \) and \( \Sigma_x = 1.50 \). Here, the choice of the relatively small geometric standard deviation arose out of discussions about the need for a sharp cut in order to prevent the unwanted intrusion of coarse mode particles into PM2.5. This criterion for PM2.5 is shown in Fig. 8, together with the inhalable \( (I) \), thoracic \( (T) \), PM10 and respirable \( (R) \) fractions.

Proposed new deposition-based aerosol fractions

Extrathoracic aerosol. Of the various standards-setting bodies, neither ISO, ACGIH, CEN nor EPA have yet proposed criteria—or developed standards—for an extrathoracic fraction. So, if a new criterion is to be proposed, it is necessary to first identify a need. ICRP has already acknowledged the importance of extrathoracic deposition in relation to dosimetry associated with inhaled radioactive aerosols. More generally, however, it is reasonable to argue that deposition in the head during mouth breathing is not of great interest since most particles deposited in this way, mainly in the larynx, are rapidly ingested. So, for the purpose of aerosol sampling criteria, such particles are already covered by the inhalable fraction. On the other hand, there are some exposure situations where nasal deposition of particles may be of significant specific interest. For example, there are some well-documented relationships between aerosol exposure and a range of nasal health effects, most particularly nasal cancers associated with the inhalation of some radioactive aerosols. For aerosol sampling to be carried out in relation to aerosol exposure assessment specifically in relation to such diseases, there is a clear need for a particle size-based sampling criterion that goes beyond the aerosol fractions that are currently defined. We therefore seek a nasal deposition fraction, say \( N(d_{ae}) \).

It is not acceptable to develop a curve for \( N(d_{ae}) \) simply by subtracting the conventionalized thoracic fraction from what was inhaled. This is because, in developing the thoracic convention, a conservative, worst-case rationale was used that involves (among other things) mouth breathing. Instead, therefore, it is necessary to go back to the original nasal deposition data, and this is most plausibly achieved by reference to the empirical models of James et al. In particular it is noted again that the deposition of particles large enough for their motion to be governed by inertial forces is confined mainly to the rear of the anterior region of the nasal passages identified earlier as ET1, for which the efficiency of particle deposition is given by the earlier eqn (13). This is an appropriate starting point for the development of \( N(d_{ae}) \), noting that the nasal deposition of very small particles will need to be treated separately.

The problem is now complicated by the fact that, for most people, inspiration is ‘partitioned’ between nose and mouth breathing. It will be mostly through the nose for low levels of activity (lower \( Q \)) but mostly through the mouth for higher levels of activity (higher \( Q \)). It is at lower levels of activity, therefore, where the greatest exposure of the nasal passages occurs. With this in mind, the discussion is focused on relatively light activity. Calculated results using eqn (13) for the efficiency of nasal deposition (\( E_{ET1} \)) as a function of \( d_{ae} \) and for relatively low \( Q \) values of 10, 20 and 30 L min\(^{-1}\) (corresponding to minute volumes 5, 10 and 15 L) respectively are shown in Fig. 9. The calculated curves reveal that \( E_{ET1} \) does not vary excessively over the range of \( Q \) indicated. So there is encouragement to seek a single function that may serve as a criterion for sampling. One possibility, expressed in the same form as for the other criteria recommended by ACGIH, CEN and ISO, is

\[ N(d_{ae}) = I(d_{ae})F(x) \]  

(24)

where \( F(x) \) is the cumulative probability function of a standardized normal variable \( x \) in the same way as described above for the thoracic and respirable fractions, but now with \( \Gamma_x = 4.0 \mu m \) and \( \Sigma_x = 2.00 \). As before, the choice of this form of expression is arbitrary. The term \( I(d_{ae})F(x) \) corresponds to the efficiency of extrathoracic deposition, and it is shown in Fig. 9 alongside the curves for the three \( Q \)-values calculated from the James et al. model.

The difficulty with writing this—or any similar expression—as a criterion for a formal health-based standard is that it is rarely possible to assume that inhalation takes place exclusively through the nose. This complication cannot readily be accommodated by means of a mathematical adjustment within a simple criterion like the one shown. But it may be possible to account for it in its practical application. For example, in a specific sampling situation with respect to such a standard, it might be possible to weigh measured concentrations by the application of a ‘partition factor’, a number between 0 and 1, which would need to be decided on the basis of the expert opinion of the professional hygienist conducting the sampling survey.

