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# Workplace air — Metals and metalloids in airborne particles — Requirements for evaluation of measuring procedures

*Air des lieux de travail — Métaux et métalloïdes dans les particules en suspension dans l'air — Exigences relatives à l'évaluation des procédures de mesure*

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# Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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This document was prepared by Technical Committee ISO/TC 146, *Air quality*, Subcommittee SC 2, *Workplace atmospheres*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

# Introduction

The health of workers in many industries is at risk through exposure by inhalation of toxic metals and metalloids. Industrial hygienists and other public health professionals need to determine the effectiveness of measures taken to control workers' exposure, and this is generally achieved by taking workplace air measurements. This document has been published in order to make available a method for making valid ultra-trace exposure measurements for a wide range of metals and metalloids in use in industry. It is intended for: agencies concerned with health and safety at work; industrial hygienists and other public health professionals; analytical laboratories; and industrial users of metals and metalloids and their workers.

This document provides a framework for assessing the performance of procedures for measuring metals and metalloids against the general requirements for the performance of procedures for measuring chemical agents in workplace atmospheres as specified in ISO 20581. It enables producers and users of procedures for measuring metals and metalloids in airborne particles to adopt a consistent approach to method validation. See also Annex B.

Although this document has been written for assessing the performance of procedures for measuring metals and metalloids, it can be used as the basis for assessing the performance of procedures for measuring other chemical agents that are present as or in airborne particles, for example, sulphuric acid mist.

This document is based on EN 13890:2009[14], published by the European Committee for Standardization (CEN).

# Workplace air — Metals and metalloids in airborne particles — Requirements for evaluation of measuring procedures

## 1 Scope

This document specifies performance requirements and test methods for the evaluation of procedures for measuring metals and metalloids in airborne particles sampled onto a suitable collection substrate.

This document specifies a method for estimating the uncertainties associated with random and systematic errors and combining them to calculate the expanded uncertainty of the measuring procedure as a whole, as prescribed in ISO 20581.

This document is applicable to measuring procedures in which sampling and analysis is carried out in separate stages, but it does not specify performance requirements for collection, transport and storage of samples, since these are addressed in EN 13205-1 and ISO 15767.

This document does not apply to procedures for measuring metals or metalloids present as inorganic gases or vapours (e.g. mercury, arsenic) or to procedures for measuring metals and metalloids in compounds that could be present as a particle/vapour mixture (e.g. arsenic trioxide).

## 2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 3696, *Water for analytical laboratory use — Specification and test methods*

ISO 7708, *Air quality — Particle size fraction definitions for health-related sampling*

ISO 13137, *Workplace atmospheres — Pumps for personal sampling of chemical and biological agents — Requirements and test methods*

ISO 18158, *Workplace air — Terminology*

ISO 20581:2016, *Workplace air — General requirements for the performance of procedures for the measurement of chemical agents*

EN 13205-1, *Workplace exposure — Assessment of sampler performance for measurement of airborne particle concentrations — Part 1: General requirements*

## 3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 18158 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at https://www.iso.org/obp
- IEC Electropedia: available at http://www.electropedia.org/

### 3.1
**test sample**
sample prepared to meet all specific conditions for a test

[SOURCE: ISO 11323:2010, 5.6]

### 3.2
**test solution**
solution prepared by the process of sample dissolution and, if necessary, having been subjected to any further operations required to bring it into a state in which it is ready for analysis

[SOURCE: ISO 8518:2001, 3.4.4]

## 4 Principle

For measuring procedures that involve sample dissolution, instrumental detection limits (IDLs) are determined by repeat analysis of blank solutions. For all measuring procedures, limits of detection (LOD) and limits of quantification (LOQ) are determined by analysis of laboratory blanks. Typically, the LOD and LOQ are calculated as three times and ten times the standard deviation of blank measurements, respectively. The determined LOQs are then assessed against the performance requirements specified in 5.2.1. Refer to ISO 18158 for definitions of these terms.

Analytical recovery is determined by one of a number of different methods, depending upon the nature of the measuring procedure under evaluation. The determined analytical recovery is then assessed against the performance requirements specified in 5.2.2.

For measuring procedures for soluble compounds of metals and metalloids, analytical recovery is determined by analysis of spiked laboratory blanks (except for procedures that incorporate a design-based sample dissolution method, see A.1.1, for which it is taken to be 100 %).

For measuring procedures for total metals and metalloids that involve sample dissolution, analytical recovery is determined by analysis of pure compounds, reference materials or reference air samples.

For measuring procedures for total metals and metalloids that involve analysis of the sample on the collection substrate, analytical recovery is determined by analysis of reference air samples, by the analysis of workplace air samples that are characterized by subsequent analysis using a reference procedure or it is estimated from theory.

Measurement uncertainty is estimated using a structured approach. Firstly, a cause and effect diagram is constructed to identify individual random and non-random uncertainty components of a measuring procedure. After simplification to resolve any duplication, the resulting diagram is used to identify components for which uncertainty estimates are required. Each of these uncertainty components is then estimated or calculated from experimental data, combined to obtain an estimate of the uncertainty of the measurement method as a whole and multiplied by an appropriate coverage factor to calculate the expanded uncertainty of the method, following the guidance in Annex C. In accordance with 5.2.3, the determined expanded uncertainty is then assessed against the general performance requirements specified in ISO 20581.

NOTE For an example for calculation of expanded uncertainty, see Annex E.

# 5 Requirements

## 5.1 Method description

### 5.1.1 Application range

The application range of the measuring procedure shall give, at minimum, information about the following:

a) the metals and metalloids covered by the measuring procedure;

b) the analytical technique(s) used in the measuring procedure;

c) the range of concentrations of metals and metalloids in air for which the measuring procedure has been shown to meet the acceptance criteria for expanded uncertainty prescribed in ISO 20581, together with the associated recommended sampled air volume (e.g. $0,01 \text{ mg} \cdot \text{m}^{-3}$ to $0,5 \text{ mg} \cdot \text{m}^{-3}$ for a sampled air volume of 960 l);

d) any form of the metals and metalloids for which the sample preparation method described is known to be, or has been shown to be, ineffective;

e) any known interferences.

If there is no procedure for measuring a particular metal or metalloid that meets the requirements of this document, a measuring procedure that gives a performance nearest to the specified requirements should be used.

