HEALTH RISK ASSESSMENT GUIDANCE FOR METALS

FACT SHEET

HERAG 02

ASSESSMENT OF OCCUPATIONAL INHALATION EXPOSURE AND SYSTEMIC INHALATION ABSORPTION

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EUROFER European Confederation of Iron and Steel Industries

EuroMetaux

ICMM International Council on Mining & Metals

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1. Introduction

It is explicitly noted here that the purpose of this fact sheet is to summarise previously developed concepts for the assessment of (i) inhalation exposure and (ii) inhalation absorption of metals and metal compounds under occupational exposure situations.

Inhalation is probably the most important exposure route to consider in the assessment of human risk from solid inorganic substances and in particular from metals in the workplace, and to a certain extent where consumer products entail exposure to an aerosol. The assessment of risk to human health due to inhalation of airborne substances needs to consider two distinct aspects: the assessment of external exposure, and the proportion of material that is retained and absorbed into the body.

This fact sheet is based on the experience gained with these issues during previous risk assessments for metals and metals compounds, conducted under the EU Existing Substances Regulation or as voluntary risk assessments in the EU. Based on these exercises, this document summarises risk assessment methodologies aimed at minimising uncertainty in the assessment of inhalation exposure and absorption. The overall aim is to assess not only external exposure, but also the systemic uptake, i.e. the amount of an inhaled substance that is absorbed into the human body as precisely as possible, before finally taking this figure forward to risk characterisation.

One key issue of this fact sheet is the influence of particle size distribution of any inhaled material on its fractional deposition in various regions of the respiratory tract. The use of particle size distribution data for the assessment of inhalation absorption has been used in previous risk assessments, and this methodology is described here in detail in chapters 2 - 4.

Historically, there are regulatory limits (designated as OELs, TLVs or WELs, etc.) in place for many metals or metal compounds, generally aimed at the control of airborne dust or fume concentrations. As a consequence, a large body of data exist that were generated to monitor compliance with these levels. The existing differences in methods of sampling which influence the quality and relevance of these data necessitates a detailed discussion of further issues of importance within the context of inhalation exposure assessment. Such methodological issues of aerosol sampling techniques and of the data collection process are discussed in chapter 5. For a structured collection of occupational inhalation exposure, a generic questionnaire is introduced.

For the sake of completeness, it is noted here that the International Council on Mining & Metals (ICMM) has recently initiated a series of workshops in an effort to promote a global harmonisation of the way in which such regulatory limits on workplace exposure are set. Further information may be obtained from ICMM (http://www.icmm.com). However, the issue of the setting of regulatory limits is not further addressed within this fact sheet, since the setting of such limits and the conduct of risk assessment occurs according to different legal standards.

Finally, whereas this fact sheet addresses particle size as relevant for occupational inhalation risk assessment, nanoparticles are not considered: under most occupational circumstances, particles in workplace aerosols aggregate or agglomerate to rather large particles. However, some exceptions for much smaller particles (< 100 nm) are given in this fact sheet (such as zinc and lead), but none of these essentially qualify as what is commonly designed as a “nanoparticle”. Instead, such particles are commercially generated by specific industrial processes. Since nanoparticles and their toxicological characterisation are currently subject of extensive research without definitive conclusions being possible at this time, this aspect was not yet considered in this inhalation fact sheet.

2. Inhalation: basic risk assessment concepts

In the absence of substance-specific inhalation absorption factors, the initial approach in previous EU risk assessments has been to use 100 % as a default absorption factor (75% is recommended for inhalation absorption for indirect exposure of man via the environment, TGD Appendix 3, Table 4). For occupational the risk assessment of metal, this is an unrealistic, unnecessarily conservative assumption as shown further below.

The fundamental basis for assessment of absorption of inhaled particles is the aerodynamic-size dependant deposition of the particles in three distinct zones of respiratory tract[1], which has been elaborated in detail in the ICRP (1994) model, and is briefly summarised here:

- Large-size material is deposited in the extra-thoracic region by impaction, and is subject to rapid clearance (usually within 2-5 minutes) and translocation to the gastro-intestinal (GI) tract. Thus, assuming minimal absorption through skin and mucous membranes in the extra-thoracic region, the GI uptake factors will actually determine the systemic bioavailability of such a compound.

- Material is deposited in the tracheo-bronchial region by sedimentation, and then subject to clearance usually on a scale of 15-20 minutes, and also then translocated to the GI tract. Similarly assuming minimal absorption through mucous membranes in this region, GI uptake factors will again apply.

- Material that penetrates to the alveolar/pulmonary fraction of the lung is subject to diffusion. Information on clearance from this area is rarely available, so as a conservative default assumption, 100 % of this material may assumed to be absorbed.

Given the availability of detailed particle size distributions (PSD) data for a particular substance and a specific occupational setting, then an mass-median-aerodynamic diameter together with it's geometric standard deviation can usually be calculated, and fractional deposition in the respiratory tract can be predicted with the aid of the MPPD model (or with the RDDR model). Please refer to A2 for details on these models.

Highest relevance should be attributed to workplace particle size distribution data, particularly where process conditions may influence significantly the particle size and the composition of aerosols.

Laboratory PSD methods (i.e. dustiness testing in combination with a cascade impactor) are highly relevant for (i) comparison between substances, (ii) exploitation of analogies, and (iii) prediction of substance-specific inhalation absorption factors, and (iv) selecting the most appropriate product/compound for inhalation toxicity testing.

Available methodology for the measurement of particle size distributions at the workplace and in the laboratory is discussed in detail in appendix A3.

The practical example of the prediction of the fractional deposition of an inhaled material in the respiratory tract using its particle size distribution together with the subsequent calculation of the overall inhalation absorption is demonstrated in the next chapter.

[1] Please refer to appendix A1 for further definitions.

3. Calculation of fractional deposition and inhalation absorption factors

This key section of this fact sheet introduces a methodology for the assessment of absorption of inhaled particles. It is based on the respective sections of the EU risk assessment for zinc and zinc compounds, in which this approach has been successfully applied and which gives a good summary of the approach chosen to derive inhalation absorption factors for (i) soluble and (ii) insoluble compounds. Further examples of the assessment of inhalation absorption in other metal risk assessments (lead, copper, nickel) are presented below.

3.1. Generic example: Zinc

For the risk assessment of zinc data were provided on the particle size distribution of zinc aerosol in three different industry sectors, i.e. the galvanising sector (three plants, 4 samples each), the brass casting sector (two plants, 3 and 4 samples respectively) and the zinc oxide production sector (one plant, 10 samples), by using personal cascade impactors with cut-off diameters of 0.52, 0.93, 1.55, 3.5, 6.0 and 21.3 µm, and a final filter diameter of 0.3 µm (Groat et al., 1999). These data served as input for the Multiple Path Particle Deposition Model (MPPDep v1.11; Asgharian and Freijer, 1999) in order to estimate the airway deposition (in head, tracheobronchial and pulmonary region) for workers, by using:

- The human – five lobar lung model.
- A polydisperse particle distribution (i.e. this distribution contains a wide range of particle sizes), by taking the mean size distribution of the 10 samples for zinc oxide production (MMAD 15.2 µm, GSD 4.0). Using this MMAD and GSD for the total polydisperse distribution is preferred above treating the polydisperse particles on individual impactor stages (with given cut-off diameters) as being monodisperse particles, also because the maximum particle size in the MPPDep model (20 µm) is lower than the largest size fraction of the cascade impactor (21.3 µm).
- Both the oral breathing and the oronasal (normal augmenter) mode, but not the nasal breathing mode. The latter is considered to present an underestimate because (i) many people are oronasal or oral breathers, independent of their activities, (i) people with a cold will not normally breath nasally, and (iii) with heavy exercise, short-term deep oral breathing will occur, resulting in increased deep pulmonary deposition.
- The possibility of inhalability adjustment for the oronasal augmenter. Inhalability is defined as that fraction of particles in an aerosol that can enter the nose or mouth upon inhalation. It must be noted that inhalability is different from respirability, which relates to the deposition of particles after making their entrance inside the airways. If “inhalability adjustment” is “off”, the calculations start by assuming that the airflow is in line with the direction of the nasal entrance. However, in reality this will not be the case because the airflow has to make turns to enter the nose. This results in losses that are larger with increasing particle size. Ménache et al. (1995) have described the relations between exposure concentration and concentration at the entrance of the airways for laboratory animals and humans.
- Two scenarios for tidal volume and breathing frequency were used in the zinc RA[2]:

  (1) For risk characterisation purposes, a representative default breathing rate of 10 m^3 for an 8-hour shift (corresponding to 1100 mL/breath and 20 breaths/min) was selected, considered to be reflective of a combination of light and heavy exercise (ICRP, 1994).

  (2) Merely for worst-case deposition model calculations, a breathing rate of 19 m^3 for an 8-hour shift was chosen, corresponding to a tidal volume of 1700 mL/breath and a breathing frequency of 23 breaths/min, and being representative of a full shift of heavy exercise only.

[2] For more information on the use of default breathing rates see appendix A7 to this fact sheet

The results of the MPPDep modelling are given in the table below. It must be noted that the MPPDep (Version 1.1) only models deposition, not clearance and retention. The modelling of clearance has been introduced in the latest version of this model (see appendix A2). However, this feature has not yet been used on a realistic data set.

Table Zinc-A: Deposition fractions for oral breathers and for oronasal augmenters, using a polydisperse particle distribution (MMAD 15.2 µm, GSD 4.0).

mode	inhalability adjustment	Tidal volume (mL)	Breaths/min	Deposition region			
				Head	Tracheo-bronchial	Pulmonary	Total
oral	off	1100 1700	20 23	0.638 0.676	0.071 0.100	0.139 0.101	0.848 0.877
oronasal	off	1100 1700	20 23	0.927 0.804	0.011 0.064	0.021 0.064	0.960 0.932
oronasal	on	1100 1700	20 23	0.519 0.585	0.011 0.063	0.021 0.064	0.551 0.713

From the table above it can be seen that for oral as well as for oronasal breathers the largest part of the deposition takes place in the head region, irrespective of the breathing rate. When inhalability adjustment is “on”, head region deposition is somewhat reduced.

The fate and uptake of deposited particles depends on the clearance mechanisms present in the different parts of the airway. In the head region, most material will be cleared rapidly, either by expulsion (not the case for oral breathers) or by translocation to the gastrointestinal tract (half-time 10 min). A small fraction will be subjected to more prolonged retention, which can result in direct local absorption. More or less the same is true for the tracheobronchial region, where the largest part of the deposited material will be cleared to the pharynx (mainly by mucociliary clearance (half-time 100 min)) followed by clearance to the gastrointestinal tract, and only a small fraction will be retained (ICRP, 1994). Higher uptake rates may be assumed for the pulmonary region than for the head and tracheobronchial region.

Once translocated to the gastrointestinal tract, uptake will be in accordance with oral uptake kinetics. Hence, for that part of the material deposited in head and tracheobronchial region that is cleared to the gastrointestinal tract, the oral absorption figures (20% for soluble zinc compounds and 12% for less soluble/insoluble zinc compounds can be taken. Given that the clearance to the gastrointestinal tract occurs within a time frame of minutes (10-100 min in head and tracheobronchial region), there will be no significant dissolution in these areas. Besides, most of the particles in the head or the TB region will have a diameter >1 µm, thus dissolution half-times for these larger particles will be longer. Based on the above information, inhalation absorption was estimated by assuming the following:

Table Zinc-B: regional absorption and clearance of zinc compounds in/from the respiratory tract

	soluble zinc compounds (chloride and sulphate)	less soluble/insoluble zinc compounds (metal, oxide, phosphate, disteareate)
fraction absorbed in airway region	20% head 50% tracheobronchial 100% pulmonary	0% head 0% tracheobronchial 100% pulmonary
fraction cleared to GI tract, followed (x) by absorption in the GI tract	80% head x 20 % 50% tracheobronchial x 20 % 0% pulmonary	100% head x 12 % 100% tracheobronchial x 12 % 0% pulmonary

These assumptions can be applied to the deposition fractions given in the table above to estimate a total absorption percentage for inhaled material. An example calculation for soluble zinc compounds (table Zinc-B), with the results from the MPPDep model obtained using the “oral” breathing mode and a tidal volume of 1100 mL (table Zinc-A) is depicted in the figure below:

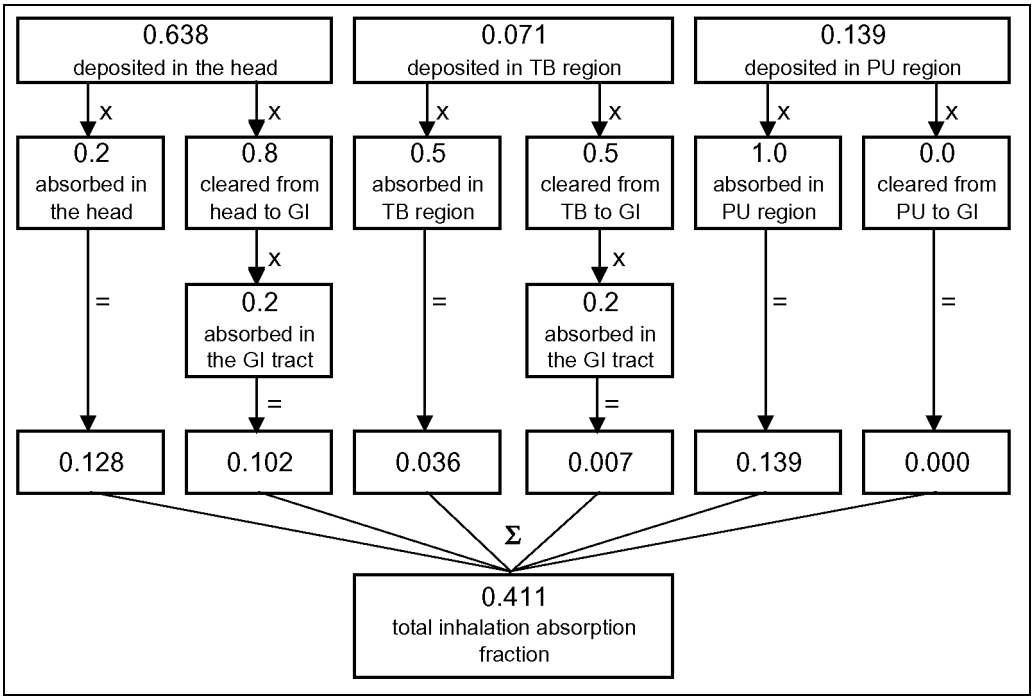


Figure: Example calculation for the estimation of inhalation absorption fraction for soluble zinc compounds (see text)

The application of this calculation also for the assumptions taken for less soluble compounds and using the deposition fractions for other breathing-modes / tidal-volume combinations gives the following results:

Table Zinc-C: Estimation of inhalation absorption fractions (given in %) for soluble and for less soluble/insoluble zinc compounds

breathing mode	inhalability adjustment	tidal volume (mL)	breaths/min	soluble zinc compounds (chloride and sulphate)	less soluble/insoluble zinc compounds
oral	off	1100 1700	20 23	41.1 40.4	22.4 19.4
oronasal	off	1100 1700	20 23	36.1 39.2	13.4 16.8
oronasal	on	1100 1700	20 23	21.4 31.2	8.5 14.2

Inhalation absorption for the soluble zinc compounds (zinc chloride and zinc sulphate) was derived at 40 %, while for the less soluble/insoluble zinc compounds (zinc metal, zinc oxide, zinc phosphate and zinc distearate) inhalation absorption is set at 20 %. These figures were taken forward to the risk characterisation as a reasonable worst case, because these figures are thought to cover existing differences between the different zinc industry sectors with respect to type of exercise activities (and thus breathing rate) and particle size distribution.