Tracheobronchial and alveolar aerosol. The criteria for the thoracic and respirable fractions discussed earlier are based on the penetration of particles to the lung and the alveolar region, respectively. They do not refer to what is actually deposited, and so do not strictly relate to the health-related dose. For most applications in standards, especially for the majority where there is a wide range of particle sizes, the thoracic and respirable criteria are sufficient. They have the advantage that they are simple in form, and so suggest relatively easy options for sampling instrumentation. However there are some exposure assessment situations where exposure information more closely associated with dose is desirable, leading to the need for criteria that more closely reflect actual particle deposition.

For a more representative measure of aerosol dose to the tracheobronchial region, a criterion that more closely follows tracheobronchial deposition deserves consideration, say \( B(d_{ae}) \). This might be especially appropriate for the sampling of...
null
The picture with respect to these is still far from complete. However, it is clear from Fig. 7b that there are two significant target regions of the human respiratory tract, the nasal passages (for nose breathing) and the alveolar region (for mouth breathing). There are distinctly different, serious health effects thought to arise from the deposition of ultrafine particles in these two regions. This is a useful starting point, and suggests the need for two criteria for ultrafine particles, one relating to each primary target exposure region.

Although, as described earlier, there are data for the particle size-dependent deposition efficiency of very small particles in the nose and alveolar region, we do not yet know the manner in which particle size influences the nature and level of the toxic response. For example, as suggested by some toxicologists, is there a particle size below which a particle of a given substance becomes intrinsically more harmful than for a larger particle of the same substance? Furthermore, we do not yet know the most appropriate metric for aerosol concentration for ultrafine particles, although some inhalation toxicology suggests that surface area concentration may be more appropriate than one based on mass.6 But, in any case, mass concentrations are not directly measurable in most practical situations because these are likely to almost always be very small for the particle size range of interest. A promising alternative involves the application of direct-reading instrumentation, which has already been applied successfully in the evaluation of ultrafine aerosols in the field. In particular, the differential mobility analyzer (DMA) has already been used extensively in both ambient and workplace atmospheric environments and can provide particle size distributions for ultrafine particles.

The experimental data for regional deposition of very small particles whose motion is dominated by diffusion are summarized in the models proposed by James et al.17 and described in the earlier set of eqn (18) and in Fig. 7. These may be used as the basis of criteria for the ultrafine nasal fraction, UN(dA), and ultrafine alveolar fraction, UA(dA), respectively. In these, one important difference is that particle size is now represented by the particle equivalent volume diameter, dA, that governs the process of Brownian diffusion (instead of particle aerodynamic diameter, d, as for all the other criteria described above). Expressed in similar mathematical form to the previous criteria, the two criteria for ultrafine particles may be given as

\[
UN(d_A) = 0.4 \left(1 - F(x)\right) \quad \text{and} \quad UA(d_A) = 1 - F(y) \quad (30)
\]

where \(F(x)\) and \(F(y)\) are cumulative probability functions of the type described above for which \(I_1 = 0.015 \, \mu m\) and \(I_2 = 3.30\), and \(I_3 = 0.055 \, \mu m\) and \(I_4 = 3.30\), respectively. These functions are shown alongside the model calculations in Fig. 12.

For the ultrafine fractions there is no mention of their relation to the inhalable fraction. This is because inhalability for such small particles will inevitably be close to unity and be independent of particle size. Two problems remain, however. The first is that we are still not able to define the particle size range for the application of these models. At present, 'ultrafine' is described notionally as comprising particles with diameter less than 0.1 \(\mu m\). But there is at present no toxicological or physical basis for this. The second applies specifically to the ultrafine nasal criterion. As described earlier for larger particles in the aerodynamic regime, it is necessary to identify the extent to which breathing takes place through the nose in any given practical situation. And how might this be written into a standard in order to protect people from nasal exposures that might relate to specific serious health effects?

Criteria for fibrous aerosols. This paper would not be complete without a discussion of fibrous aerosols. The inhalation of fine fibrous aerosols poses uniquely serious risks to health, especially for durable materials such as asbestos. Because of their distinctive morphological properties, such particles are not specifically covered by any of the aerodynamically-defined particle size-selective criteria described above. Particle size selection on the basis of particle aerodynamic diameter alone is not sufficient for such particles. Instead a new set of criteria are needed that take into account of both: (a) the aerodynamic properties of fibres that govern their regional deposition in the alveolar region of the respiratory tract after inhalation; and (b) the biological effects and responses following deposition.