### 5.1.2 Method performance

For all metals and metalloids included in the application range of the method, the measuring procedure shall give comprehensive information about method performance, including the following:

a) the LOQ and, if required, LODs of the measuring procedure;

b) the analytical recovery for all test materials for which the sample preparation method has been shown to be effective;

c) all random and non-random uncertainty components of the measuring procedure, together with their estimated or experimentally determined values, and the resulting expanded uncertainty;

d) full details of any known interferences, including suitable and sufficient information on how to minimize their effects, if applicable.

### 5.1.3 Safety information

The measuring procedure shall provide suitable and sufficient information on the safety hazards associated with the reagents and equipment used in the procedure.

### 5.1.4 Samplers

The measuring procedure shall:

- require the user to select samplers that are designed to collect an appropriate fraction of airborne particles, as defined in ISO 7708, according to the particle size fraction(s) that is(are) applicable to the OELV for the metals and metalloids of interest (e.g. an inhalable sampler, a thoracic sampler or a respirable sampler);
- specify that the samplers shall conform to the provisions of EN 13205-1;

— require, if appropriate, for procedures that do not involve sample dissolution, that calibration of the analytical instrument to be used [e.g. X-ray fluorescence (XRF) spectrometry] is specific to the sampler to be used.

### 5.1.5 Sampling pumps

The measuring procedure shall require the user to use sampling pumps that conform to the provisions of ISO 13137.

### 5.1.6 Other requirements

Where necessary, the measuring procedure shall give other requirements (e.g. for the collection substrate).

## 5.2 Performance requirements

### 5.2.1 Limit of quantification (LOQ)

For each metal and metalloid included in the application range of the measuring procedure, the lower limit of the working range of the method that will be satisfactory for the intended measurement task shall be determined. For example, if the measurement task is testing compliance with long-term OELVs, Formula (1) is used to calculate the least amount of the metal or metalloid that needs to be quantified when it is to be determined at a concentration of 0,1 times its OELV:

$$m_{\mathrm{low}} = 0{,}1 \rho_{\mathrm{LV}} \cdot q_{\mathrm{v,a}} \cdot t_{\mathrm{s,min}} \quad (1)$$

where

$m_{\mathrm{low}}$ is the lower limit of the required analytical range of the metal or metalloid, in micrograms;

$\rho_{\mathrm{LV}}$ is the OELV for the metal or metalloid, in milligrams per cubic metre;

$q_{\mathrm{v,a}}$ is the design flow rate of the sampler to be used, in litres per minute;

$t_{\mathrm{s,min}}$ is the minimum sampling time that will be used, in minutes.

For procedures that involve sample dissolution, the lower limit of the required working range is calculated for each metal and metalloid, in micrograms per millilitre, by dividing the lower limit of the required working range, in micrograms, by the volume of the test solution, in millilitres. When tested in accordance with 8.1.2.1, the determined LOQs shall be lower than the resulting values.

For procedures that do not involve sample dissolution, when tested in accordance with 8.1.2.2, the determined LOQs for each metal and metalloid shall be lower than the lower limit of the required working range in micrograms.

### 5.2.2 Analytical recovery

When tested in accordance with one of the procedures prescribed in 8.2, the mean analytical recovery shall be at least 90 % for all material types included within the application range of the measuring procedure and the coefficient of variation of the analytical recovery shall be less than 5 %.

NOTE The predecessor term to “coefficient of variation” is “relative standard deviation”, which is deprecated. See also ISO 3534-1:2006, 2.38, Note 2 to entry[1].

### 5.2.3 Expanded uncertainty

The expanded uncertainty of the measuring procedure shall conform to the requirements specified in ISO 20581.

# 6 Reagents and materials

## 6.1 Reagents

During the analysis, only reagents of analytical grade, and only water conforming to the requirements for ISO 3696 grade 2 water (electrical conductivity less than 0,1 mS · m$^{-1}$, i.e. resistivity greater than 0,01 MΩ · m, at 25 °C) may be used.

The water used should be obtained from a water purification system that delivers ultrapure water having a resistivity greater than 0,18 MΩ · m (usually expressed by manufacturers of water purification systems as 18 MΩ · cm water).

## 6.2 Standard solutions

Standard solutions with concentrations of the metals and metalloids of interest that are traceable to national and/or international standards shall be used.

If commercial standard solutions are used, the manufacturer's expiry date or recommended shelf life shall be observed.

## 6.3 Test materials

For each metal or metalloid, a range of test materials shall be used that is representative of the substances of interest that could be present in the workplace atmosphere.

The test materials shall be pure compounds of known composition, certified reference materials (CRMs) or other well-characterized materials (e.g. materials characterized in an interlaboratory comparison).

When using CRMs, the supplier's instructions shall be followed.

If there is an OELV for a specific compound, that compound should be included in the range of reference materials.

For a method that is intended to have general applicability, the range of reference materials should include compounds and materials in industrial use and compounds and materials that could be generated by the work activity.

NOTE 1 It is important that the particle size of the reference materials be as close as possible to that of the particles analysed, since, compared to coarse bulk materials, inhalable particles are often much smaller and more readily soluble.

NOTE 2 CRMs that have been characterized with respect to a particular sample dissolution method might not be suitable for use as a test material.

## 6.4 Reference air samples

Samples of dust on collection substrates (e.g. airborne particles collected on filters using a multiple simultaneous sample collection system) having a known or measured loading of the metal or metalloid of interest shall be used. The loading should be within the working range of the method.

Special techniques for the preparation of reference air samples, as described in A.3, should be considered when sample dissolution is not required.

# 7 Apparatus

Usual laboratory apparatus and resources and, in particular, the following test equipment.

**7.1 A system** for applying a known volume of standard solution to collection substrates with a precision of better than 1 %.

**7.2 An analytical balance** capable of weighing to at least 0,01 mg, calibrated with weights traceable to national standards, checked before use by means of a test weight.

**7.3 An instrument or instruments** for analysing each metal or metalloid of interest.

# 8 Test methods

## 8.1 LOD and LOQ

### 8.1.1 Instrumental detection limit (IDL)

For measuring procedures that involve sample dissolution, analyse the calibration blank solution at least ten times under repeatability conditions.

If there is no measurable response from the analytical instrument, prepare a test solution with concentrations of the metals or metalloids of interest near their anticipated instrumental limits of detection by diluting the standard solutions (6.2) by an appropriate factor. Analyse the test solution at least ten times under repeatability conditions.