This chapter has demonstrated the use of particle size distribution data for the calculation of fractional deposition in the respiratory tract and further the calculation of an overall inhalation absorption factor for different zinc compounds. Comparable approaches were also used in the EU risk assessments for lead and copper and their compounds, as summarised in the next two subchapters.

3.2. Lead

Laboratory particle size information of all thirteen lead compounds covered in the VLRA is presented below. These values were obtained from the airborne fraction generated during dustiness testing, and are thus considered to be reflective of exposure under conditions of normal handling and use.

Detailed investigations of particles size distribution of real workplace aerosols are given in Appendix 4.2, which principally confirm that the laboratory measurements are largely reflective of real circumstances. One exception are “hot” processes (such as smelter operation), where close proximity to the furnace may yield a higher proportion of freshly generated, smaller particles.

The mass median aerodynamic diameters and the corresponding GSD values are summarised in the table below. Based on these data, the MPPDep model (v1.11) (Asgharian & Freijer, 1999) was then used to predict fractional deposition behaviour in the human respiratory tract for workers. In brief, based on morphological data on the human respiratory tract and the aerodynamic diameter of a particle under scrutiny, the model predicts the fraction of inhaled material that is deposited in the extrathoracic (ET), tracheobronchial (TB) and alveolar (PU) regions.

The results of the MPPDep modelling are given in the table below. From the predicted fractional deposition, inhalation absorption factors were calculated based on the following basic assumptions:

- Firstly, particles deposited in the ET region will be translocated to the GI tract with typical clearance times of a few minutes only; from the GI tract, absorption at a rate of 8% is assumed.
- Secondly, particles deposited in the tracheobronchial region will be subject to mucociliary escalation and therefore also transferred to the GI tract; in both cases, the poor solubility of all 13 lead compounds under assessment is assumed to render any dissolution prior to reaching the GI tract negligible; again, 8 % absorption is assumed.
- Finally, particles that penetrate to the alveolar fraction and are deposited will be assumed to be subject to dissolution and ultimately 100 % absorption.

In conclusion, with the exception of basic lead carbonate, all other lead compounds are anticipated to have absorption factors for inhalation between 5 and 10 %. It is therefore proposed to use a factor of 10 % for all lead compounds for risk assessment purposes, albeit realising that this is a mild underestimation for basic lead carbonate (predicted value: 11.6%).

Table: MPPDep model predictions of deposition behaviour in the respiratory tract, and derivation of proposed inhalation absorption factors

Substance	CAS-No.	relative density	d50 [µm] MMAD*	d50 GSD	Predicted fractional deposition			Inhalation absorption [%]
					ET	TB	PU	
lead metal powder	7439-92-1	11.4	33.7	4.1	48.9*	0.9*	1.3*	5.3
lead oxide	1317-36-8	9.5	35.9	3.6	50.6*	0.9*	1.1*	5.2
lead tetroxide	1314-41-6	9.0	14.0	3.9	54.2	1.2	2.6	7.0
dibasic lead phthalate	69011-06-9	4.5	13.4	4.0	54.0	1.2	2.9	7.3
basic lead sulphate	12036-76-9	6.5	15.4	4.5	51.7	1.1	2.2	6.4
tribasic lead sulphate	12202-17-4	6.6	12.9	3.9	55.7	1.3	3.0	7.6
tetrabasic lead sulphate	12065-90-6	7.4	10.0	3.7	63.4	1.5	4.2	9.4
neutral lead stearate	1072-35-1	1.4	28.6	3.6	50.3*	0.9*	1.0*	5.1
dibasic lead stearate	12578-12-0	2.0	24.2	4.0	48.6*	0.9*	1.2*	5.2
dibasic lead phosphite / sulphite	62229-08-7 12141-20-7	6.9	104.2	6.0	48.8*	0.9*	1.2*	5.2
polybasic lead fumarate	90268-59-0	6.5	55.4	4.8	48.8*	0.9*	1.2*	5.2
basic lead carbonate	1319-46-6	6.6	6.0	3.3	73.3	1.9	5.6	11.6
dibasic lead phosphite	12141-20-7	7.0	54.0	4.9	48.8*	0.9*	1.2*	5.2
zinc oxide (3)	1314-13-2	5.6	36.0	3.7	50.0*	0.9*	1.1*	5.2

* Due to the largeness of some particles, input values for MMAD and GSD were sometimes above the linear range of the model, and were reset by the model to maximum values of 20 µm and 4.0 (GSD), where applicable.

For these calculations, the following model assumptions were used in assessing conditions reflective of workplace conditions:

Table: MPPDep model parameters

Parameter	**Used option/value**	**comment**
Airway morphometry	human five lobar lung model	
Particle density	density	as given for each compound in the table above
Particle diameter	polydisperse distribution	was assumed for all particles, as characterised by MMAD and GSD values stated in the table above
inhalability adjustment	on	selected in view of the overall particle size distributions of the lead compounds (for a more detailed description of this parameter please refer to section 7.4 on zinc below)
Exposure conditions	constant	
aerosol concentration	100 µg/m³	considered reflective of exposure at the occupational exposure limit level
breathing mode	oronasal normal augmenter	selected because most humans breath through nose and mouth simultaneously
Shift breathing volume	10 m³/8 h	Corresponding to the ICRP (1994) standard data for occupational breathing volume*
Breathing frequency	20 breaths/min	
Tidal volume	1,042 mL	

* Occupational breathing volume defined by ICRP is 9.6 m³/8-hour shift, composed of 7h light exercise, plus 1 h heavy exercise. For more information on “default breathing rates” please refer to appendix A7 of this fact sheet.

3.3. Copper

The copper risk assessment derives absorption factors specific for several copper compounds (sulphate pentahydrate, oxychloride, (I) oxide and (II) oxide, and copper powder, based on Multiple Path Particle Deposition (MPPD) modelling and the particle size distribution data of the individual substances. Particle size information of all five copper compounds was determined with a laboratory method (Heubach), and at the workplace for selected operations using a Respicon 3-stage virtual impactor. For these calculations, the following MPPD model assumptions were used in assessing conditions reflective of workplace conditions:

Airway morphometry	Human five lobar lung model	Otherwise, standard model defaults were employed
particle density	density	as given for each compound
particle diameter	polydisperse distribution	was assumed for all particles, as characterised by MMAD and GSD values stated in the table below
inhalability adjustment	yes	selected in view of the overall particle size distributions of the copper compounds
exposure conditions	constant	
aerosol concentration	1000 µg/m³	considered reflective of occupational exposure levels in the copper industry
breathing mode	oronasal normal augmenter	selected because most humans breath through nose and mouth simultaneously
shift breathing volume	10 m³/8 h	Corresponding to the ICRP (1994) standard data for occupational breathing volume*
breathing frequency	20 breaths/min	
tidal volume	1,042 ml	

The following resulting inhalation absorption factors were derived for five different copper compounds:

Substance	CAS	rel. density [g/cm³]	D50 [µm] MMAD(1)	D50 GSD(1)	predicted fractional deposition			inhalation absorption(2) [%]
					ET	TB	PU	
copper powder	7440-50-8	5.9	71.7	3.9	49.2	0.9	1.2	14
copper (I) oxide	1317-39-1	6.3	9.9	3.3	67.5	1.4	3.8	21
copper (II) oxide	1317-38-0	2.3	60.7	3.8	49.4	0.9	1.1	14
copper (II) sulphate pentahydrate	7758-99-8	3.6	90.3	5.2	48.6	1.0	1.2	14
Dicopper chloride trihydroxide	1332-40-7; 1332-65-7	8.9	12.2	4.1	56.2	1.4	3.5	18

(1): MMAD/GSD values above the linear range of the model are reset by default to max. values of 20 µm and 4.0 (GSD)
(2): rounded values

For actual workplace particle size monitoring data (Respicon sampling), by assuming that extrathoracic and tracheobronchial fractions are translocated to the GI tract (subject to "dose"-dependant uptake factors in the range of approx. 25%) and 100% absorption for alveolar deposition, the following inhalation absorption factors were derived:

	particle size distribution (%)			inhalation absorption [%]
	respirable	tracheo-bronchial	extra-thoracic	
smelter, converter	12	33	55	27
furnace opn, copper powder production	39	23	38	29
bagging copper oxychloride	20	25	55	27
bagging copper(I)oxide	12	47	41	27

3.4. Nickel

It is worthy of note that the EU risk assessment on nickel and nickel compounds did not make use of the MPPD model and any subsequent calculation of inhalation absorption factors, presumably because of the availability of other data considered relevant. For this reason, the approaches used there are briefly summarised here for comparative purposes:

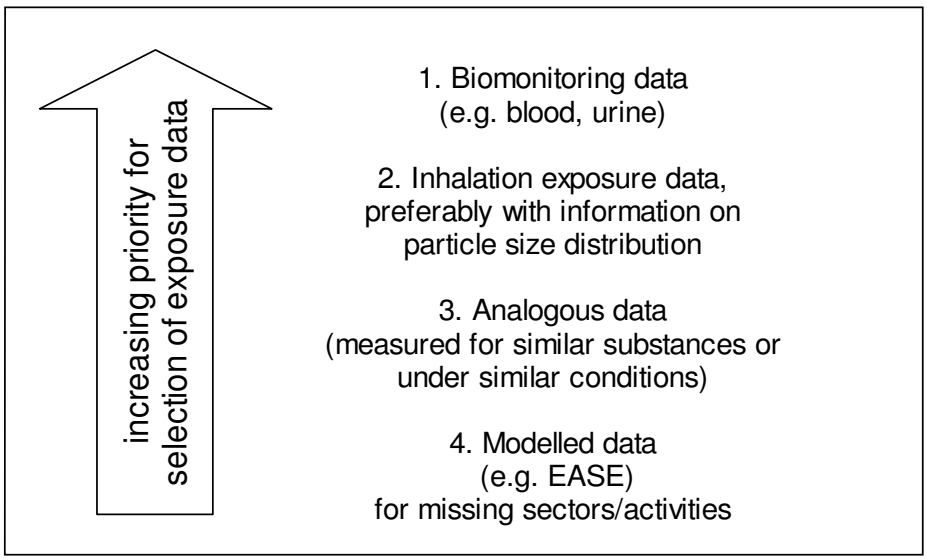
Animal studies with radio-labelled water-soluble nickel compounds (MMAD ~ 2 µm) indicate that inhalation absorption of Ni(II) is high (80-100%). Nickel is removed from the lung with a retention half time of 24 hours. In the EU RA documents, it was concluded that inhalation absorption of respirable particles (< 5 µm) is expected to be 100 %, while inhalation absorption of larger size particles will occur mostly via the gastrointestinal tract and would therefore amount to 5-30 %. These values were applied to all assessed water soluble nickel compounds such as the sulphate, chloride, and nitrate.

For nickel metal, the results from a 90-day inhalation study with nickel metal powder (MMAD 1.9 µm) were used by the rapporteur to calculate an inhalation absorption factor of 6 % for respirable particles. The clearance half time was 30-60 days. Industry considers this value to be an overestimate since the animals were exposed "whole body" and there will be considerable oral intake of nickel through grooming. Calculations using data from the inhalation study recovery period suggest that 1.5 to 3 % absorption may be more realistic. Nevertheless, the rapporteur used 6 % for respirable particles for risk characterisation but stated that the inhalation absorption of larger particles will be mostly via the GI tract (0.05-0.3% absorption).