As background to the development of criteria for fibres, it is also important to note that concentrations of fibres of materials such as asbestos are usually very low in practical situations. In addition, the fibres are invariably accompanied by much larger relative concentrations of non-fibrous particles. So gravimetric sampling, or any other assessment of aerosol mass concentration, for such particles is rarely a viable option. It has therefore become an almost-universal convention that fibres should be assessed in terms of their number concentration; also that they should be selected according to criteria that relate to shape and dimensions when fibres collected onto a filter are viewed—post-sampling—under an optical microscope. It is therefore important to note that the concept of a ‘respirable’ fibre diverges sharply from the aerodynamic definition that has been described above for respirable aerosols more generally, and should not be confused with it.

Particle size-selective criteria for the routine assessment of fibres depend inextricably on the microscopic methods that are used to visualize them. This is because differences in the techniques for sample preparation and microscope set-up, including magnification and type of light used (e.g., wavelength, state of polarization, etc.), can greatly influence the way in which micrometre-sized objects appear to the observer. For these reasons, therefore, the evolution of fibre selection criteria has taken place alongside the development of microscopy procedures. The ‘phase contrast microscopy’ (PCM) method was developed to optimize the visibility of thin fibres that are
Table 2 Summary of particle size-selective sampling criteria: established criteria that have already been applied in occupational or environmental hygiene standards, and potential criteria that might be useful in specific occupational and environmental health situations

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Term</th>
<th>Rationale</th>
<th>Function</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Established criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalable</td>
<td>$I(d_{90})$</td>
<td>Penetration into the nose and/or mouth in moving air environments</td>
<td>$0.5[1 + \exp(-0.06 d_{90})] + 10^{-1} U^{-2/3} \exp(0.055 d_{90})$</td>
<td>$d_{90} \leq 100 \mu m$; $0.25 &lt; U &lt; 9 \text{ ms}^{-1}$</td>
</tr>
<tr>
<td>Thoracic PM$_{10}$</td>
<td>$T(d_{90})$</td>
<td>Penetration into the lung</td>
<td>$I(d_{90}) {1 - F(x)}$</td>
<td>$I_y = 11.64 \mu m$; $\Sigma = 1.5$</td>
</tr>
<tr>
<td>Respirable PM$_{2.5}$</td>
<td>$R(d_{90})$</td>
<td>Penetration into the alveolar region</td>
<td>$I(d_{90}) {1 - F(x)}$</td>
<td>$I_y = 4.25 \mu m$; $\Sigma = 1.5$</td>
</tr>
<tr>
<td>Fine fibres</td>
<td>‘Respirable’ fibres</td>
<td>Penetration into the alveolar region and exhibit toxic behavior there</td>
<td>$NIOSH: l &gt; 5 \mu m$; $AIA: l &gt; 5 \mu m$; $l/d_4 \geq 3$</td>
<td>Particle sizes as determined in terms of geometrical dimensions by optical microscopy</td>
</tr>
<tr>
<td>Potential criteria</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalable</td>
<td>$I(d_{90})$</td>
<td>Penetration into the nose and/or mouth in calm air environments</td>
<td>$1 - 0.0038 d_{90}$</td>
<td>$d_{90} \leq 100 \mu m$; $U &lt; 0.25 \text{ ms}^{-1}$</td>
</tr>
<tr>
<td>Nasal</td>
<td>$N(d_{90})$</td>
<td>Deposition in the nasal passages</td>
<td>$R(d_{90}) F(x)$</td>
<td>$I_y = 4.0 \mu m$; $\Sigma = 2.0$</td>
</tr>
<tr>
<td>Tracheobronchial</td>
<td>$B(d_{90})$</td>
<td>Deposition in the conducting airways</td>
<td>$R(d_{90}) {1 - F(x)} F(y)$</td>
<td>$I_y = 6.0 \mu m$; $I_y = 6.0 \mu m$; $\Sigma = 2.2$; $\Sigma = 1.6$</td>
</tr>
<tr>
<td>Alveolar</td>
<td>$A(d_{90})$</td>
<td>Deposition in the alveolar region</td>
<td>$R(d_{90}) {1 - F(x)} F(y)$</td>
<td>$I_y = 4.5 \mu m$; $I_y = 2.0 \mu m$; $\Sigma = 2.0$</td>
</tr>
<tr>
<td>Ultrafine</td>
<td>$U(d_{4})$</td>
<td>Ultrafine particles deposited in the nasal passages</td>
<td>$0.4[1 - F(x)]$</td>
<td>$I_y = 0.015 \mu m$; $\Sigma = 3.3$</td>
</tr>
<tr>
<td>Ultrafine</td>
<td>$U(d_{4})$</td>
<td>Ultrafine particles deposited in the alveolar region</td>
<td>${1 - F(y)}$</td>
<td>$I_y = 0.05 \mu m$; $\Sigma = 3.3$</td>
</tr>
</tbody>
</table>