NOTE An IDL is of use in identifying changes in instrument performance, but it is not the same as a method LOD. An IDL is likely to be lower than a method LOD because it only takes into account the variability between individual instrumental readings; determinations made on one solution do not take into consideration contributions to variability from the matrix or sample.

### 8.1.2 Method LOD and LOQ

**8.1.2.1** For measuring procedures that involve sample dissolution, prepare at least 10 test solutions from laboratory blanks, following the sample preparation method described in the measuring procedure, and analyse the test solutions for the metals or metalloids of interest under repeatability conditions.

If there is no measurable response from the analytical instrument, spike 10 laboratory blanks with an appropriate volume of working standard solution containing appropriate known masses of the metals or metalloids of interest, such that the test solutions produced from them will have concentrations near their respective anticipated LODs. Prepare test solutions from the spiked laboratory blanks, following the sample preparation method described in the measuring procedure, and analyse the test solutions for the metals or metalloids of interest under repeatability conditions.

Calculate the method LOD and the LOQ for each metal or metalloid of interest as three times and ten times the standard deviation, respectively[22].

**8.1.2.2** For measuring procedures that do not involve sample dissolution, analyse at least 10 laboratory blanks under repeatability conditions.

Calculate the method LOD and the LOQ for each metal or metalloid of interest as three times and ten times the standard deviation, respectively.

**8.1.2.3** Compare the LOQs obtained with the requirements of 5.2.1.

## 8.2 Analytical recovery

### 8.2.1 General

Different test methods are applicable for the determination of analytical recovery, depending on the sample preparation method used. These are detailed separately in 8.2.2, 8.2.3 and 8.2.4. See Annex A for guidance.

### 8.2.2 Measuring procedures for soluble compounds of metals and metalloids

#### 8.2.2.1 Measuring procedures that incorporate a design-based sample dissolution method

Unless there is a contra-indication (see A.1.2), take the analytical recovery to be 100 % for procedures for soluble compounds of metals and metalloids that incorporate a design-based sample dissolution method (see A.1.1).

#### 8.2.2.2 Other measuring procedures

For measuring procedures that do not incorporate a design-based sample dissolution method or for which there could be a problem of chemical compatibility between the analyte and the substrate, prepare a minimum of six replicate test samples by spiking laboratory blanks with an appropriate volume of working standard solution containing a known mass of each metal or metalloid of interest. Then use the sample dissolution method described in the measuring procedure to prepare test solutions from the test samples and analyse the resulting solutions using the analytical method described in the measuring procedure.

Repeat the test on laboratory blanks spiked with other masses of each metal or metalloid of interest to determine the analytical recovery across the working range of the measuring procedure.

Calculate the mean analytical recovery and coefficient of variation for each of the tests performed and compare the results with the requirements of 5.2.2. If the requirements are not met, take corrective measures (e.g. use an alternative collection substrate), if possible, and repeat the analytical recovery test.

### 8.2.3 Measuring procedures for total metals and metalloids that involve sample dissolution

#### 8.2.3.1 Determination of analytical recovery using pure compounds

Prepare a minimum of six test solutions from each of the selected pure compounds (6.3) using the sample preparation method described in the measuring procedure. Use a mass of the pure compound that can be weighed with an accuracy of at least 1 %. Analyse the test solutions as described in the measuring procedure.

NOTE It is usually not necessary to include water-soluble compounds in the range of compounds tested.

It is preferable to use the smallest mass of pure compound that can be easily weighed, to scale up the volume of reagents and to adjust the final test solution volume so that the experiment is as representative as possible of the analysis of workplace air samples.

#### 8.2.3.2 Determination of analytical recovery using reference materials

Carry out the same test procedure prescribed for pure compounds in 8.2.3.1. Use a suitable mass of each of the selected reference materials (6.3), taking into consideration the concentration of each metal or metalloid of interest in the reference material and the supplier's instructions on the minimum amount of material that is required for a homogenous sample.

It is preferable to use the smallest mass of reference material that can be easily weighed, to scale up the volume of reagents and to adjust the final test solution volume so that the experiment is as representative as possible of the analysis of workplace air samples.

#### 8.2.3.3 Determination of analytical recovery using reference air samples

Prepare and analyse test solutions from a minimum of six reference air samples (6.4) using the method described in the measuring procedure.

#### 8.2.3.4 Comparison of results with the acceptance criteria

Calculate the mean analytical recovery and coefficient of variation for each of the tests performed and compare the results with the requirements of 5.2.2. If the requirements are not met for a test material, the analytical recovery test may be repeated using material with a smaller particle size and/or using a larger volume of reagents. If the requirements are still not met, the materials of a type similar to the test material concerned shall be excluded from the scope of the measuring procedure.

### 8.2.4 Measuring procedures that do not involve sample dissolution

#### 8.2.4.1 Experimental determination of analytical recovery

##### 8.2.4.1.1 Reference air samples

Analyse a minimum of six reference air samples (6.4) using the method described in the measuring procedure.

##### 8.2.4.1.2 Workplace air samples

Analyse a minimum of six workplace air samples using the method described in the measuring procedure. Then re-analyse the samples using an independent measuring procedure with known analytical recovery to obtain reference values for each metal or metalloid of interest.

##### 8.2.4.1.3 Comparison of results with the acceptance criteria

Calculate the mean analytical recovery and coefficient of variation for each of the tests performed and compare the results with the requirements of 5.2.2. If the requirements are not met, ensure that the limitations of the measuring procedure are fully described in its application range.

#### 8.2.4.2 Theoretical estimation of analytical recovery

Estimate the analytical recovery by theoretical consideration of the principles of the technique involved and compare results with the analytical recovery requirements of 5.2.2.

NOTE For example, the maximum sample loading for quantitative determination of metals and metalloids in air by X-ray fluorescence spectrometry can be estimated from theory[20].

## 8.3 Measurement uncertainty

### 8.3.1 Identification of random and non-random uncertainty components

See Table B.1 for a list of random and non-random uncertainty components that typically should be considered.

### 8.3.2 Estimation of individual uncertainty components

#### 8.3.2.1 General

For each of the significant uncertainty components identified in 8.3.1, estimate individual uncertainties or calculate them from experimental data as prescribed in 8.3.2.2 to 8.3.2.6, following the guidance given in Annex C.

Where appropriate, convert a range ± $A$, into a non-random uncertainty equal to $A/\sqrt{3}$, assuming a rectangular probability distribution or into a non-random uncertainty equal to $A/\sqrt{6}$, assuming a triangular probability distribution, as appropriate.