4. Proposed scheme for assessing occupational inhalation exposures and subsequent systemic absorption

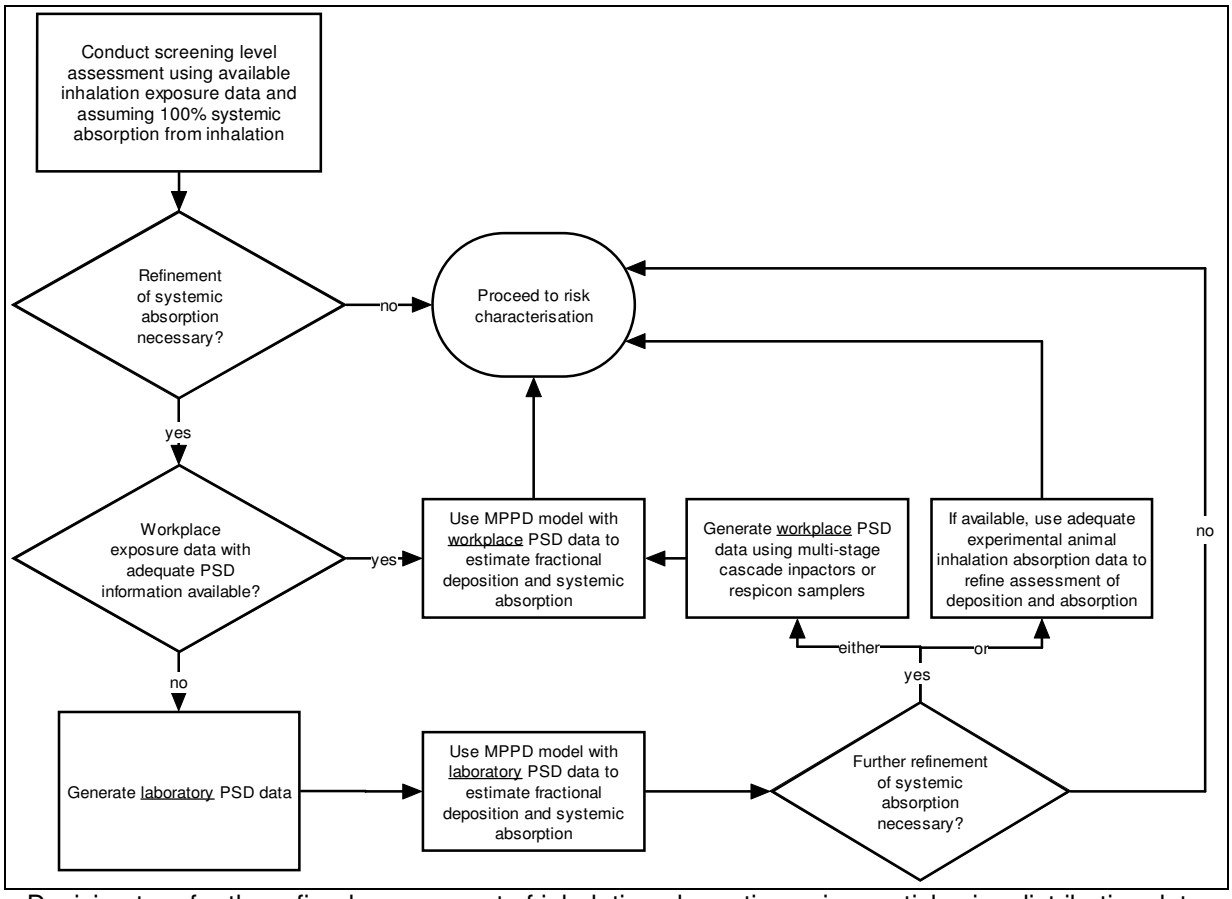
This sub-chapter refers to scientific principles that apply predominantly to the assessment of occupational inhalation exposures. Under workplace conditions, it is well-established that the aerosols present are of comparatively large particle size. In contrast, exposure of consumers and indirect exposure via ambient air is usually associated with very fine particulate matter, for which the scientific principles set forth below also apply, but have much less quantitative influence.

For some substances (examples: lead and cadmium), a large body of biomonitoring data is available. Given that biomonitoring data reflect actual body burdens most correctly by reflecting intakes as well as absorption/toxicokinetics, these will be given preference over "external" exposure data that are intrinsically affected by uncertainties. Thus, for risk characterisation, the priority of exposure data according to relevance can be schematically summarised as follows:



Priority ranking of exposure data by relevance for risk characterisation

However, the focus of this fact sheet is not on risk characterisation, but rather on the collection of exposure data of high relevance, and the subsequent refinement of inhalation exposure and absorption. The highest possible refinement of the two latter aspects is required in order to define risk as closely as possible, and to offer advice to possible subsequent risk management measures. For this purpose, the following **step-wise procedure** is suggested for the assessment of systemic uptake from inhalation exposure, which is summarised in the following decision tree:



Decision tree for the refined assessment of inhalation absorption using particle size distribution data

The individual stages of this step-wise procedure are described in detail below:

Step 1 – screening level (using worst-case default assumptions)

In lack of any information whatsoever on inhalation deposition and/or absorption, including a complete lack of relevant particle size information, an initial screening assessment may be conducted, using a default inhalation absorption factor of 100 % an also 100 % deposition in the respiratory tract, which are unrealistic, but conservative screening assumptions only.

At this initial screening level, the exposure data based upon which the assessment is made could be either measured data, “analogous” data or model predictions (e.g. EASE). Further refinements of exposure data are outlined in Step 4 below

Step 2 – refined assessment of the level of absorption by the use of laboratory data

Dust particles originating from inorganic materials can be experimentally investigated for particle size (see methodology described in appendix A3). Relevant information on particle size must allow the calculation of an MMAD and GSD from the available data. Determinations of physical particle sizes with techniques such as sieve analysis or laser diffraction are of little use, since they do not monitor the aerodynamic diameter of a substance.

One preferred (laboratory) method is the measurement of total dustiness including particle size distribution. This is considered to adequately reflect the particle size of aerosols under conditions of mechanical handling, and as such is useful in the assessment of the PSD under workplace conditions (such as for example packaging, weighing or mixing of a substance/product).

It can be expected that for most aerosols generated under industrial conditions (exceptions: welding fumes, nanoparticles etc., which are not considered here), particle aggregation will occur while particles are suspended. In addition, particles above 8 µm in aerodynamic diameter are statistically unlikely to penetrate quantitatively to the respiratory tract. As one consequence, retention in the respiratory tract is usually much less than 100 % (the remainder of the material being exhaled again).

The following calculation procedures can then be applied:

- first, an MMAD (with GSD) needs to be derived for the existing PSD data.

- next, this data can be used as input to the MPPD model, from which a regional deposition pattern for the extra-thoracic (ET), tracheo-bronchial (TB) and pulmonary regions (PU) of the lung is obtained. For examples see chapter 3 above.

The percentage of material in these three regions is subject to the following clearance mechanisms:

ET: rapid clearance to the GI tract within minutes
TB: mucociliary escalation within 15-20 minutes, also to the GI tract
PU: for lack of other information, 100 % absorption is assumed

As an overall result, the fractions translocated to the ET and TB region will be subject to gastrointestinal absorption (usually less than 100% for metal/inorganics), and the sum of these three fractions can be calculated to an overall inhalation absorption factor (see example in section 7.4 on zinc)

Step 3 (a)
Further refined assessment by use of workplace PSD data

The limitations of the step 2 procedure lie in the fact that merely mechanical agitation is considered as a process. Whereas this is reflective of many industrial settings, for example high temperature processes such as smelting and refining which are predominant features of the metal industry may be considered as not covered by the laboratory type particle size distribution analysis as discussed above. Examples can be found in the Appendix I to this fact sheet, such as for lead and zinc.

In such circumstances, a refinement of inhalation absorption factors relevant to a particular process can only be done with the aid of workplace-specific PSD data, the collection of which is of course considerably more cumbersome and costly than the laboratory method. For applicable measuring methodologies, please refer to chapter 6 above.

However, the calculation procedure is otherwise identical to the one presented for Step 2 above.

Step 3 (b)
Further refined assessment by the use of animal-derived metal-specific absorption rates

In the case that sophisticated and reliable information on inhalation absorption rates of a respirable-size aerosol is available from animal studies, these data may of course also be incorporated into the risk assessment, but also taking into consideration the particle size (e.g., only a fraction of the total inhalation exposure will be deposited in the lung, and only a sub-fraction of this may be absorbed).

Step 4
Possibilities for further refinement

Apart from refining the rate of inhalation absorption as outlined above, the adequacy of inhalation exposure data should be carefully evaluated. It is recognised that step 1 “screening level” assessments are of merely orientating character, which in most occupational settings will not provide an adequate analysis required for risk characterisation.

The various options to refine the exposure assessment are as follows:

(i) in a first refined step, consider replacing modelled data by “analogous” data generated either for a “similar” substance or under “similar” process conditions,

(ii) as the preferred option, generating workplace-specific personal exposure monitoring data should be considered.

5. Further aspects of occupational inhalation exposure assessment

A precise quantification of the amount of contaminant in air is essential for a meaningful risk assessment. Several aspects of this required particular attention in previous metal risk assessments, and are therefore addressed here for future consideration: first, an introduction to available measurement techniques and their efficiency of sampling is given. Secondly, an adequate reflection of auxiliary information concerning the tasks performed is required for a proper risk assessment. For this purpose, a "generic" questionnaire for the collection of occupational inhalation exposure data is introduced, with the example questionnaire being presented in appendix A7.

5.1. Measurement techniques

Workplace air monitoring of metal and metal-compound aerosols provides the base data for assessing occupational exposure. Reviews of available measurement techniques and comparisons of sampling equipment have been conducted previously for various purposes. Therefore such an exercise is not repeated here but reference is made to such a review, which appears comprehensive and useful to the authors of this fact sheet:

Within the SMOPIE[3] project, Witschger[4] reviewed the monitoring devices and methods used in aerosol sampling studies in workplaces for exposure assessment. Whereas small parts of the document deal with radiation dosimetry issues, the major part addresses aerosol sampling issues in general. Key issues addressed amongst others in the review are:

Performance consideration for workplace aerosol samplers
- Factors influencing the sampling performance
- Evaluation of sampling performance in laboratory
- Field tests

Sampling strategies for exposure assessment
- Area vs. personal sampling
- Transfer studies and modelling

Aerosol Sampling in the workplaces
- Aerosol concentration, particle size and shape
- Aerosol measurement errors
- Personal aerosol samplers
- Inhalable Samplers
  - The filter plastic cassettes
  - The IOM Inhalable Sampler
  - The Button Inhalable Sampler
  - The GSP Sampler
  - The PAS 6 Sampler
- Thoracic and Respirable Cyclonic Samplers
- Environmental Samplers
- Area aerosol samplers
- Aerosol spectrometer
- Direct-reading devices

Filtration and Quantification of the sampled aerosols
- Gravimetric analysis
- Chemical analysis

[3] SMOPIE: Strategies and Methods for Optimisation of Internal Exposures of workers. Funded by the European Commission in 2001. For more information see http://www.nrg-nl.com/product/re/norm/smopie001.html [link checked 2006-07-11].
[4] Reference: Witschger, O.: Sampling for particulate airborne contaminants - Review and analysis of techniques. Report IRSN No. DPEA/SERAC/LPMAC/02-18 in the final report on the SMOPIE project (Annex 3, Appendix 1). Available for download: http://www.nrg-nl.com/docs/smopie2004/SMOPIE_Annex3_Appendix1.pdf [link checked 2006-07-11].

5.2. Methodical aspects – sampling efficiency of dust samplers

General remarks

Methodical aspects of aerosol sampling are discussed in the sections on occupational exposure assessment in the RARs on nickel and copper. This chapter is based on these sections (for the full extracts see appendix A6 to this fact sheet).

Different measurement methods and sampling devices are in use across the EU for the assessment of inhalation exposure at the workplace, and several studies have been conducted to determine the performance of used sampling devices in relation to the three biologically relevant aerosol fractions (inhalable, thoracic and respirable fraction (CEN, 1993; ISO, 1992)). The focus of most studies comparing the various types of samplers is on the sampling efficiency for the inhalable fraction.

Comparative studies on sampling efficiency

Recently, Kenny et al. (1997) summarised the technical characteristics of commonly used (EU, statutory or recommended) instruments for personal sampling of aerosols. The sampling efficiencies of the instruments were compared in the laboratory at well defined ambient air velocities (wind tunnel experiments) and with near-monodisperse particles. It is noted that the sampling efficiency for many sampler types decreased as wind speed increased. In agreement with similar studies, large variability was found for all samplers at high wind speeds (>1.0 m/s) at higher aerodynamic diameters (20 to 30 µm). Better performance at lower particle sizes was observed for several samplers. Based on this, suggested correction factors for performance in field conditions for each sampler type were derived.

Table A: Correction factors to obtain aerosol concentrations in terms of inhalable aerosols (Kenny et al., 1997)

Sampler type	Manufacturer	Correction factor 0.5 m/s*	Correction factor 1.0 m/s*
IOM	SKC	0.9 (filter and cassette) 1.0 (filter only)****	1.0 (filter and cassette)
Seven-hole	Casella, SKC, JS Holdings	1.0	1.2
GSP	Ströhlein	1.0	1.0
PAS-6	University of Wageningen	1.0	1.25
PERSPEC	Lavoro e Ambiente	1.0**	NA***
CIP10-I	Arelco	1.15	1.15
37-mm open face	Millipore	1.15	1.15
37-mm closed face	Millipore	1.0	1.2

* Ambient air velocity; ** Inlet losses recovered and included in sample; *** Not available.
**** Quote from Kenny et al. (1997): In the case of the IOM sampler the filter deposits were weighed separately in order to examine the division of collected particles between the filter and the inner walls of the cassette. This is important because some methods for analysing the composition of aerosols such as X-ray fluorescence are typically used directly with particles collected on filters, and extra sample preparation would be required in order to analyse the complete IOM cassette deposit. The percentage of the sample mass on the filter was found to decrease from 100% at small particle sizes to around 75% at 100pm. At 0.5m/s wind it was found that analysis of the IOM filter deposit alone gave good agreement with the inhalable convention.

It has to be noted that it is difficult to simulate workplace conditions in the laboratory (wind tunnel). For example, the laboratory test by Kenny et al. were limited in scope to well defined aerosol particles (sizes from 6 to 100 µm) and external wind speed in the range 0.5 – 4 m/s. In contrast, in the actual workplace there may be larger particles, localized aerosol sources and ambient air velocities well below 0.5 m/s.