*Function $F(x)$ is the cumulative probability function of standardized normal variable, $x$, given by eqn (21) for $d_{90}$; and similarly for forms involving $d_{4}$. 

close to the limits of observability under visible light. The PCM method involves the use of cellulose ester membrane filters, mounting them on a glass slide, and ‘clearing’ them in an atmosphere of acetone vapor. The cleared filter is observed under the microscope under phase contrast illumination at a magnification of ×400 and with an appropriate graticule that permits accurate evaluation of individual fibres. 

The parallel development of laboratory methods and criteria for the visual selection and counting of ‘respirable’ fibres when observed under the microscope by the PCM method has been led by the United States National Institute for Occupational Safety and Health (NIOSH) and the European-based Asbestos International Association (1982), starting in the late 1970s and continuing into the 1990s. There are slight differences between the two approaches as they have evolved. The criteria in the NIOSH 7400 method specify that a ‘respirable fibre’ should be taken to be one with length ($l$) greater than 5 μm and aspect ratio ($l/d_4$) greater than or equal to 3 (where $d_4$ is fibre width). The AIA criteria specify that, in addition to $l_4 > 5 \mu m$ and $l/d_4 \geq 3$, $d_4$ should be less than 3 μm. Other differences include how to deal with fibres that appear to be in contact with non-fibrous particles, or with fibres that lie partially outside the graticule area, or with split fibres or fibre bundles. Such issues have been treated in successive refinements of the NIOSH and AIA methods. Similar methods and criteria (referred to as ‘rules’) have also been published by other bodies, including the Australian National Health and Medical Research Council and the World Health Organization (WHO). Indeed, nowadays, it appears that most countries outside the United States apply the WHO rules. Again, it is important to reiterate that such criteria for fibrous aerosols are only loosely based on what is known about lung deposition in humans (where, as already stated, little is known because of the hazardous nature of the experiments that would be required to obtain such information), but relate also to the biological effects that are known to ensue. That said, however, there has been some work to use aerodynamic particle size classification methods in order to eliminate coarse fibrous and non-fibrous particles from samples that would subsequently be analyzed by the PCM method, one of which involved the application of respiratory preselection. 

The particle size-based criteria that are summarized above were intended initially for asbestos fibres. However to complete what is needed for a standard, criteria are also needed to define the material of the fibre. The PCM method is not ideally suited to identifying asbestos fibres in the presence of other non-asbestiform fibres. Therefore in the application of the PCM method, it has become customary to assume that all fibres meeting the geometrical criteria are, in fact, asbestos. In any case, in recent years the health-related concerns about fine asbestos fibres have been extended to all fine fibres that are similarly durable in the lung after inhalation.

**Overview**

**Summary**

A set of criteria for aerosol fractions relevant to inhalation and penetration to—and deposition in—the various regions of the human respiratory tract after inhalation has been described. Taken together these form a framework for health-related aerosol sampling for which the philosophy for each particle size-selective criterion is: (a) it should embody recognition of the various processes by which particles eventually come into contact with the human respiratory system; (b) it should reflect the wide range of people and environmental situations that
pertains to the standard in which it will be used, taking account worst-case scenarios where appropriate; (c) it should provide a realistic basis for practical sampling instrumentation; and (d) it should be defined in terms of a consistent mathematical form in order that users may understand the general shape of any particular curve and be able to define it with as few, and easily understandable, parameters as possible. The criteria that provide the modern basis for aerosol exposure standards are summarized in Table 2. It includes those criteria that have already been accepted by the occupational and environmental hygiene community and many regulatory bodies. It also includes some criteria that have not yet been widely discussed, but which point towards the development of criteria and standards for aerosol fractions that might be applied in the future in certain special situations.