#### 8.3.2.2 Uncertainty associated with sampled air volume

Estimate the random and non-random uncertainty components of the sampled air volume, referring to the guidance in C.2.

If the measurement uncertainty is being estimated for the general use of a published method, make a worst-case estimate of the uncertainty components concerned.

If the measurement uncertainty is being estimated for the use of the method under specific conditions (e.g. by a particular organization using particular sampling equipment and a particular sampling protocol), estimate the uncertainty components for the specific equipment concerned (e.g. flow meter, sampling pump, timer), taking account of any specific additional requirements of the sampling protocol (e.g. number of flow rate measurements, sampling time).

#### 8.3.2.3 Uncertainty associated with sampling efficiency

Estimate the random and non-random uncertainty components for aerosol samplers referring to the guidance in C.3.

#### 8.3.2.4 Uncertainty associated with sample storage and transportation

Estimate the non-random uncertainty components associated with sample storage and transportation, referring to the guidance in C.4.

#### 8.3.2.5 Uncertainty associated with analytical recovery

Estimate analytical recovery and the non-random uncertainty components associated with analytical bias, referring to the guidance in C.5.

#### 8.3.2.6 Uncertainty associated with analytical variability

Estimate the random uncertainty components associated with analytical variability referring to the guidance in C.6.

### 8.3.3 Calculation of expanded uncertainty

Calculate the expanded uncertainty of the measuring procedure by combining the random and non-random components of sampling uncertainty and analytical uncertainty (see C.7.1, C.7.2 and C.7.3) and multiplying by a coverage factor of two (see C.8).

## 9 Test report

The test report shall include at least the following:

a) a reference to this document, i.e. ISO 21832;

b) identification of the test laboratory, including brief information concerning any relevant accreditation;

c) identification of the procedure tested;

d) information about the sampling equipment for which the performance of procedure was assessed;

e) information about the reference materials used and, for reference air samples, how they were prepared;

f) a brief description of the analytical method tested, including information about the analytical instruments used;

g) information about which of the test methods prescribed in Clause 8 were followed;

h) a list of the metals and/or metalloids evaluated;

i) information about any operation not included in this document that could have influenced the results;

j) test results;

k) a statement concerning whether the acceptance criteria were met and, if so, over which ranges of concentration of metal or metalloid in air and sampled air volumes;

l) technical justification for omitting any relevant tests.

# Annex A
(informative)

# Guidance on determination of analytical recovery

## A.1 Procedures for soluble compounds of metals and metalloids

**A.1.1** In general, procedures for the determination of soluble compounds of metals and metalloids in workplace air incorporate a design-based sample dissolution method, i.e. soluble compounds of metals and metalloids are defined as such by the specific leach solution and leach conditions prescribed or envisaged for sample dissolution when the corresponding OELVs were set. (For soluble metal and metalloid compounds that have an OELV that does not have an associated prescribed measuring procedure, the sample dissolution procedure prescribed in ISO 15202-2[5] should be used.) This is because, except for compounds that have a very high or very low solubility in water, solubility is dependent upon the nature of the leach solution and other factors, such as particle size, solute/solvent ratio, temperature etc. Consequently, by definition, the analytical method gives 100 % recovery and the analytical bias is zero.

**A.1.2** However, there are circumstances in which procedures for the determination of soluble compounds of metals and metalloids in workplace air can give incorrect results. In particular, results can be incorrect if a soluble compound reacts with the collection substrate, or a contaminant on it, to produce an insoluble compound. For example, a low recovery will be obtained for soluble silver compounds if the filter used is contaminated with chloride[15]. Consideration should, therefore, be given to chemical compatibility when selecting collection substrates for soluble compounds of metals and metalloids. For more information, see ISO 15202-1[4]. If it is believed that there could be a chemical compatibility problem, tests should be performed to confirm that analytical recovery is satisfactory.

## A.2 Procedures that involve sample dissolution

**A.2.1** Most procedures for measuring metals and metalloids in airborne particles involve sample dissolution, for example, procedures in which the analysis is carried out by atomic absorption spectrometry (AAS), inductively coupled plasma–atomic emission spectrometry (ICP–AES) and inductively coupled plasma-mass spectrometry (ICP-MS). The major source of analytical bias for this type of procedure is usually incomplete dissolution of the metals or metalloids of interest. The analytical bias can, therefore, be estimated by testing the effectiveness of the sample dissolution method on a range of suitable, well-characterized bulk materials (e.g. CRMs or pure compounds of the metal or metalloid of interest).

**A.2.2** The analytical method should normally not exhibit a bias. If there are clearly identifiable sample types for which the measuring procedure as a whole is not suitable because the sample dissolution method gives poor recoveries, these should be excluded from the scope of the procedure.

**A.2.3** In some instances, the use of results obtained from the analysis of CRMs and/or pure compounds can lead to an over-estimate of the analytical bias because air samples containing a much smaller amount of material of much smaller particle size are much more readily taken into solution. If this could be the case, it might be possible to obtain a more relevant estimate of analytical bias by repeating the sample dissolution experiments on test filters prepared by generating a homogenous dust cloud from the test material and collecting replicate samples using a multiport sampling device.

## A.3 Procedures that do not involve sample dissolution

Some procedures for measuring metals and metalloids in airborne particles involve analysis of the sample on the collection substrate using a non-destructive technique (e.g. X-ray fluorescence spectrometry). Such measuring procedures can exhibit an analytical bias resulting from physical or chemical differences between the samples and calibration materials. It is, therefore, necessary to design special experiments to test these procedures, or to estimate the analytical bias by theoretical consideration of the processes involved. In some instances, it might be possible to produce test samples suitable for use in estimation of the analytical bias by depositing CRMs or pure compounds on collection substrates in a controlled manner. However, it is necessary to ensure that there are no differences in sample deposition characteristics between the test samples and workplace air samples that could significantly influence results.

# Annex B
(informative)

# Experiments for method validation

Table B.1 gives an example how to perform experiments for method validation of both sampling and analytical methods for metals and metalloids in workplace air in order to fulfil the requirements specified in this document.