Some comparison-of-sampler-types-studies under workplace conditions have been carried out, most extensively for the IOM and 37-mm closed face samplers, the IOM and 37-mm open-face samplers, and the IOM and seven-hole samplers. Limited data are also available comparing the CIP10-I and the IOM samplers. As reviewed by Kenny et al. (1997) the field comparisons of IOM and 37-mm samplers (both closed and open face) generally show the IOM samplers collecting 2-3 times as much as the 37-mm sampler in contrast to the factor of 1.2 listed in table A. The comparisons of IOM and seven-hole samplers showed a median IOM/seven-hole ratio of 1.17, and the comparisons of IOM and CIP10-I showed a median IOM/CIP10-I ratio of 1.5. Both of these latter results are reasonably consistent with the data listed in Table A but are based on a relatively small number of field tests.

Several reasons may explain the 2-3 fold difference observed between the IOM and the 37-mm sampler in the field:

- In the work of Kenny and co-workers, the cassette body of the 37-mm samplers was coated with conducting paint in order to minimise electrostatic effects and the study design may therefore have underestimated negative bias in respect of these samplers.
- Open-faced 37mm samplers used as purchased do indeed appear to show lower collection efficiencies for particles >10 µm when similarly tested on manikins in wind tunnel experiments (Buchan et. al., 1986).
- In addition, localised air currents in workplace settings may create conditions which are not replicated in wind tunnel experiments and which may increase bias arising from inertial factors.
- Conversely, the IOM sampler moderately over-samples particles of all sizes at a wind speed of 0.5 m/s (Kenny et al., 1997) which is considered most representative of actual wind speeds under workplace conditions. Hence, the deviation of the 37-mm sampler from the CEN convention may be less marked than the comparison with the IOM sampler may suggest.

Recently, personal sampling data from comprehensive field studies in the nickel-producing and -using industries were published (Tsai et al., 1995; Tsai et al., 1996a; Tsai et al, 1996b) in which the closed-face 37-mm filter holder was compared with inhalable aerosol as measured using the IOM sampler. Data were also obtained by an approach of static sampling using mannequins to simulate personal sampling (Tsai and Vincent, 2001). The statistical analysis of the personal sampling results has been summarized (NIPERA, 1996) and the regression results are listed in table B for each sampled industry sector. The static sampling results were in good agreement with the personal sampling results for most of the work sites. Priority is given to personal sampling and the static sampling results are not further discussed.

Table B: Comparison between the IOM and the 37-mm samplers in the nickel-producing and -using industries. Regression results from each sampled facility process.

Industry sector	Regression results*					
	analysed as overall dust (by mass)			analysed as total nickel (by ICP-AES)		
Mining	3.64±0.50	N=30	R^2=0.88	3.20±0.48	N=32	R^2=0.86
Milling	2.61±0.46	N=20	R^2=0.88	2.72±0.67	N=21	R^2=0.78
Smelting	1.97±0.23	N=39	R^2=0.89	1.65±0.17	N=35	R^2=0.92
Smelting	2.43±0.69	N=23	R^2=0.71	2.84±0.73	N=23	R^2=0.75
Refining	2.50±0.34	N=37	R^2=0.86	2.12±0.45	N=36	R^2=0.72
nickel alloy production	1.94±0.45	N=45	R^2=0.86	2.29±0.39	N=46	R^2=0.76
Electroplating	2.77±0.44	N=25	R^2=0.87	2.02±0.53	N=21	R^2=0.76
Electroplating	3.29±0.70	N=26	R^2=0.79	3.01±0.93	N=21	R^2=0.70

*The values in the table correspond to 'S±standard error' in the relationship $E_{IOM}=S\times E_{37,}$ thus giving the factor by which the IOM sampler collected more material than the 37-mm sampler. N corresponds to the number of samples analyzed; R^2 corresponds to the regression coefficient.

The nickel data (table B, 5th column) show the levels of 'total' aerosol exposure to be markedly lower than those of inhalable aerosol, with the bias ranging from about 1.7 to 3.2 depending on the industry sector and workplace in question. Consistent with what would be expected from aerosol sampling theory, the observed biases tended to be greater for workplaces where aerosols are coarser.

Studies employing unmodified open-face 37mm samplers for personal sampling in field conditions indicate much greater deviation from the performance of more accurate alternatives such as the IOM sampler. Data from a wide range of industries are shown in Liden et al. (2000).

Conclusions as drawn in the VRA on copper

In the copper Risk Assessment Report, the open-faced 37-mm sampler is assumed to under-sample under field conditions by a factor of two. The correction factor of two is based on an approximately median estimate of performance in the field. This correction factor is applied to exposure data submitted for these samplers. This adjustment is considered moderately conservative in the RA. Factors of 1.25 and 1.2 were applied for the PAS-sampling head and for the seven hole head sampler, respectively. Where the sampling method was not specified, a factor 2 was applied.

Conclusions as drawn in the EU RAR on nickel and nickel compounds

In the nickel Risk Assessment Report, exposure levels measured with the 37-mm closed-face cassette are converted to inhalable aerosols taking into account the conversion factors listed above in table B. Perhaps droplets are the predominant aerosol in the nickel sulphate production scenarios. For such cases, the two conversion factors for electroplating are considered useful for the assessment, and representing the upper range of factors, a factor of 3.0 was taken forward for risk assessment. For other cases, a factor of 2.5 is used as recommended for dust by Werner et al. (1996).

Aerosols as measured with the seven-hole sampler are converted to inhalable aerosols by a factor of 1.17, while aerosols collected with the CIP10-I sampler are converted to 'inhalable' taking into account a conversion factor of 1.5. Aerosols collected with the GSP sampler are considered inhalable. It is recognized in the nickel metal RAR, that “the factor used for the 37-mm closed face cassette is derived from rather solid data (work place sampling in the nickel industry). In contrast the factors used for other types of samplers were derived from work place sampling in other industries or from experiments in the laboratory."

Other available data

The Norwegian National Institute of Occupational Health (Internet: http://www.stami.no) has conducted recent field studies in the primary Aluminium industry, measuring inhalation exposure using personal and static sampling at several plants. Some of the data were used to compare the “Respicon” sampler and the “IOM” sampler with respect to their sampling efficiency of the inhalable fraction. The difference between the IOM and Respicon was roughly 20 % in this study, with the IOM showing higher results. However, the data have not been analysed properly yet and further evaluation is currently being undertaken (E. Nordheim, European Aluminium Association, personal communication, March 2006). Further information may be available in the future at the before mentioned website.

5.3. Generic questionnaire for occupational inhalation exposure data surveys

For many metals or metal compounds, a large body of occupational exposure data exist that were generated during compliance monitoring. For the purpose of retrospective analysis of such existing data, a generic questionnaire was developed to facilitate the collection of core information requirements for a proper risk assessment by the TGD, such as:

- process descriptions,
- frequency and duration of exposure,
- amount and nature of substance handled,
- engineering controls and PPE in use,
- sampling details and quality controls.

Based on the principles given in the TGD, the experiences gained in previous data collection exercises and a consideration of available scientific literature (Ritchie and Cherrie 2001; Rajan et al. 1997; Vincent 1998), a generic questionnaire template has been developed and is included in appendix A7). This questionnaire focuses on inhalation exposure, since the monitoring of dermal exposure is currently not so wide-spread and also methodologies are not yet standardised in a way that such exercises are common to any industry sector.

The purpose of this questionnaire is not to aid in epidemiological surveys. For this, it has been commented during SRP discussions that the additional collection of information would be useful on other aspects such as confounders etc..

For the prospective generation of a workplace data base a standardised approach could be taken, based on a modification of the current template. CEMAS, developed by IOM under funding by CEFIC through their Long-range Research Initiative (LRI), was suggested as potentially suitable, but the HERAG team had no experience in its use.

It is recognised that the majority of risk assessments are single-substance based, and the proposed questionnaire is reflective of this. However, in specific situations other substances/ contaminants at the workplace or even mixed exposures may be of higher relevance (example: exposure of workers to hydrogen fluoride in the Aluminium industry). Such an assessment would require separate attention.

Recommendations for the data collection process

A process description derived based on a site inspection, which is first reviewed by the companies of such an industry sector and finally agreed to be representative, should be the first step in the compilation of such a questionnaire. Based on this description of production processes, scenarios and tasks/processes, the questionnaire can be tailored to the specific requirements of this particular industry.

The questionnaire should be accompanied by introductory wording explaining the legal background of the data collection exercise. A remark that quality and regulatory acceptance of the data is achieved only if all fields are filled out is beneficial. Adding a confidentiality agreement could increase willingness to disclose all necessary information. A glossary of terms, explaining individual items, should be included.

Experience shows that providing a “drop down” set of responses to some items is useful, instead of allowing “free text” entries which may lead to a variation in responses that are difficult to evaluate in the end. In this example questionnaire, such suggestions for possible answers are given in brackets.

In the case that co-exposures, mixed exposures or exposures to more than one metal are anticipated (for example based on the process description developed at the beginning), then multiple copies of Section 2 (measurement strategy), and the corresponding sets of Section 3 sheets would be required.

Some aspects of this questionnaire will probably also be useful for the development of "exposure scenarios" under the upcoming new European chemical policy REACH.

6. Summary and conclusions

A precise assessment of occupational inhalation exposure is essential for a correct human health risk assessment for workers. This fact sheet therefore firstly summarises principles that should be applied in the collection and evaluation of inhalation exposure data.

Further, metals and their inorganic compounds present in workplace aerosols are most adequately characterised not only by the amount of metal present in the air, but also by chemical speciation and particle size. The latter parameter critically determines the deposition in the respiratory tract and subsequent translocation, with ultimate consequences on overall absorption of inhaled particles.

This fact summarises the experience gained in previous EU Risk Assessments. The methodology described herein is aimed at minimising uncertainty in the assessment of inhalation exposure and the amount of an inhaled substance that is absorbed.

The key aspects of this fact sheet are the following:

(i) collection of exposure data:
for most metals, the large number of occupational exposure data that exist were generated during compliance monitoring, according to a large diversity of sampling protocols. For a meaningful statistical analysis and interpretation, relevant auxiliary information additionally needs to be collated. The minimum requirement for the retrospective collection of such data has been the basis of a proposed “generic” exposure questionnaire, as given in Appendix 7 of this fact sheet. It is acknowledged that the use of this questionnaire for epidemiological surveys would require collection of additional information.

(ii) interpretation of exposure data:
the diversity of sampling protocols and analytical equipment mentioned above may have a large impact on the reported result. For example, sampling conventions such as “total” and “inhalable” fractions may impact the measured results considerably. Corrections for sampling efficiency are therefore required to transform these data, as summarised in Chapter 5 of this fact sheet.

(iii) particle size information:
apart from chemical speciation, particle size distribution of any inhaled material is decisive for its fractional deposition in the respiratory tract. The generation of laboratory or workplace particle size distributions is described in Appendix 3 of this fact sheet. Some abbreviated practical examples are given in Appendix 4.

(iv) derivation of inhalation absorption factors from particle size data:
inhalation absorption rates have been derived from particle size data in previous risk assessments using the MPPD model. Examples of such calculations and the underlying principles are summarised in Chapter 3 of this fact sheet, and a scheme illustrating the proposed step-wise approach is presented in Chapter 4.

In a combination of these four aspects, not only a consistent approach for the precise assessment of external occupational inhalation exposures is facilitated, but also a refinement of amounts likely to be absorbed into the body with a perspective of subsequent risk characterisation is possible

7. References & abbreviations

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Abbreviations

AAS	atom absorption spectroscopy
ATO	Antimony trioxide
CEFIC	Conseil Européen de l'Industrie Chimique / European Chemical Industry Council.
CEMAS	CEFIC Exposure Management and Analysis System
EASE	Estimation and Assessment of Substance Exposure (model), see e.g. Creely et al. (2004)
ET	extra-thoracic
EU	European Union
FRC	functional residual capacity
GI	gastro intestinal
GSD	geometric standard deviation
ICMM	International Council on Mining & Metals
IOM	Institute of Occupational Medicine (UK)
LRI	Long-range Research Initiative

MFF	metal fume fever
MMAD	mass median aerodynamic diameter
MPPD	Multiple Path Particle Deposition (Model), name of the current version
MPPDep:	Multiple Path Particle Deposition (Model), name of previous versions, reference Asgharian, B. and Freijer, J.I. (1999)
NiPERA	Nickel Producers Environmental Research Association
OEL	Occupational Exposure Level
PIDS	Polarization Intensity Differential Scattering
PSD	particle size distribution
PU	alveolar/pulmonary
RA(R)	risk assessment (report)
RDD	Regional Deposited Dose: The deposited dose of particles calculated for a respiratory tract region of interest (r) as related to an observed toxicity. For respiratory effects of particles, the deposited dose is adjusted for ventilatory volumes and the surface area of the respiratory region effected (mg/min-sq. cm). For extra respiratory effects of particles, the deposited dose in the total respiratory system is adjusted for ventilatory volumes and body weight (mg/min-kg).
RDDR	Regional Deposited Dose Ratio: The ratio of the regional deposited dose calculated for a given exposure in the animal species of interest to the regional deposited dose of the same exposure in a human. This ratio is used to adjust the exposure effect level for interspecies dosimetric differences to derive a human equivalent concentration for particles.
RfC	reference concentration
SMOPIE	Strategies and Methods for Optimisation of Internal Exposures of workers. Funded by the European Commission in 2001. For more information see http://www.nrg-nl.com/product/re/norm/smopie001.html [link checked 2006-07-11].
SRP	Scientific Review Panel
TB	Tracheo-bronchial
TGD	technical guidance document
TLV	threshold limit value
URT	upper respiratory tract
US EPA	United States Environmental Protection Agency
VLRA	voluntary lead risk assessment
WEL	Workplace exposure limit

A 1: Definitions

Physical particle size

This term is used in the context of "optical", "measured" or "geometric" diameters which are representations of actual diameters, but which in themselves cannot be related to deposition within the respiratory tract.