Differences between criteria

Differences between criteria aimed at sampling for essentially the same fraction can produce significant differences when they are applied in the real world. For example, the thoracic fraction and the PM$_{10}$ criteria are intended to represent essentially the same fraction in relation to the same range of health effects. But, as seen in Fig. 8, the curves differ slightly, in particular for larger particle sizes. Here, the thoracic fraction allows for the sampling of particles with finite collection efficiency for $d_{50}$ up to about 25 µm, whereas the PM$_{10}$ curve cuts off at around 15 µm. It is therefore clear that, for a hypothetical pair of samplers that exactly follow the respective conventions, the one designed for the thoracic fraction will collect more than the one designed for PM$_{10}$. Further, the magnitude of the difference will be greater for coarser aerosol.

More generally, similar differences will occur for: (a) a sampler designed to match a single given criterion but does not exactly follow the target performance curve, in which case the collected sample will be consistently biased with respect to the ideal; and (b) a pair of samplers designed to match a single given criterion but where their performances are not identical, in which case they will collect different amounts of aerosol. These were first discussed in 1986 by Bartley and Doemeny with particular reference to the earlier ACGIH criterion for the respirable fraction. They demonstrated that so-called ‘acceptable’ samplers may yield mass concentrations that vary—depending on the particle size distribution—by even as much as a factor of six.

Such biases are recognized in the implementation of criteria like those described at the point where a specific sampler is chosen to do the job. For this, test methods are being developed by which sampler performance may be assessed relative to given sampling criteria. In its published sampler performance protocol, CEN describes procedures in which not only is the collection efficiency of a sampler as close as possible to the curve identified in the target criterion, but also the collected particulate mass must fall within ±10% of that which would be collected by a hypothetical ideal sampler that follows the curve perfectly. In general, such considerations must underpin all discussions of precision and tolerance bands pertaining to the application of such criteria in the design and choice of sampling instruments.

International harmonization of sampling criteria

In the early years, there were wide differences in the criteria proposed by different bodies. This was especially true for the respirable fraction which attracted so much attention during the early years of occupational and environmental hygiene. Some differences still remain. However, considerable progress has been made towards international harmonization of the main set of criteria for the inhalable, thoracic and respirable fractions for applications in occupational health standards, involving ISO, CEN and ACGIH. It has become clear that considerable work is required before they can become fully effective and of true practical value. In due course, therefore, it is hoped that all such standards will be harmonized in those areas where, at present, they differ both qualitatively and quantitatively.

Aerosol-related health effects

Diseases of the respiratory tract. Table 3 lists examples of some non-infectious, non-cancerous diseases that are listed for regions of the respiratory tract that are known to be associated with aerosol exposure. It also identifies regions of the respiratory tract corresponding to the criteria that have been elaborated above for the purpose of aerosol sampling. It also indicates the criterion that would apply for sampling in relation to the health effect in question. The list includes not only the criteria that have already been agreed, and so are already widely-accepted as conventions, but also some plausible additional ones that have been discussed but not yet adopted.

In the simplest view of aerosol-related disease it is assumed that when there is a sufficient dose of toxic particles to a given type of surface in the respiratory tract, it may initiate a range of biological responses leading to a disease outcome specifically at that surface. This is true for most forms of the pneumococci, spores and other infectious or antigenic proteins usually act through an immunological response, which too can be remote from the site of deposition. For example, insoluble particles which are deposited in the alveolar region may be captured by alveolar macrophages which in turn migrate into the bronchioles and other proximal parts of the pulmonary system where disease processes can develop in the respiratory tract remote from the original site of deposition.

Aerosol-related diseases beyond the respiratory tract. For soluble particles, dissolution in pulmonary fluids may occur through physico-chemical reactions such that toxic molecules may enter the systemic circulation. One well-known example is exposure to aerosols containing soluble species of lead, where inhalation may lead to serious diseases of the central nervous system. Such exposures are experienced in both occupational and in ambient atmospheric environments. Another example is exposure to particles containing soluble cadmium species, leading to kidney damage and prostate cancer; another is exposure to soluble nickel species, leading to effects in the cardiovascular system, kidneys and central nervous system. For such aerosols, exposure assessment by aerosol sampling is an important part of the process of hazard surveillance. Here, since the particles are available for dissolution after deposition at any point in the respiratory tract, albeit at different regional rates, the inhalable fraction represents the most appropriate criterion for a standard. However, for soluble substances like the examples mentioned, additional exposure assessment metrics are available in the form of biological indices—for example, lead in blood, protein products in urine directly associated with cadmium aerosol inhalation, and nickel in urine. For such substances, biological exposure indices (BEIs) represent important complementary tools, to be applied alongside air sampling for overall exposure assessment and hazard evaluation. For such substances, ACGIH lists limit values for BEIs.