**Table B.1 — Method validation example**

| Objective | Analytes[a] | Determination | Number of samples | Requirements |
|---|---|---|---|---|
| Analytical repeatability | Filter spiked with<br>0,1; 0,5; 2 OELV<br>0,5; 2 ST-OELV | Standard deviation | 6 | Coefficient of variation less than 5 % |
| Instrumental detection limit (see 8.1.1) | Blank solutions | Three times standard deviation (blank calibration standard) | ≥ 10 | Total mass of analyte less than 0,03 OELV |
| Limit of detection, limit of quantification (see 8.1.2) | Blank sample solution with filter | Three times (for LOD) and ten times (for LOQ) standard deviation<br>(blank samples or spiked samples at the estimated LOQ) | ≥ 10 | LOQ less or equal than 0,1 OELV |
| Analytical recovery (including particle digestion) (see 8.2) | Filter spiked with<br>0,1; 0,5; 2 OELV<br>0,5; 2 ST-OELV | Pure compounds | ≥ 6 | More than 90 % |
| Reproducibility (including particle digestion) | Filter spiked with 0,1 OELV to 2 OELV | a) Certified reference material (preferred)<br>b) Reference air samples | ≥ 6 | Coefficient of variation less than 5 % |
| Sample storage[b] | Filter spiked with 0,1; 2 OELV | Storage test at least for four weeks | ≥ 3/day | Recovery more than 90 % |

[a] OELV 8h: 0,1; 0,5; 2 OELV for 0,1 OELV × 30 min, 0,5 OELV × 120 min, 2 OELV × 480 min, respectively; ST-OELV: 0,5; 2 ST-OELV for 0,5 ST-OELV × 15 min, 2 ST-OELV × 15 min, respectively.

[b] If necessary, the storage test can be shortened (e.g. for $As_2O_3$, $Cr^{VI}$).

# Annex C
(informative)

# Estimation of uncertainty of measurement

## C.1 General

Methods for measurement of chemical agents in airborne particles involve two major steps: sampling and analysis.

The following is a typical, but non-exclusive, list of random and non-random uncertainty components:

a) sampling:
   1) uncertainty associated with sampled air volume (see C.2);
   2) uncertainty associated with sampling efficiency (see C.3);
   3) uncertainty associated with sample storage and transportation, if any (see C.4);

b) analysis:
   1) uncertainty associated with analytical recovery (see C.5);
   2) uncertainty associated with analytical precision (see C.6.3.1 or C.6.4.1);
   3) uncertainty associated with the calibration (see C.6.3.2 and C.6.3.3 or C.6.4.2 and C.6.4.3);
   4) uncertainty associated with dilution of sample solutions, if applicable (see C.6.3.4 or C.6.4.4);
   5) uncertainty associated with instrument response drift (see C.6.3.5 or C.6.4.5);
   6) uncertainty associated with blank subtraction (see C.6.5).

For additional guidance not contained in this annex, see References [17], [18] and ISO/IEC Guide 98-3[9].

## C.2 Uncertainty associated with sampled air volume

See ISO 20581:2016, C.2.1.

## C.3 Uncertainty associated with sampling efficiency

### C.3.1 General

Each collection stage of a sampler for airborne particles should follow a sampling convention for one of the health-related fractions for the airborne particles, as described in ISO 7708. Aerosol sampling methods have random and non-random uncertainty components that arise from how closely the samplers used match the required sampling convention(s).

EN 13205-2[12] and EN 13205-4[13] describe two test methods to determine whether a sampler collects the required aerosol fraction(s) correctly. In the EN 13205-2[12] method, this is done by determining the mean sampling efficiency curve from the individual values of sampling efficiency of the tested sampler as a function of particle aerodynamic diameter. The sampling efficiency is calculated based on the aerosol concentration determined using samples from the tested sampler divided by ambient aerosol concentration estimated from the isokinetic sampler values for at least nine particle aerodynamic sizes.

In the EN 13205-4[13] method, this is done by comparing the concentration measured by the candidate sampler and that measured by a validated (reference) sampler for at least three test aerosols with widely different particle size distributions. It is not possible to determine the sampling efficiency curve by using the method described in EN 13205-4[13].

### C.3.2 Uncertainty for aerosol samplers tested in accordance with the EN 13205-2 method

#### C.3.2.1 Principle

In this method, sampling efficiency is determined as a function of particle aerodynamic diameter.

#### C.3.2.2 Sources of uncertainty for sampling efficiency

The sampling efficiency has the following sources of uncertainty:

- calibration of sampler test system (see C.3.2.3);
- estimation of sampled aerosol concentration (see C.3.2.4);
- bias relative to the sampling convention (see C.3.2.5);
- flow excursion from the nominal flow rate (for respirable samplers and thoracic samplers) (see C.3.2.6);
- individual sampler variability (for respirable samplers and thoracic samplers) (see C.3.2.7).

#### C.3.2.3 Calibration of sampler test system

In a properly designed and performed experiment, the random and non-random uncertainty components associated with calibration of the sampler test system should be very small. They can be calculated by propagation of errors from the uncertainty of the diameter of the calibration particles (and possibly by the use of calibration functions for particle sizers) to the uncertainty in sampled mass fraction. See EN 13205-2[12] and CEN/TR 13205-3[10].

#### C.3.2.4 Estimation of sampled aerosol concentration

The random uncertainty component associated with the mean sampled aerosol concentration depends on how well the model used for the sampling efficiency describes the sampling efficiency data. For both, the polygonal approximation method and the curve-fitting method described in EN 13205-2[12], it is calculated by propagation of errors as how the uncertainties incorporated in each of these methods translate into the uncertainty of the calculated aerosol concentration. See EN 13205-2[12] and CEN/TR 13205-3[10].

#### C.3.2.5 Bias relative to the sampling convention

The bias variability of the sampled aerosol concentration stems from the difference between the average actual sampling efficiency of the tested sampler and the sampling convention. The non-random uncertainty of the mean sampled aerosol concentration due to the difference of the average sampling efficiency curve of the tested sampler and the sampling convention is calculated as specified in EN 13205-2[12].

#### C.3.2.6 Flow excursion from the nominal flow rate (for respirable samplers and thoracic samplers)

The penetration of samplers for the respirable and thoracic sampling conventions is highly dependent on the sampling flow rate. The non-random uncertainty component associated with flow excursion from the nominal flow rate is calculated from propagation of error in flow rate to variability in sampled mass fraction as specified in EN 13205-2[12]. This uncertainty component incorporates the uncertainty component of the sampled air volume (see C.2).