Aerodynamic diameter

The aerodynamic diameter d_a is the parameter that determines the sampling behaviour in personal inhalation sampling devices and is related to the physical particle diameter d_p with the following formula by correcting for the particle density ρ_p as follows:

$$d_a = d_p \cdot \sqrt{\rho_p}$$

Mass Median Aerodynamic Diameter

The "aerodynamic" diameter is the diameter of a sphere of unit density which behaves aerodynamically as the particle of the test substance. It is used to compare particles of different sizes, shapes and densities and to predict where in the respiratory tract such particles may be deposited. Given that polydisperse particles dominate for example in the occupational setting, the Mass Median Aerodynamic Diameter (MMAD) and its Geometric Standard Deviation (GSD) are calculated to describe the size distribution of airborne particles. As such, the MMAD is a statistically derived figure for a particle sample: for instance, an MMAD of 5 µm means that 50 % of the total sample mass will be present in particles having aerodynamic diameters less than 5 µm, and that 50 % of the total sample mass will be present in particles having an aerodynamic diameter larger than 5 µm.

Dustiness

“Dustiness” is defined as the propensity of a material to become airborne, and thus serves as an indicator of the mobility under workplace conditions. In dustiness tests with the Heubach “rotating-drum” method, the test material is introduced into a rotating drum apparatus, intended to simulate mechanical stress under conditions of industrial processes involving handling/manipulation of these materials. Any dust generated is conveyed in a stream of air to a collection chamber, where it precipitates and where it is weighed. If coupled to a cascade impactor, a discrimination of the airborne material according to particle size (aerodynamic) is additionally possible. In a recent EU draft guidance document (ECB, 2002) it is explicitly mentioned that the rotating drum method (see section 6) is the only standardised method to disperse the dust and to give a separation by mass based on the respirable, thoracic and inhalable fractions.

Size fractions relevant for inhalation toxicology

Particle size distribution measurements relevant for inhalation toxicology should determine the appropriate fractions as defined in EN481 (CEN, 1993), using the aerodynamic diameter as the basis of the measurement. The fractions as defined in EN481 (1993) are:

– inhalable fraction (the mass fraction of particles which can be inhaled by nose or mouth); since there are no experimental data on inhalable fraction of particles with an aerodynamic diameter of > 100 µm, particles > 100 µm are not included in the inhalable convention,

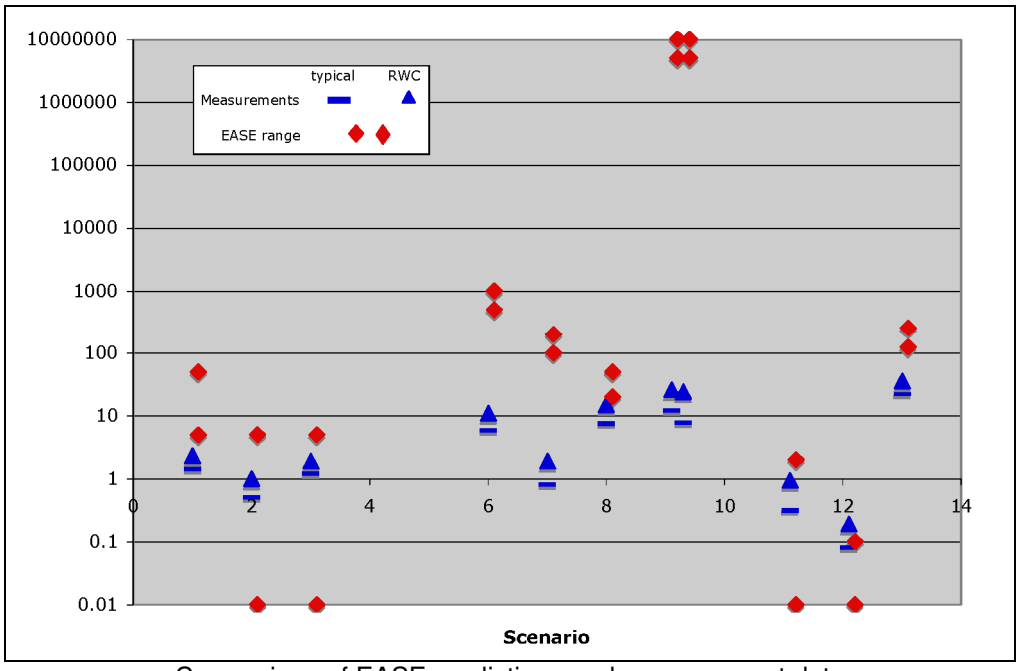
– thoracic fraction (the mass fraction of particles that passes the larynx); the median value of the particle size is 11.64 µm with a geometric standard deviation (GSD) of 1.5 µm. It has been shown that 50 % of the particles in air with an aerodynamic diameter of 10 µm belong to the thoracic fraction,

– respirable fraction (the mass fraction of particles that reaches the alveoli); the median value is 4.25 µm with a GSD of 1.5 µm. It has been shown that 50 % of the particles with an aerodynamic diameter of 4 µm belong to the respirable fraction.

A 2: Relevant Models

A 2.1: Models relevant for inhalation exposure assessment

Inhalation exposure in previous EU risk assessments for metals and their inorganic compounds has often been assessed with the aid of the EASE model. The reliability of this model is rarely questioned, despite it being the subject of several recent review reports by the Institute of Occupational Medicine:



Comparison of EASE predictions and measurement data
Source: Cherrie et al. (2004)

Based on a detailed comparison of recent measured data and EASE predictions (see graph above), the conclusion was drawn that the EASE predictions were comparable to measured data for only a very limited set of data, whereas in all other cases the EASE estimates were higher, sometimes by two or more orders of magnitude. In fact, the ratio of the average of the EASE exposure endpoints to the average of the exposure measurements ranged from 0.7 to 990,000, with the mean of these ratios (excluding the two highest values) being 40, from which the authors concluded that EASE estimates were about 40 times higher than the average measured exposure level (Cherrie et al., 2004).

A major review of the performance of EASE concluded that there was a pressing need to completely revise the model used in higher tier exposure assessments in Europe. As one reason for this, the authors stated that the information used to define the exposure ranges in EASE is likely to be more than 20 years old and there have been many changes in European workplaces during this time (Cherrie et al., 2003).

A 2.2: Models relevant for derivation of inhalation absorption factors

Multiple Path Particle Deposition (MPPD) Model

The MPPD model was developed by the CIIT Centre for Health Research, USA, in collaboration with the National Institute of Public Health and the Environment, The Netherlands (RIVM), and the Ministry of Housing, Spatial Planning and the Environment, The Netherlands. The most recent version was published in September 2006 on the CIIT website under:
http://www.ciit.org/techtransfer/tt_technologies.asp.

The MPPD model, amongst other feature, predicts particle-size dependant deposition patterns in the respiratory tract. The algorithms can calculate the deposition of both mono-disperse and polydisperse[5] aerosols in the respiratory tract of rats and humans for particles, ranging from ultra-fine (0.01 microns) to coarse (20 microns) sizes. The models are based upon single-path and multiple-path methods for tracking air flow and calculating aerosol deposition in the lung. The single-path method calculates deposition for a typical path, while the multiple-path method is capable of incorporating the asymmetry in lung structure and providing lobar specific and airway specific information. Within each airway or airway bifurcation, deposition is calculated using theoretically derived efficiencies for deposition by diffusion, sedimentation and impaction. Filtration of aerosols by the head is determined using empirical efficiency functions. Results using this software show good agreement with experimental data for regional deposition in the rat and human lung. User input options include particle characteristics, breathing patterns (e.g. nasal, oral or oronasal), breathing parameters, functional residual capacity (FRC) and the upper respiratory tract (URT) volume. One major improvement of the current version of this model compared the previous ones is the possibility to include calculations of particle clearance in the lung following deposition. Two types of clearance plots are available to the user: The amount cleared per day during post-exposure and the retained mass in the tracheobronchial and pulmonary regions and in the lymph nodes during exposure and post-exposure times.

Note: a previous version of MPPD with the original designation MPPDep (Version 1.11, Asgharian and Freijer, 1999) was used for example in the ESR risk assessment reports on zinc and lead to predict particle-size dependant deposition patterns in the respiratory tract.

RDDR model

The US EPA in its Reference Concentration (RfC) assessments has introduced a concept that allows adjustments for differences between occupational and environmental exposure scenarios, and also for differences in particle sizes between exposures to be made. Such adjustments are needed before extrapolation from exposure conditions in animal studies to practically relevant exposure conditions for humans can be made. For this, a “regional deposited dose ratio“ (RDDR) is calculated (using the RDDR program available from U.S. EPA, 1994). The RDDR represents the ratio between the dose deposited in a given region of the respiratory tract when animals are exposed to a given concentration of the particle in air, and the dose to the same respiratory tract region received by humans exposed to the same air concentration.

The RDDR is normalised by regional surface area whereas other dosimetry methods, such as that used by Oberdörster (1993), normalise based on tissue weight. In addition to the particle size distribution, inputs to the calculation of the RDDR include the animal and human body weight, the surface area of the respiratory tract region of interest, and the minute volume of respiration.

In consequence, the pulmonary dose for humans may be considerably higher when exposure is considered to the particle size distribution used in the animal studies (which is usually required to be low, i.e. 1-4 µm), compared to the pulmonary dose when exposure is to the particle size distribution found under occupational conditions. The latter is often quite different to that of the laboratory studies, tending towards much higher size distributions. As an outcome, the high exposure under occupational conditions will lead to a relatively lower tissue dose than predicted based on aerosols from animal studies.

[5] In the occupational setting, airborne particulate matter will be characterised by a process- and substance-driven particle size distribution, rendering “polydisperse” the only relevant model option for this setting.

A 3: Measurement of particle size

A 3.1: Laboratory methods

A wide range of methods exist for the assessment of the particle size distribution of a substance. A comprehensive review of these is given in a draft guidance document by the ECB (2002).

One of the recommended methods is the modified Heubach method for dustiness testing, which is also standardised in Germany as an industrial norm (DIN Norm 55 992).

In this method, the test material is introduced into a rotating drum apparatus, intended to simulate mechanical stress under conditions of industrial processes involving handling/manipulation of these materials, such as bagging/unpacking, filling, weighing and mixing. Any dust generated is conveyed in a stream of air to a collection chamber, where it precipitates and is determined gravimetrically. The test result is expressed in “mg/g” of dust/sample. In addition, by adding a cascade impactor, a discrimination of dust particles according to particle size is possible.

Examples of such determinations using lead and zinc compounds are contained in Appendix A4 to this fact sheet.

A 3.2: Workplace particle size monitoring

Multi-stage cascade sampling

For the assessment of (aerodynamic[6]) particle size distribution of workplace aerosols, both stationary and personal cascade sampling devices are available. However, the conduct of such measurements is offered only by a narrow range of specialise expert laboratories/consultancies, which is why a detailed presentation is not given here. However, as a general rule, personal sampling with portable cascade impactor should always be given preference over a static methodology, since the former may be considered more reflective of personal exposure under practically relevant conditions.

The aerosol size characteristics of the airborne dust are usually determined using personal cascade impactors (e.g. Thermo Electron Corporation, SE298), which are attached to an operator for the major part of a working shift. Such cascade impactors can contain up to 8 collection stages. Particles larger than the cut-off point of the first stage impact onto the collection substrate, and the continuing stream of air through the sampler causes a size-selective impaction onto the subsequent stages. The particle size distribution is obtained by measuring the mass of dust collected on each stage.

Static sampling for particle size information is commonly done with the aid of portable aerosol spectrometers. In these, ambient-air is drawn through a sample cell past a laser diode detector, and sampled on cellulose ester membrane filters (analysed gravimetrically). Such instruments are usually capable of analysing airborne dust in a particle size ranges of 0.2 to >20 µm.

Three-stage Respicon® sampling

An alternative method of obtaining particle size distributions is to use a “Respicon” 3-stage virtual impactor. The aerodynamic particle cut sizes of the three stages are respectively 4 µm (respirable), 10 µm (tracheobronchial) and 100 µm (extrathoracic)[7]. The Respicon sampler is calibrated at a flow rate of 3.1 L/min (± 2 %) and dust is collected on 37 mm diameter glass fibre filters. Sample and blank filters are analysed by atomic absorption spectrometry. Inhalable dust is measured as the sum of the three fractions. The performance of this instrument as an inhalable dust sampler, and its operation as a virtual impactor, are described in detail elsewhere (Li et. al., 2000; Koch et. al., 2002; Tatum et. al., 2002). The incorporation of optical detectors in each stage allow for short-time sampling, relevant for the identification of local sources of high dust exposures.

[6] Samplers used for occupational monitoring purposes are intrinsically designed to reflect aerodynamic particle sizes.
[7] It should be noted that, consistent with the principles outlined in this fact sheet, the selection of the cut-off stages for this sampler intrinsically render an over-prediction of fractional deposition in the respiratory tract, and therefore represent a “conservative” assessment.

A 4: Workplace particle size data from previous/current EU Risk Assessments

A 4.1: Zinc

The investigations described here were performed in the context of the EU risk assessment on zinc and zinc compounds, currently being conducted under the existing substances regulation 793/83/EEC (rapporting member state: The Netherlands).

The following is a summary of a paper presented at the Fraunhofer conference on inhalation toxicity in 2003, and at meetings of the German Chemical Society's exposure modelling group (2003), the working group for regulatory toxicology of the German Society for Pharmacology and Toxicology, and subsequently published (Battersby & Boreiko, 2004).

One major concern for a large portion of the workforce in various zinc industries has been the potential risk of "metal fume fever", which is a phenomenon that has frequently been associated with inhalation of zinc oxide fumes: The exposure of humans to artificially generated ultrafine aerosols (< 100 nm) is reported to elicit pulmonary effects characteristic of inflammatory response already at 5 mg/m³, including elevated cytokine levels and polymorphonuclear leukocyte counts, as well as fever-like symptoms. In contrast, in acute inhalation studies in rats with zinc oxide aerosol at 5.7 mg/l (mass median aerodynamic diameter 4 µm), no toxicologically relevant effects were seen.