Aerosols of biological origin, including bacteria, viruses, spores and other infectious or antigenic proteins usually act through an immunological response, which too can be remote from the site of deposition. Microorganisms such as bacteria, many of which are as small as 1 to 2 µm, and viruses, even smaller down to 0.01 to 1 µm, penetrate quite readily to the alveolar region, and may either remain at the site of deposition or elicit antibodies that enter the systemic circulation, leading
to responses elsewhere in the body. Fungal spores typically have \(d_{ae}\) from 3 to 30 \(\mu m\) and most of those inhaled are captured largely in the extrathoracic region where they are commonly linked with allergic rhinitis. But they may also be associated with asthma through systemic responses. In short, from the above, it should not necessarily always be assumed that health effects are experienced in the same region of the respiratory tract where the particles are deposited. This means that the choice of a sampling criterion for particle size—selective sampling, and ultimately a limit value in relation to a given aerosol-related health effect, needs to be carried after due consideration of all available physical, chemical, toxicological and medical information.

**Health effects associated with inhaling aerosols in the ambient atmosphere.** Aerosol in the ambient atmospheric environment has long been associated with excess mortality and morbidity. The strength of the association was quite strong even early on where epidemiological studies depended on crude aerosol indices based on black smoke (BS) and total suspended particulate matter (TSP). But more recent epidemiological studies, many of them using monitoring data for thoracic particulate matter, as measured according to the PM10 criterion, have generally produced stronger associations between ambient aerosol and mortality and morbidity in the general population. And recent studies have shown that those associations are even stronger for indices of exposure based on the still finer PM2.5 criterion.62

Epidemiological evidence for health effects attributable to exposures to the PM2.5 fraction is more limited than for PM10. But some important studies have been reported. One major study for which fine particles were measured selectively along with the PM10 and TSP fractions has become known as the ‘Harvard Six-Cities Study’. It was shown not only that the PM2.5 fraction correlates better with daily mortality than PM10 but also that there is an especially good correlation with the sulfate chemical subfraction. Further, it has been shown that the excess deaths reflected in these results were accounted for by cardiopulmonary effects and lung cancer. In another study in 22 US and Canadian cities, adverse effects on the lung capacity and bronchitis in children were also shown to correlate best with the finer aerosol fraction.63,64

**Health effects associated with inhaling ultrafine particles.** Interest in the health effects of ultrafine particles comes from the growing awareness of health effects associated with exposures to particles finer than those contained just within the aerosol fractions which underpin current EPA air quality regulations in the United States. Such interest is being driven by current concerns that such particles in ambient air, as yet poorly defined and whose properties are as yet poorly understood, may be associated with the observed increases in mortality linked to cardiopulmonary disease in vulnerable populations.65,66 During this line of enquiry, evidence has emerged to support the view that extremely small particles are very important in relation to health, perhaps increasingly so. Seaton and colleagues67,68 considered the possible causative factor linking exposure and the observed mortality in the general population. They proposed a hypothesis in which exposure to ultrafine particles in the size range around 50 nm characteristic of air pollution (may) provoke alveolar inflammation leading to acute changes in blood coagulability and release of mediators able to provoke attacks of acute respiratory illness in susceptible individuals. The blood changes result in an increase in the exposed population’s susceptibility to acute episodes of cardiovascular disease; the most susceptible suffer the most. This hypothesis, being based on the number, composition and size—rather than on the mass—of particles accounts for the observed epidemiological relations.