#### C.3.2.7 Individual sampler variability (for respirable samplers and thoracic samplers)

The random uncertainty component associated with individual sampler variability for respirable samplers and thoracic samplers is calculated in accordance with EN 13205-2[12] from the measured/calculated standard deviations of the aerosol concentration sampled by the test sampler individuals. See also CEN/TR 13205-3[10].

### C.3.3 Uncertainty for aerosol samplers tested in accordance with the EN 13205-4 method

#### C.3.3.1 Principle

In this method, sampling efficiency is determined by comparing the concentration measured by the test sampler and that measured by a validated reference sampler.

#### C.3.3.2 Sources of uncertainty for sampling efficiency

The sampling efficiency has the following sources of uncertainty:

- test aerosol (reference) concentration, as determined using the validated reference sampler(s) (see C.3.3.3);
- reference sampler (see C.3.3.4);
- sampler bias (see C.3.3.5);
- individual sampler variability (for respirable samplers and thoracic samplers) (see C.3.3.6);
- flow excursion from the nominal flow rate (for respirable samplers and thoracic samplers) (see C.3.3.7).

#### C.3.3.3 Test aerosol (reference) concentration, as determined using the validated reference sampler(s)

The random uncertainty component associated with the test aerosol (reference) concentration is determined directly from experimental data, as specified in EN 13205-4[13].

#### C.3.3.4 Reference sampler

The non-random uncertainty component associated with concentration measurements made using the reference sampler is obtained from the reference sampler test report. The random uncertainty component associated with concentration measurements made using the reference sampler is incorporated in the uncertainty of the test aerosol (reference) concentration (see C.3.3.3).

#### C.3.3.5 Sampler bias

The average systematic difference between the tested sampler and the reference sampler has random and non-random uncertainty components. These are calculated as specified in EN 13205-4[13].

#### C.3.3.6 Individual sampler variability (for respirable samplers and thoracic samplers)

The random uncertainty component associated with individual sampler variability can be determined as specified in EN 13205-4[13] if several test samplers of the same type are included in the performance test.

#### C.3.3.7 Flow excursion from the nominal flow rate (for respirable samplers and thoracic samplers)

The penetration for respirable samplers and thoracic samplers is highly dependent on the sampling flow rate. The non-random uncertainty component associated with flow excursion from the nominal flow rate is calculated by propagation of error (flow rate deviation) to variability in sampled mass fraction, as specified in EN 13205-4[13]. This uncertainty component incorporates the uncertainty component of the sampled air volume (see C.2).

## C.3.4 Uncertainty for aerosol samplers

### C.3.4.1 Inhalable samplers

### C.3.4.1.1 Experimental data

Experimental data have been determined for the expanded measurement uncertainty for selected inhalable samplers. They are described in Table C.1.

**Table C.1 — Expanded measurement uncertainty for selected inhalable samplers [Experimental data provided by G. Liden to M. Brisson, private communication, 13 February 2017]**

| Sampler type | Measurement procedure | Flow rate<br>litres· min$^{-1}$ | Expanded uncertainty<br>% |
|---|---|---|---|
| 7-hole | MDHS 14/4 Inhalable Dust[a] | 2,0 | 13,9 |
| IOM | MDHS 14/4 Inhalable Dust[a] | 2,0 | 36,8 |
| GSP | BGIA #7284 Inhalable Dust[b] | 3,5 | 16,2 |
| CIP 10-I | Métropol M-279 Inhalable Dust[c] | 10 | 47,7 |
| FH37-CF | MTA/MA-014/A88 Inhalable Dust,<br>Closed-Face 37 mm Filter Holder[d] | 2,0 | 34,9 |
| FH37-OF | Metodserien #1010 Inhalable Dust,<br>Open-Face 37 mm Filter Holder[e] | 2,0 | 49,5 |

NOTE Data presented in this table are for sampler-only expanded (k = 2) measurement uncertainty exclusive of interlaboratory uncertainty.

[a] UK Health and Safety Executive, http://www.hse.gov.uk

[b] Institut für Arbeitsschutz (IFA), https://www.dguv.de/ifa/index.jsp

[c] Institut National de Recherche et de Sécurité (INRS), http://www.inrs.fr

[d] Instituto Nacional de Seguridad e Higiene en el Trabajo (INSHT), http://www.insht.es

[e] Swedish Work Environment Authority (SWEA), https://www.av.se

### C.3.4.1.2 Estimates for general use

The following estimates of uncertainty components, which are those that were used in the EU project BC/CEN/ENTR/000/2002-16, *Analytical methods for chemical agents,* can be applied for inhalable samplers not listed in Table C.1[19]:

| | |
|---|---|
| — calibration of sampler test system (non-random) | 0,5 %; |
| — estimation of the sampled concentration (random) | 4 %; |
| — bias relative to the sampling convention (non-random) | 7,5 %. |

CEN/TR 15230[11] lists examples of inhalable samplers which were or had been available on the market up to 2004 with the potential to meet the requirements of ISO 7708 and EN 13205-1.

### C.3.4.2 Respirable samplers

#### C.3.4.2.1 Experimental data

Experimental data have been determined for the expanded measurement uncertainty for selected respirable samplers. They are described in Table C.2.

**Table C.2 — Expanded measurement uncertainty for selected respirable samplers [Experimental data provided by G. Liden to M. Brisson, private communication, 13 February 2017]**

| Sampler type | Measurement procedure | Flow rate<br>litres min$^{-1}$ | Expanded uncertainty<br>% |
|---|---|---|---|
| Higgins-Dewell 9.5 Cyclone | BGIA #6068 Respirable Dust HD9.5[a] | 2,0 | 45,8 |
| Higgins-Dewell 9.5 Cyclone | MDHS 14/4 Respirable Dust[b] | 2,2 | 18,8 |
| Higgins-Dewell 9.5 Cyclone | NMAM 0600 Respirable Dust[c] | 2,2 | 18,8 |
| Higgins-Dewell 2.3 Cyclone | BGIA 6068 Respirable Dust HD2.3[a] | 10 | 50,5 |
| Dorr-Oliver DO-10 (Nylon) | MDHS 14/4 Respirable Dust[b] | 1,7 | 23,2[d] |
| Dorr-Oliver DO-10 (Nylon) | NMAM 0600 Respirable Dust[c] | 1,7 | 21,5 |
| GK-26.9 | MDHS 14/4 Respirable Dust[b] | 4,2 | 18,8 |
| CIP 10-R | Métropol M-281Respirable Dust[e] | 10 | 39,4 |

NOTE Data presented in this table are for sampler-only expanded ($k$ = 2) measurement uncertainty exclusive of interlaboratory uncertainty.