Occupational exposure limits have nevertheless been established for zinc oxide "fume" in many EU countries. In the above mentioned risk assessment, the specific question was raised whether workers in several major zinc industries (i. e. hot dip galvanizing, brass casting, zinc oxide production) may be at risk of metal fume fever. This paper summarizes the results of the investigation of particle size distribution of workplace aerosols in these three industry sectors, showing the absence of quantitatively relevant amounts of ultrafine zinc oxide aerosols.

Further, with the aid of particle-size deposition modeling (ICRP, 1996) it could be demonstrated that in the studied industrial settings, the size range of the airborne zinc oxide predominant yields extra-thoracic deposition with subsequent translocation to the GI tract. Thus, it could be demonstrated that in these industries, the risk of metal fume fever is practically minimal. However, this is in contrast to processes such as welding and cutting of galvanized steel, in which the prevalence of such ultrafine aerosols has been shown and for which there is clear epidemiological evidence of this risk.

Inhalation studies in human volunteers (Gordon et al., 1992) have reported subjective symptoms (fever, chills, dry/sore throat, chest tightness, headache) of metal fume fever at and above exposure levels of 5 mg/m³ already after 2 hours of exposure. The zinc oxide fume was generated in an electrical furnace, with an aerosol particle size typically below 0.1 µm. In later investigations, the nature of this phenomenon as an inflammatory response of lung tissue was further verified (Blanc et al., 1991, 1993; Kuschner et al., 1995) by documented rises in body temperature, and bronchioalveolar lavage revealing an elevation of tumor necrosis factor and various interleukins, as well as an increase in polymorphonuclear leukocytes. In contrast to the effects seen in inhalation studies in humans with ultrafine aerosols, the acute toxicity of commercially available zinc oxide powder was investigated in rats (4 hours exposure, MMAD 4 µm) with an LC50 > 5.7 mg/l (Klimisch et al., 1982), without any signs of respiratory irritation or any other clinical observations.

Based on particle size dependent respiratory deposition modeling, it was hypothesized that the exposure to ultrafine (< 0.1 µm) zinc oxide aerosols which may freely penetrate to the alveolar fraction of the lung will elicit symptoms of metal fume fever at and above a given concentration, whereas commercial grade zinc oxide powder would not, since this would largely be deposited in the extra-thoracic fraction of the respiratory system, with rapid subsequent translocation to the GI tract.

Thus, a decision was taken to investigate the particle size distribution of zinc oxide aerosols in occupational settings in a range of industries in which the potential for the formation of zinc oxide "fume" was thought to be of quantitative relevance.

The particle size (laboratory determinations) of zinc oxide in comparison to other zinc compounds is shown in Figure 1, indicating a d50 for ZnO of just under 1 µm. However, it should be noted that such

determinations are performed to ensure compliance with technical specifications, usually conducted in an inert solvent with previous ultra-sonification to disaggregate particles, followed by laser diffraction measurements.

It is known that such laboratory particle size assays rarely reflect the particle size in the occupational setting. Thus, a refined attempt was made to assess particle size of airborne zinc oxide in a dustiness test according to the Heubach method. In this system, the test material is mechanically agitated in a rotating drum apparatus with a flow of air directed laterally through the chamber. By equipping the outlet with a cascade impactor, the particle size distribution of any material that becomes airborne can be determined, as shown for zinc oxide in Figure 2.

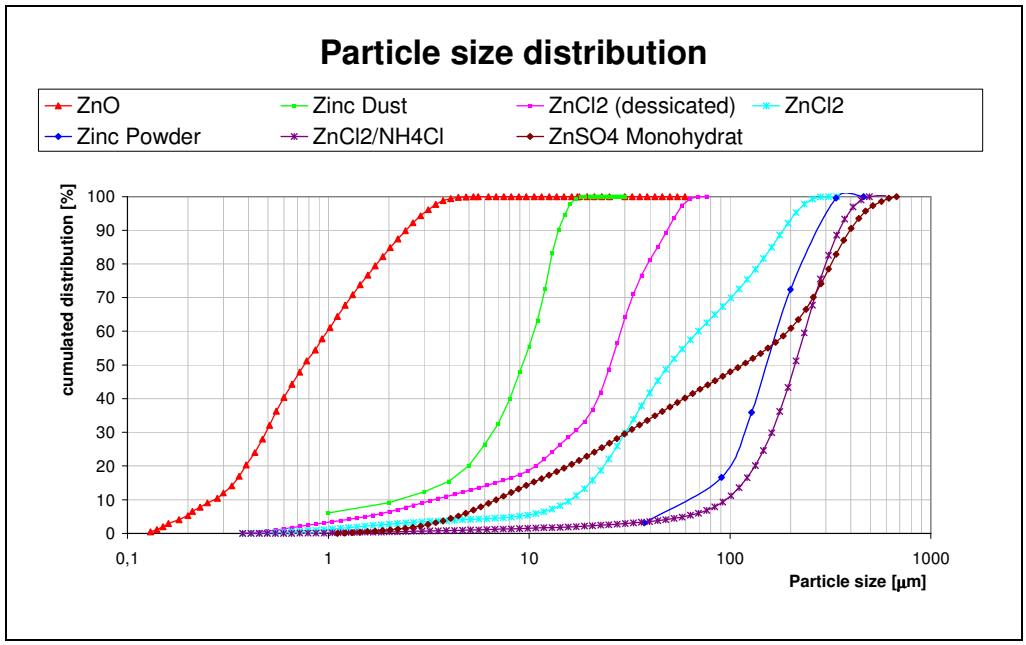


Figure 1: Physical particle size distribution of various zinc compounds

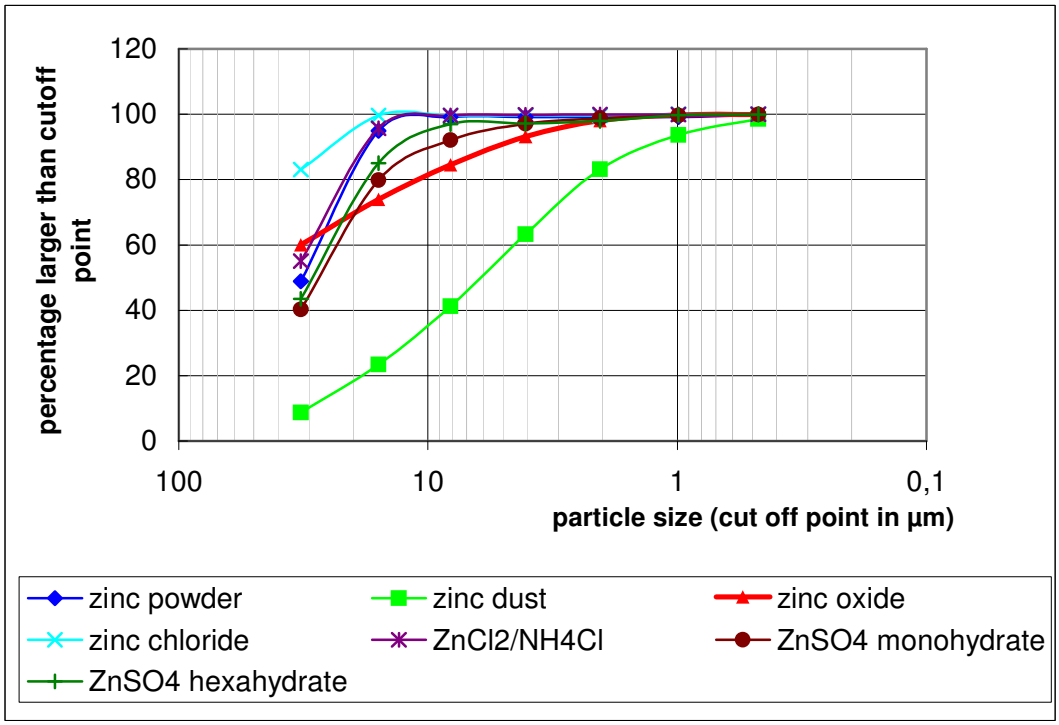


Figure 2: Particle size distribution (Heubach apparatus, plus cascade impactor) of zinc compounds

The results of this analysis show that airborne zinc oxide may be expected to aggregate extensively, since 80 % of the airborne material had particle diameters clearly in excess of 10 µm, with only a negligible amount of fine (< 1 µm) material. In view of the obvious necessity to verify this finding, it was decided to investigate the particle size distribution of zinc particle at the workplace in several industries, which are all characterized by a potential to generate ”fume” in relevant amounts: zinc oxide production, brass casting, hot-dip galvanizing.

Whereas all of these industries operate sophisticated local exhaust ventilation systems, the extent to which workers may be exposed to ultra-fine zinc/zinc oxide aerosols was of prime interest. For this purpose, personal samples (total inhalable fraction) were taken full-shift with the aid of cascade impactors, and analyzed for zinc. The following three figures show an example of the results obtained in each one of the three industries:

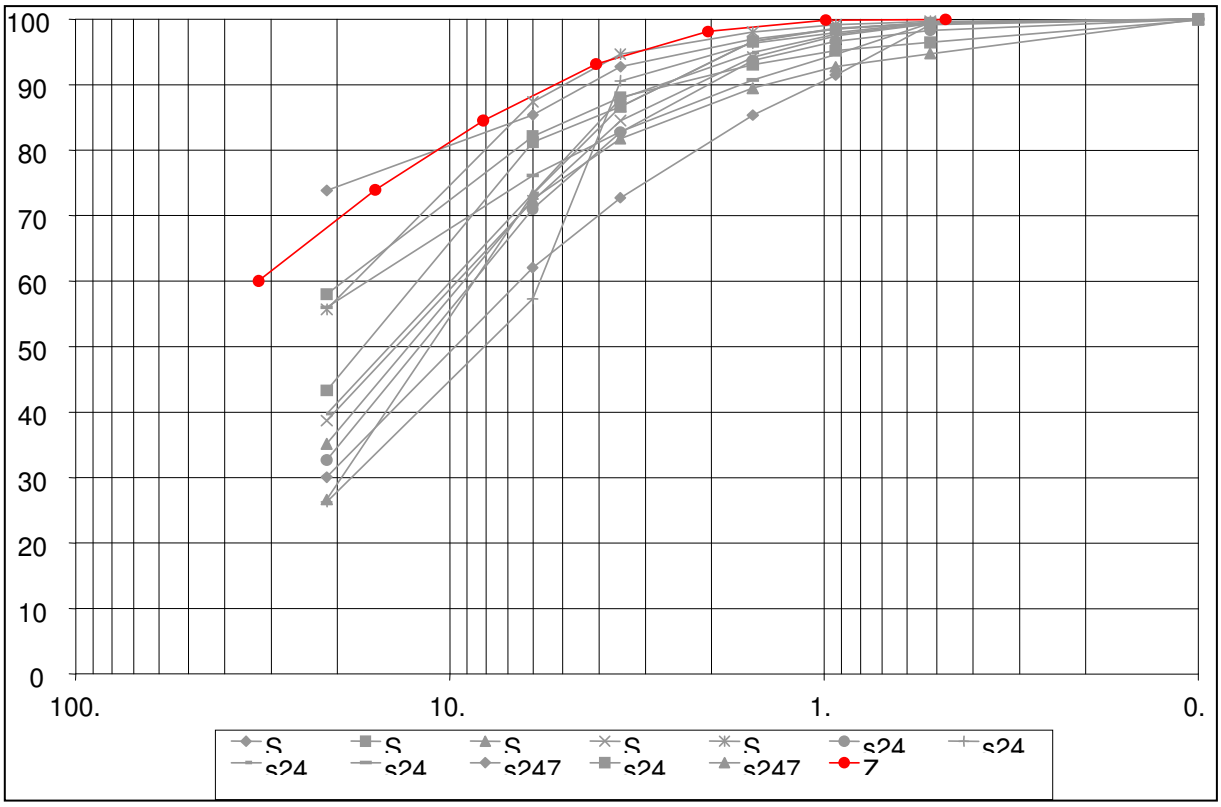


Figure 3: Workplace particle size distributions (personal sampling) of airborne zinc aerosols in one plant of the zinc oxide producing industry (twelve workers sampled).

Discussion

The results show that in all three industries, the bulk of the material present is above 10 µm in particle size, and thus predominantly prone to extra-thoracic deposition. The cumulative particle size patterns show that there is a negligible content (if any) of ultrafine zinc oxide to be expected in the workplace air of these three industries. It is merely noted here that, as a kind of reality check, during the extensive occupational exposure assessment conducted for a wide range of zinc oxide producing and consuming industries, questionnaires were issued to the occupational physicians in these facilities, who reported not a single case of metal fume fever in the past two decades.