The Seaton hypothesis relates to ultrafine particles that deposit in the alveolar region of the lung, and embodies the suggestion that such small particles are readily translocated

### Table 3 Examples of some health conditions associated with aerosol exposure, listed together with the part of the respiratory tract affected for each and the particle size-selective (PSS) criteria that might be most appropriate to each

<table>
<thead>
<tr>
<th>Disease</th>
<th>Region of deposition</th>
<th>PSS criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute rhinitis</td>
<td>Extrathoracic—nasal breathing</td>
<td>Inhalable, (I(d_{ae})); nasal,(^a) (N(d_{ae}))</td>
</tr>
<tr>
<td>Chronic rhinitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic pharyngitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic sinusitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic laryngitis</td>
<td>Extrathoracic—mouth breathing</td>
<td>Inhalable, (I(d_{ae}))</td>
</tr>
<tr>
<td>Chronic laryngotraehitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis, not specific as acute or chronic</td>
<td>Tracheobronchial</td>
<td>Thoracic, (T(d_{ae})); PM10, tracheobronchial,(^a) (B(d_{ae}))</td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic airway obstruction, not elsewhere classified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic allergic alveolitis</td>
<td>Alveolar</td>
<td>Respirable, (R(d_{ae})); alveolar,(^a) (A(d_{ae}))</td>
</tr>
<tr>
<td>Coalworkers’ pneumoconiosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumoconiosis due to other silica and silicates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumoconiosis due to other inorganic dust</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumopathy due to inhalation of other dust</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emphysema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical pulmonary edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extrinsic allergic alveolitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asbestosis</td>
<td>Alveolar</td>
<td>‘Respirable’ fibres as defined by the PCM method</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Suggested criteria, not yet adopted by any of the standards setting bodies referred to in this paper.
into the blood. A plausible particle size-selective criterion for sampling relative to this health effect is the $\frac{U(d_v)}{V}$ fraction described in the preceding section, see eqn (30). More recently, there has been discussion about the deposition of ultrafine particles in the nasal passages, and their direction translocation through the olfactory nerve into the olfactory bulb and thence to the brain and central nervous system. The potential importance of this specifically to ultrafine particles generated during certain welding processes has been raised. Here a plausible criterion for health-related sampling is the $\frac{U(d_v)}{V}$ fraction, again see eqn (30). It is clear that there is a need for further research to confirm the plausibility of such hypotheses or to provide a basis for new ones. At the time of writing this paper, vigorous efforts are being undertaken to better understand the relationship between exposure to ultrafine particles in the nanometre regime and health effects.

**Exposure limits.** As stated at the beginning of this paper, the particle size-selective criteria that have been discussed are a first, important part of the overall framework by which standards for the protection of people for the adverse health effects associated with aerosol exposure may be achieved. The final part is the development of the actual quantitative limit values that are the bases by which achievement of the standard is measured, whether it be for ambient atmospheric or workplace environments. These are not the subject of this paper, but copious information is available in the literature. 61, 71, 72

**Appendix**

It is widely acknowledged that the cumulative log-normal mathematical form that features widely throughout this paper—as for example in eqn (20) and (22)—is unwieldy when applied to aerosol sampling, and so is not convenient for routine use. With this in mind the following simple analytical form provides results very close to the formal definition:

$$T(d_v) = \left(1 - \frac{\exp [a + b \ln(d_v)]}{\exp [a + b \ln(d_a)]}\right)$$

(A1)

where

$$b = 1.658/\ln(2) \quad \text{and} \quad a = -b \ln(T)$$

(A2)

**Acknowledgements**

The author wishes to thank the large number of colleagues—too many to name individually—in many countries around the world that have contributed over many years to the discussion of the issues raised in this paper.

**References**


2 R. F. Phalen, in Particle Size-Selective Sampling for particulate Air Contaminants, ed. H. J. Vincent, American Conference of Governmental Industrial Hygienists (ACGIH), Cincinnati, OH, USA, 1999, pp. 29–49.


14 R. F. Phalen, Particle size-selective sampling in the workplace, Report of the ACGIH Air Sampling Procedures Committee, American Conference of Governmental Industrial Hygienists (ACGIH), Cincinnati, OH, 1985.


* Many such issues touched on this paper were discussed at the First International Symposium on the Occupational Health Implications of Nanomaterials held in Buxton, England, UK in October 2004, and will be discussed at the Second International Symposium on Nanotechnology and Occupational Health to be held in Minneapolis, MN, USA in October 2005.

54 G. Oberdörster, The ash of silicotic lungs, the South African Institute of Medical Research, Johannesburg, 1913.
57 Asbestos International Association (AIA), Airborne asbestos fiber concentrations at workplaces by light microscopy (membrane filter method), AIA health and safety publication RTM1, AIA, Paris, 1979.
61 American Conference of Governmental Hygienists (ACGIH), Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices, ACGIH, Cincinnati, OH, 2004.