[a] Institut für Arbeitsschutz (IFA), https://www.dguv.de/ifa/index.jsp

[b] UK Health and Safety Executive, http://www.hse.gov.uk

[c] US National Institute for Occupational Safety and Health, https://www.cdc.gov/niosh/index.htm

[d] Expanded uncertainty at 0,1 times the OELV is 20,6 %; at 0,5 and 2,0 times the OELV it is 23,2 %.

[e] Institut National de Recherche et de Sécurité (INRS), http://www.inrs.fr

#### C.3.4.2.2 Estimates for general use

The following estimates of uncertainty components can be applied for respirable samplers, not identified in Table C.2, that are optimized for collection of the respirable fraction of airborne particles, as defined in ISO 7708:

| | |
|---|---|
| — calibration of sampler test system (non-random) | 1 % |
| — estimation of the sampled concentration (random) | 1 % |
| — bias relative to the sampling convention (non-random) | 8 % |
| — flow excursion from the nominal flow rate for inertia-based pre-separators, e.g. cyclones and impactors: | |
| (when the sample volume is calculated from the nominal flow rate) | 3 % |
| (when the sample volume is calculated from the average flow rate) | 6 % |
| — individual sampler variability | 7 % |

The estimate for the uncertainty associated with bias relative to the sampling convention given above assumes that the nominal flow rate specified for the sampler is within 5 % of the optimum value for collection of the respirable fraction of airborne particles. CEN/TR 15230[11] lists (without optimum flow rates) examples of respirable samplers which were or had been available on the market up to 2004 with the potential to meet the requirements of ISO 7708 and EN 13205-1.

The non-random uncertainty component associated with flow excursion from the nominal flow rate for inertia-based pre-separators is higher when the sample volume is calculated from the average flow rate than when it is calculated from the nominal flow rate because respirable samplers (based on inertial separation) are largely self-compensating for excursions from the nominal flow rate[23].

The non-random uncertainty component associated with flow excursion from the nominal flow rate for sedimentation-based pre-separators (e.g. a horizontal elutriator) can be calculated from theory.

### C.3.5 Efficiency of collection substrate

#### C.3.5.1 Filter materials

Filter materials should be selected to have high collection efficiency for the particle size range of interest, in which case the uncertainty associated with collection efficiency is negligible. See ISO 15767[7].

#### C.3.5.2 Foams

When a foam is used as the collection substrate, sampling efficiency and collection efficiency are interrelated and no uncertainty components need to be added.

## C.4 Uncertainty associated with sample storage and transportation

### C.4.1 Sample storage

Metals and metalloids and their inorganic compounds are generally stable. However, if desired, the uncertainty associated with sample storage can be estimated by the analysis of replicate samples collected from a test atmosphere using a multiport sampler or prepared by spiking sampling collection media.

Assuming a rectangular probability distribution, the uncertainty associated with sample storage is given by Formula (C.2):

$$u_{st} = \frac{\Delta_{st}}{\sqrt{3}} \tag{C.2}$$

where

$u_{st}$ is the relative standard uncertainty associated with sample storage;

$\Delta_{st}$ is the difference between the mean results of replicate samples analysed immediately after sampling or preparation and replicate samples analysed after the maximum storage time, in per cent.

### C.4.2 Transportation

The transport of aerosol samples normally has a component of uncertainty associated with loss of sample from the collection substrate during transportation. This non-random uncertainty component can be determined from the acceptance criteria for the upper limit of sample loss on transportation, which EN 13205-1 and ISO 15767[7] require is less than 5 %. For methods that are validated in accordance with these standards, the uncertainty component associated with transportation is, therefore, $5/\sqrt{3}$ %, assuming a rectangular probability distribution.

If a measuring procedure specifies a more stringent requirement for the upper limit of sample loss on transportation, or if such a requirement is specified in a sampling protocol that will be used in conjunction with a measuring procedure, the uncertainty component of transportation should be calculated from the acceptable range, assuming a rectangular probability distribution.

If it can reasonably be assumed that there is negligible sample loss on transportation, the uncertainty component of transportation can be disregarded.

## C.5 Uncertainty associated with analytical recovery

### C.5.1 General

Bias is normally eliminated during the development of an analytical method, but this is not always possible. According to ISO/IEC Guide 98-3[9], measurement results should be corrected for bias, if it is significant. However, this is often not practicable in procedures for measurement of metals and metalloids in workplace air samples, since analytical bias can vary with the sample matrix. Analytical bias, therefore, has to be estimated and treated as an uncertainty component.

The non-random uncertainty component of the analytical bias can be estimated from

- results from the analysis of CRMs and/or pure compounds (see C.5.2),
- results from interlaboratory comparisons (see C.5.3),
- results from recovery tests carried out on spiked laboratory blanks (see C.5.4),
- an acceptable bias range (see C.5.5), or

it can be taken to be zero for procedures that incorporate a design-based sample preparation (see C.5.6).

### C.5.2 Analysis of certified reference materials and/or pure compounds

**C.5.2.1** The non-random uncertainty component of the analytical bias can be estimated by determining analytical recovery when the method is tested on well-characterized bulk materials, such as CRMs or pure compounds of the metals and metalloids of interest, which are representative of substances that could be present in workplace air. This can be achieved by replicate analysis of a single CRM or pure compound or, preferably, by replicate analysis of several CRMs and/or pure compounds. The test samples should be analysed in a minimum of five analytical series (e.g. on five different days).