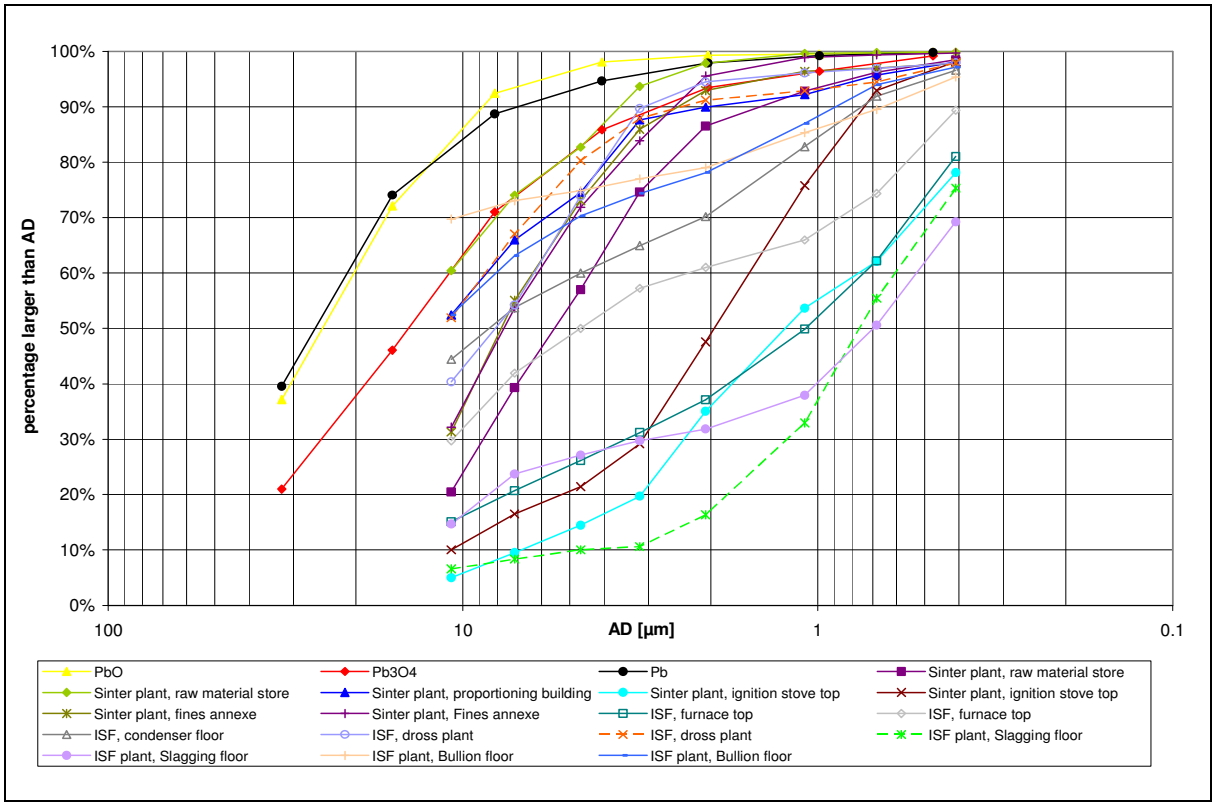
Occupational respiratory effects related to zinc oxide such as metal fume fever (MFF) are elicited by ultrafine zinc oxide particles. It is well-known that MFF occurs primarily in welding/cutting operations, largely due to improper use or omission of respiratory protective equipment (RPE). In contrast, exposure to zinc oxide powder/dust has failed to induce such symptoms in the occupational setting. In

order to more accurately define any such potential occupational health risk, particle size distributions in the laboratory and the workplace were conducted in three major zinc industries. These investigations have shown a negligible exposure of workers in zinc oxide production, brass-casting and hot-dip galvanizing to ultrafine zinc oxide particles. In consequence, the current EU risk assessment report concludes “no risk” of acute toxic effects or respiratory irritation in any of the industries assessed.

A 4.2: Lead (voluntary risk assessment)

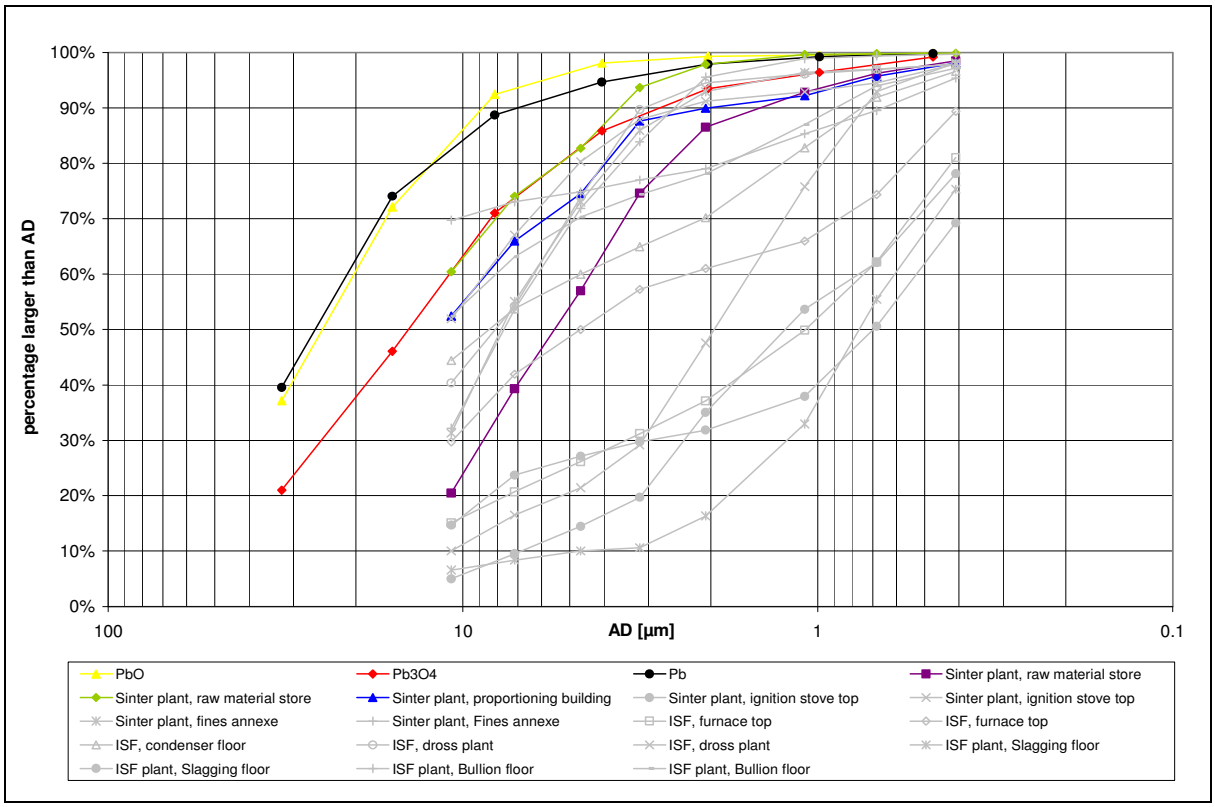
The Voluntary Risk Assessments on Lead contains a wide range of particle size investigations of workplace aerosols, so that reference to this source should be made for further information. Below, merely one example is given from a primary lead smelter (Avonmouth, Harrison & Williams, 1981).

Airborne particulate mater was characterised for particle size distribution at a primary zinc-lead smelter, operating an Imperial Smelting Blast Furnace (ISF, Avonmouth, UK). Sampling was conducted with low and high volume static Andersen cascade impactors with cut-offs ranging from 0.4-10 µm. Subsequent analytical follow-up included AAS and X-ray diffraction for chemical speciation. The workplaces that were monitored included ore storage, various areas of the sinter plant, furnace top, condenser floor, dross plant, slagging floor, bullion floor, and the refinery. The publication presents detailed particle size distributions, chemical speciation (into sulphides, sulphates, and oxides) for each workplace, and MMAD values for each workplace. The authors note that airborne particles were generally much larger than in ambient air outside of the plant (Harrison & Williams, 1981). The figure below contains the particle size distributions for the various locations within the smelter.



Workplace aerosol particle size distributions in a UK ISF-plant

At first sight, it seems that the particle size distributions from the lab are not particularly well correlated to the PS distributions given in this publication. However, considering that most of the measurements represent hot metal processes which are likely to produce smaller particles, and deducting these from the comparison leads to a more consistent picture. Therefore, in the figure below, all distributions which were deemed to represent this kind of processes have been shaded in grey. The remaining particle size distributions which are all related to mechanical processes fit much better to the approach discussed above.



A 4.3: Particle size data for other metals

Detailed particle size investigations have also been undertaken by the Copper, Nickel and Diantimonytrioxide industries for their currently on-going risk assessments. However, both procedures have not yet been finalised, so that these documents are not officially publicly available, and are therefore not further considered here.

Similarly, data on chromium metal had not been released prior to finalisation of this fact sheet.

A 5: Experience from previous RA procedures with relative sampling efficiencies of inhalation monitoring devices

A 5.1: Extract from copper VRA

Different measurement methods and sampling devices are in use across the EU, and several studies have been conducted to determine the performance of widely used sampling heads in relation to EN 481. One of the most extensive studies available investigated the performance of several samplers in collecting near-monodisperse particles while mounted on a manikin in a large scale wind tunnel (Kenny *et. al.*, 1997). In agreement with similar studies, large errors were found for all samplers at high windspeeds (>1.0 m.sec-1) at higher aerodynamic diameters (20-30 µm). Better performance at lower particle sizes was observed for several samplers. Based on this, suggested correction factors for performance in field conditions for each sampler type may be derived.

The open and closed-face 37mm samplers are not designed specifically for size selective sampling and have been adapted from other applications. They are used in methods for "total" dust in the US including total nuisance dust (NIOSH 0500) collected at 1-2 l/min, and for metals in total dust (NIOSH 7300) collected at 1-4 l/min. They are also widely used in Scandinavian countries. Inaccuracies in their use as inhalable samplers occur partly due to aspiration efficiency, arising from inlet geometry/flow rate, and also from electrostatic effects from the non-conductive plastic construction.

Studies employing unmodified open-face 37mm samplers for personal sampling in field conditions indicate much greater deviation from the performance of more accurate alternatives such as the IOM sampler. Data from a wide range of industries are shown in Liden *et al.,* (2000).

Kenny and co-workers acknowledged earlier work showing the disparity between the performance of these samplers in field and laboratory conditions. They refer to a differential of 2-3, broadly consistent with the later findings of Liden et al. (2000), suggesting undersampling in laboratory studies.

Several reasons may explain these differences:

- in the work of Kenny and co-workers, the cassette body was coated with conducting paint in order to minimise electrostatic effects and the study design may therefore have underestimated negative bias in respect of these samplers.
- open-faced 37mm samplers used as purchased do indeed appear to show lower collection efficiencies for particles >10 µm when similarly tested on manikins in wind tunnel experiments (Buchan *et. al.,* 1986).
- in addition, localised air currents in workplace settings may create conditions which are not replicated in wind tunnel experiments and which may exacerbate bias arising from inertial factors.
- conversely, the IOM sampler moderately oversamples particles of all sizes at a windspeed of 0.5 m/sec (Kenny *et al.,* 1997) which is considered most representative of actual windspeeds in workplace conditions. Hence the deviation of the 37mm sampler from the CEN convention may be less marked than comparison with the IOM sampler may suggest.

In conclusion, the open-faced 37mm sampler is assumed to undersample in field conditions by a factor of two. The correction factor of two is based on an approximately median estimate of performance in the field. This correction factor is applied to exposure data submitted for these samplers. This adjustment is considered moderately conservative.

A 5.2: Extract from nickel RAR

Over the years, different aerosol sampling and subsequent analytical procedures have been applied in worker exposure assessment which may compromise a comparison of results. In the workplace or the ambient atmosphere health-related sampling of aerosols should be based on biologically relevant fractions. Three aerosol fractions are defined; the inhalable, thoracic, and respirable fractions (CEN, 1993; ISO, 1992). The inhalable fraction is the mass fraction of airborne particles which is inhaled through the nose and mouth. The thoracic fraction is the mass fraction of inhalable aerosols penetrating beyond the larynx, and the respirable fraction is the mass fraction of inhalable aerosols penetrating to the unciliated airways.

The IOM sampler is the most common for personal sampling of the inhalable fraction. Comprehensive data on the sampling characteristics of the IOM sampler are available (Mark *et al*., 1986; Vincent *et al*., 1990; Mark *et al*., 1994). For comparison of results it is important to establish conversion factors to translate traditional data of 'total' aerosol into inhalable aerosol. Such conversion factors should take into account the design of the 'total' aerosol sampler and the size distribution of the aerosol under consideration. Thus there is no simple relationship from concentrations given as 'total' aerosols to concentrations given as inhalable aerosols. However, it has to be noted that a concentration in terms of inhalable aerosols often is high compared to the concentration of 'total' aerosols due to an insufficient sampling efficiency of a 'total' aerosol sampler.

Recently Kenny *et al*. (1997) summarized technical characteristics of common (statutory or recommended) instruments within Europe for personal sampling of aerosols. The sampling efficiency of the instruments were compared in the laboratory at well defined ambient air velocities (wind tunnel experiments) and the obtained correction factors to obtain satisfactory performance in sampling inhalable aerosols are listed in Table 4.1.1.2.1.1.A. It is noted that the sampling efficiency for many sampler types decreased as wind speed increased. In typical workplaces wind speeds range from 0.04 to 2.02 m/s and have an arithmetic mean value of 0.3 m/s. Therefore, the current inhalable convention, which is based on tests conducted at higher wind speeds (0.5-4.0 m/s) may not fully reflect human inhalability at lower wind speeds (Li *et al*., 2000). In low air movement environments (wind speed less than 0.1 m/s) Aitken *et al*. (1999) found that human inhalability is significantly greater than the current inhalable convention.

Table 4.1.1.2.1.1.A. Correction factors to obtain aerosol concentrations in terms of inhalable aerosols (Kenny et al., 1997)

Sampler type	Manufacturer	Correction factor 0.5 m/s (1)	Correction factor 1.0 m/s (1)
IOM	SKC	0.9	1.0
Seven-hole	Casella, SKC, JS Holdings	1.0	1.2
GSP	Ströhlein	1.0	1.0
PAS-6	University of Wageningen	1.0	1.25
PERSPEC	Lavoro e Ambiente	1.0 (2)	NA (3)
CIP10-I	Arelco	1.15	1.15
37-mm open face	Millipore	1.15	1.15
37-mm closed face	Millipore	1.0	1.2

1): Ambient air velocity; 2): Inlet losses recovered and included in sample; 3): Not available.

It is difficult to simulate workplace conditions in the laboratory. Thus the correction factors listed in Table 4.1.1.2.1.1.A may not be valid to convert 'total' aerosol concentrations into 'inhalable' aerosols. Some workplace comparisons of sampler types have been carried out most extensively for the IOM and 37-mm closed face samplers, the IOM and 37-mm open-face samplers, and the IOM and seven-hole samplers. Limited data are also available comparing the CIP10-I and the IOM samplers. As reviewed by Kenny *et al*. (1997) the field comparisons of IOM and 37-mm samplers (both closed and open face) generally show the IOM samplers collecting 2-3 times as much as the 37-mm sampler in contrast to the factor of 1.2 as listed in Table 4.1.1.2.1.1.A. The comparisons of IOM and seven-hole samplers showed a median IOM/seven-hole ratio of 1.17, and the comparisons of IOM and CIP10-I showed a median IOM/CIP10-I ratio of 1.5. Both of these latter results are reasonably consistent with the data listed in Table 4.1.1.2.1.1.A but are based on a relatively small number of field tests. Recently personal sampling data from comprehensive field studies in the nickel-producing and -using industries

were published (Tsai *et al*., 1995; Tsai *et al*., 1996a; Tsai *et al*, 1996b) in which the closed-face 37-mm filter holder was compared with inhalable aerosol as measured using the IOM sampler. Data were also obtained by an approach of static sampling using mannequins to simulate personal sampling (Tsai & Vincent, 2001). The statistical analysis of the personal sampling results has been summarized (NIPERA, 1996) and the regression results are listed in Table 4.1.1.2.1.1.B for each sampled industry sector. The static sampling results were in good agreement with the personal sampling results for most of the work sites. As already mentioned priority is given to personal sampling and the static sampling results are not further discussed.

Table 4.1.1.2.1.1.B. Comparison between the IOM and the 37-mm samplers. Regression results from each sampled facility process.

Industry sector	Regression results					
	Total aerosol			Total nickel		
Mining	3.64±0.50	N=30	R^2=0.88	3.20±0.48	N=32	R^2=0.86
Milling	2.61±0.46	N=20	R^2=0.88	2.72±0.67	N=21	R^2=0.78
Smelting	1.97±0.23	N=39	R^2=0.89	1.65±0.17	N=35	R^2=0.92
Smelting	2.43±0.69	N=23	R^2=0.71	2.84±0.73	N=23	R^2=0.75
Refining	2.50±0.34	N=37	R^2=0.86	2.12±0.45	N=36	R^2=0.72
nickel alloy production	1.94±0.45	N=45	R^2=0.86	2.29±0.39	N=46	R^2=0.76
Electroplating	2.77±0.44	N=25	R^2=0.87	2.02±0.53	N=21	R^2=0.76
Electroplating	3.29±0.70	N=26	R^2=0.79	3.01±0.93	N=21	R^2=0.70

The values in the table correspond to 'S±standard error' in the relationship $E_{IOM}=S\times E_{37}$; N corresponds to the number of samples analyzed; R^2 corresponds to the regression coefficient.

The nickel data (Table 4.1.1.2.1.1.B) show the levels of 'total' aerosol exposure to be markedly lower than those of inhalable aerosol, with the bias ranging from about 1.7 to 3.2 depending on the industry sector and workplace in question. Consistent with what would be expected from aerosol sampling theory, the observed biases tended to be greater for workplaces where aerosols are coarser.

In this part of the assessment exposure levels measured with the 37-mm closed-face cassette are converted to inhalable aerosols taking into account the conversion factors listed in Table 4.1.1.2.1.1.B. Aerosols as measured with the seven-hole sampler is converted to inhalable aerosols by a factor of 1.17 while aerosols collected with the CIP10-I sampler is converted to 'inhalable' taking into account a conversion factor of 1.5. Aerosols collected with the GSP sampler is considered inhalable. It is recognized that the factor used for the 37-mm closed face cassette is derived from rather solid data (work place sampling in the nickel industry). In contrast the factors used for other types of samplers were derived from work place sampling in other industries or from experiments in the laboratory.

A 6: The use of default breathing rates

For future reference, the recommendations given by the US Environmental Protection Agency and by the International Commission on Radiological Protection on default breathing rates are summarised here using the following sources:

US-EPA, 1997: Exposure Factors Handbook. U.S. Environmental Protection Agency, National Center for Environmental Assessment, Office of Research and Development. Available on the internet: http://www.epa.gov/ncea/exposfac.htm [link checked: 1 March 2006].

ICRP, 1994: ICRP Publication 66: Human Respiratory Tract Model for Radiological Protection. Annals of the IRCP, Volume 24, No. 1-3, p- 23-24.

Recommendations of the United Stated Environmental Protection Agency

The US-EPA addresses factors commonly used in exposure assessment in their Exposure Factors Handbook. Recommended mean values of breathing rates were derived for different sexes, age groups and types of activity. When an activity pattern is known, the short-term breathing rates can be used to calculate an overall breathing volume. If an activity pattern is not available, the long-term (daily) breathing volumes may be used.

Table: Summary of recommended values for inhalation (US-EPA, 1997, Table 5-23)

Long-term Exposures		Short-term Exposures	
Infants		Adults	
<1 year	4.5 m^3/day	Rest	0.4 m^3/hr
Children		Sedentary Activities	0.5 m^3/hr
1-2 years	6.8 m^3/day	Light Activities	1.0 m^3/hr
3-5 years	8.3 m^3/day	Moderate Activities	1.6 m^3/hr
6-8 years	10 m^3/day	Heavy Activities	3.2 m^3/hr
9-11 years			
males	14 m^3/day	Children	
females	13 m^3/day	Rest	0.3 m^3/hr
12-14 years		Sedentary Activities	0.4 m^3/hr
males	15 m^3/day	Light Activities	1.0 m^3/hr
females	12 m^3/day	Moderate Activities	1.2 m^3/hr
15-18 years		Heavy Activities	1.9 m^3/hr
males	17 m^3/day		
females	12 m^3/day	Outdoor Workers	
Adults (19-65+ yrs)		Hourly Average	1.3 m^3/hr
females	11.3 m^3/day	Slow Activities	1.1 m^3/hr
males	15.2 m^3/day	Moderate Activities	1.5 m^3/hr
		Heavy Activities	2.5 m^3/hr

Recommendations of the International Commission on Radiological Protection:

In their handbook on a human respiratory tract model for radiological protection, the ICRP has published default breathing rates for workers and members of the public. The default ventilation rates, which are based on a large dataset, are summarised below.

Table: Ventilation rates in m³/h for a general Caucasian population at different levels of activity (ICRP, 1994)

	Resting	Sitting awake	Light exercise	Heavy exercise
3 month	0.09	-	0.19	-
1 year	0.15	0.22	0.35	-
5 years	0.24	0.32	0.57	-
10 years male	0.31	0.38	1.12	2.22
10 years female	0.31	0.38	1.12	1.84
15 years male	0.42	0.48	1.38	2.92
15 years female	0.35	0.40	1.30	2.57
Adult male	0.45	0.54	1.5	3.0
Adult female	0.32	0.39	1.25	2.7

Two activity patterns (i.e. light and heavy work) are suggested by the ICRP for workers, dividing the day into three 8-hour sections:

1. Sleep: 8 h
2. Non-occupational time: 4 h sitting + 3 h light exercise + 1 h heavy exercise
3a. Occupational time “light worker”: 5.5 h light exercise + 2.5 h sitting
or
3b. Occupational time “heavy worker”: 7 h light exercise + 1 h heavy exercise

Using the ventilation rates for the adult male from the table above, this results in a total volume of air breathed during a whole day of 23 m³ for a “light worker” (3a) and 27 m³ for a “heavy worker” (3b), both figures rounded.

Calculating the volume breathed during the 8 hours of work gives 9.6 m³ for the light worker and 13.5 m³ for the heavy worker. The value of 9.6 m³/8h (rounded to 10 m³/8h) was used for example as the basis of the occupational exposure assessment in the EU RAR on zinc, as well as the VRA on lead and copper RAR (see section 7. of this fact sheet).

A 7: Generic occupational inhalation exposure questionnaire

For the majority of key metals, a large body of data exits that originate form compliance monitoring. In order to make these available for a retrospective analysis, a standardised format has been developed to facilitate the collection of auxiliary information relevant for risk assessment.

Questionnaire structure:

The questionnaire consists of the following three sections, and reflects the minimum core data set of auxiliary information required to qualify a data set as reliable:

Section 1: General company information (self-explanatory)

Section 2: Measurement procedure and strategy (self-explanatory)

Section 3: Workplace specific information

(i) In primary/secondary production, a minimum of three workplace categories are anticipated to exist, namely “raw material handling”, “production” and “packaging/shipping department”. Thus, a separate “section 3” questionnaire sheet should be provided for each workplace. However, further workplace definitions can be developed based on the requirements of the industry being assessed, or in some cases even a subdivision may need to be done depending on the process.

(ii) For downstream user industries, the number of workplace categories may be substantially less than the minimum of three anticipated for the primary/secondary production sector, and usually will be limited to only one process type that is of relevance for exposure.

(iii) For each workplace, several tasks may be applicable and these should be described in detail, especially with respect to their duration and frequency.

(iv) The amounts of material handled per shift/task and the type of material handled or packed are also crucial for a correct assessment. The material workers are exposed to may change during the process, in which case this needs to be noted.

(v) Information on the use of PPE (personal protective equipment) should also be requested as an evaluation of data with and without PPE is probably required.

Section 1: General information

[to be completed in all cases]

Address

Company name:

Address:

Facility identification (where appropriate):
[Note. please provide a section 1 and section 2 sheet for each facility!]

Contact details

Contact person (name, job title):

Phone:

Fax:

Email:

Production details for the facility given above:

Annual operating days:	[days/year]
Number of working days per week	[days/week]
Number of working hours per day	[hours/day]
Number of shifts per day	[shifts/day]
Annual production of the *"substance under investigation"*:	
2001:	[t/year]
2002:	[t/year]
etc…:	[t/year]

Number of employees

Total number:

Involved in production:

Section 2: Measurement procedure and strategy

[to be completed in all cases]

Identification of workplace contaminant to be monitored

Substance identification:
[Chemical Name, CAS number]

Exposure to multiple contaminants: [Yes / No]
[specify which]

Air monitoring

Measurement target:
[indication required whether only one metal (or metal compound) or several substances (co-exposure) are to be considered]

Measurement strategy:
[representative survey; worst-case survey; compliance testing; short-term exposure monitoring; personal or static]

Sampling method or standard:
[e.g. national legislation]

Analytical method:
[e.g. ICP-MS; AAS]

Sampling device:
[the monitoring equipment]

Measured particle size/fraction:
[e.g. total inhalable dust, respirable fraction, PM10]

Unit of resulting concentrations:
[e.g. mg/m³]

Medical biomonitoring

Measurement strategy:
[representative survey; worst-case survey; compliance testing; short-term exposure monitoring]

Sampling method:
[e.g. blood, urine, etc.]

Analytical method:
[e.g. ICP-MS; AAS]

Number of workers monitored:
[e.g. in total, or each month/year. Was one worker monitored repeatedly?]

Sampling frequency:
[measurements/year]

Unit of resulting concentrations:
[e.g. µg substance / dL blood]

Room for comments

Please provide a separate "Section 3" for each workplace

Section 3: *"Workplace"-specific data reporting*

[to be completed if the initial process analysis suggests that any of these factors influence overall exposure]

General information

Task(s) performed by employee	Frequency, Period and Duration
Example "Bag filling"	performed 2 times per day for 10 minutes
Task 1	*[is performed x times a period for x minutes]*
Task 2	*[is performed x times a period for x minutes]*
Task x…	*[is performed x times a period for x minutes]*
Other, minor tasks	*[are performed x times a period for x minutes]*

Type and amount of material handled per task/shift (where relevant):
[eg. kg/8 h]

Size and nature of packaging (where relevant):
[e.g. big bags, IBC, etc.]

Approximate composition of materials workers are exposed to:

Type 1:	(%)
Type 2:	(%)
Others:	(%)

Number of employees at this workplace

Total number of employees:

Number of employees exposed to metal or metal compound:

Number of exposed female employees of child-bearing capacity:

Exposure pattern:
[e.g. intermittent, continuous]

Exposure settings:
[e.g. confined space, open air]

Pattern of exposure control:
[e.g. dilution ventilation, local exhaust ventilation]

Personal protective equipment (PPE) for this workplace

Respiratory protection equipment (RPE)

Pattern of use:
[mandatory, voluntary, nor required? If mandatory: Is there a written PPE programme?]

Face piece:
[e.g. quarter mask, etc.]

Protection class (particles):
[e.g. P1 etc.]

Gloves

Pattern of use:
[mandatory, voluntary, nor required]

Type of glove:
[description]

Comments

Example of a data reporting form

entry	industry sector	workplace	task(s)	St / P	sampling location	workers age	workers sex	sample date	duration	particle size	ID-No.	result / concentration	unit of result	comments
(optional) for future reference: entry into assessors database etc…	*general description of industry*	*workplace descriptor acc. to section 3 of questionnaire*	*task(s) performed by worker or at workplace*	*static or personal sample*	*(optional) further description of sampler location*	*if assignable to the measurement datum*	*if assignable to the measurement datum*	*date at which sample was taken*	*duration of the sample collection in minutes*	*the sampled fraction of particles*	*(optional) e.g. internal sample ID of the reporting company*	*the individual figure *)*	**)*	*(optional) room for further comments*
23/03/2006	Primary lead	furnace	manual filling	p		45	male	29/06/2000	300	respirable	ABXY-1	0.010	mg/m³	
23/03/2006	Primary lead	packing	operating the sacking machine	s	2 m from sacking machine	-	-	18/07/2000	300	inhalable	ABXY-2	0.080	mg/m³	
23/03/2006	Primary lead	foreman office		s		-	-	05/07/2000	301	PM_{10}	2000-01s	0.060	ounces/cubic foot	
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

*) Please specify at the beginning of the table whether the measured value relates to the contaminant in question (e.g. PbO) or to the species chemically analysed (e.g. Pb by AAS)