**C.5.2.2** If a single CRM or pure compound is used, the relative standard uncertainty of the analytical bias (non-random) is given by Formula (C.3):

$$u_{\mathrm{ab}} = \sqrt{\left(\frac{B_{\mathrm{a}}}{k}\right)^2 + \frac{\left(K_{\mathrm{v,r}}\right)^2}{n} + \left(u_{\mathrm{cnv}}\right)^2} \qquad \text{(C.3)}$$

where

| | |
|---|---|
| $u_{\mathrm{ab}}$ | is the relative standard uncertainty of the analytical bias, in per cent; |
| $B_{\mathrm{a}}$ | is the bias of the mean result of replicate analyses for the CRM or pure compound from the certified or nominal value, in per cent; |
| $k$ | is the coverage factor used in the calculation of the expanded uncertainty (see C.8); |
| $K_{\mathrm{v,r}}$ | is the coefficient of variation of the replicate samples, in per cent; |
| $n$ | is the number of replicate samples of the CRM or pure compound analysed; |
| $u_{\mathrm{cnv}}$ | is the relative standard uncertainty of the certified or nominal value, in per cent (e.g. a 95 % confidence interval, divided by 1,96 to convert to a standard uncertainty, then divided by the mean result and multiplied by 100 convert it to a relative value). |

**C.5.2.3** If several different CRMs or pure compounds are used, the relative standard uncertainty of the analytical bias (non-random) is, in general, given by Formula (C.4):

$$u_{\mathrm{ab}} = \sqrt{\sum_{i=1}^{n} \frac{\left(B_{\mathrm{a},i}\right)^2}{n} + \left(\bar{u}_{\mathrm{cnv}}\right)^2} \qquad \text{(C.4)}$$

where

$\sum_{i=1}^{n} \frac{\left(B_{\mathrm{a},i}\right)^2}{n}$ is the mean square bias, in per cent, where $B_{\mathrm{a},i}$ is the bias of mean result for the $i^{\mathrm{th}}$ CRM or pure compound analysed and $n$ is the total number of CRMs and/or pure compounds analysed;

$\left(\bar{u}_{\mathrm{cnv}}\right)^2$ is the mean square relative uncertainty of the certified or nominal values of the CRMs and/or pure compounds analysed, in per cent.

### C.5.3 Interlaboratory comparisons

The non-random uncertainty component of the analytical bias can be estimated from the results of interlaboratory comparisons, as described in Reference [18]. However, this approach has limited applicability in the case of measuring procedures for metals and metalloids in workplace air.

Interlaboratory comparison results are generally not useful for estimating the uncertainty of the bias for methods that involve sample dissolution. This is because the test samples used in most interlaboratory comparisons are collection substrates spiked with standard solution and the analysis of such samples does not test the performance of the sample dissolution method in an effective manner. However, in instances when this is not the case (e.g. for interlaboratory comparisons in which the test samples are prepared by the deposition of airborne particles on collection substrates) or in instances for which the effectiveness of sample dissolution is not an issue (e.g. measuring procedures for soluble metals and metalloids) the use of results from interlaboratory comparisons is a good approach for estimating the uncertainty of the analytical bias.

Interlaboratory comparison results can also be used to estimate the uncertainty of the bias for methods that do not involve sample dissolution (e.g. X-ray fluorescence methods), but only if it can be shown that any physical differences between the test samples and workplace air samples will not significantly influence results.

The procedure for estimation of the uncertainty of the analytical bias from interlaboratory comparisons is similar to that used for several different CRMs and pure compounds. To produce a good estimate of the analytical bias, a laboratory should participate at least six times within a reasonable time period.

The relative standard uncertainty of the analytical bias (non-random) is given by Formula (C.5):

$$u_{\mathrm{ab}} = \sqrt{\sum_{i=1}^{n} \frac{\left(B_{\mathrm{a},i}\right)^2}{n} + \left(\bar{u}_{\mathrm{ref}}\right)^2} \qquad \text{(C.5)}$$

where

$\sum_{i=1}^{n}\frac{\left(B_{\mathrm{a},i}\right)^2}{n}$ is the mean square bias, in per cent, where $B_{\mathrm{a},i}$ is the bias of the result for the $i^{\mathrm{th}}$ interlaboratory comparison sample and $n$ is the total number of interlaboratory comparison samples analysed;

$\left(\bar{u}_{\mathrm{ref}}\right)^2$ is the mean square relative uncertainty of the reference value, $\frac{\bar{K}_{\mathrm{v,bL}}}{\sqrt{n}}$, in per cent, where $\bar{K}_{\mathrm{v,bL}}$ is the average between-laboratory coefficient of variation for the interlaboratory comparisons, and $n$ is the average number of participants in the interlaboratory comparisons.

Uncertainty estimates from interlaboratory comparison results are usually a little higher than when results from the analysis of CRMs are used. This is partly because certified values of CRMs are normally better defined than the nominal or assigned values in an interlaboratory comparison.

### C.5.4 Analysis of spiked collection substrates

The non-random uncertainty component of the analytical bias can be estimated from the results of the analysis of spiked collection substrates, in much the same way as results from interlaboratory comparisons. However, this approach is only applicable to methods for which the effectiveness of sample dissolution is not an issue, such as methods for soluble metals and metalloids, and to methods that do not involve sample dissolution, but only if it can be shown that any physical differences between the test samples and workplace air samples will not significantly influence results.

Laboratory blanks should be spiked with known volumes of standard solution containing the analyte or analytes of interest at a number of different spiking levels within the working range of the method. The test samples should be analysed in a minimum of five analytical series (e.g. on five different days).

The relative standard uncertainty of the analytical bias (non-random) is given by Formula (C.6):

$$u_{\mathrm{ab}}=\sqrt{\sum_{i=1}^{n}\frac{\left(B_{\mathrm{a},i}\right)^2}{n}+\left(\bar{u}_{\mathrm{sp}}\right)^2} \quad (C.6)$$

where

$\sum_{i=1}^{n}\frac{\left(B_{\mathrm{a},i}\right)^2}{n}$ is the mean square bias, in per cent, where $B_{\mathrm{a},i}$ is the bias of the mean result for the $i^{\mathrm{th}}$ spiking level from its nominal value and $n$ is the number of spiking levels at which the bias was determined;

$\left(\bar{u}_{\mathrm{sp}}\right)^2$ is the mean square relative uncertainty of the nominal values of the spikes, in per cent.

Provided that the same standard solution is used to spike the sampling media and prepare the calibration solutions, assuming a rectangular probability distribution for the bias of the micropipette and assuming that the effect of temperature on the dispensed volume is negligible, the relative uncertainty of the nominal value of the spike is in turn given by Formula (C.7):

$$u_{\mathrm{sp}}=\sqrt{\frac{\left(B_{\mathrm{max,s}}\right)^2}{3}+\left(u_{\mathrm{p1}}\right)^2} \quad (C.7)$$

where

$B_{\max,s}$ is the maximum bias of the solution volume dispensed by the micropipette used to spike the blank sampling media, in per cent;

$u_{p1}$ is the relative uncertainty of the solution volume dispensed by the micropipette used to spike the blank sampling media, in per cent.

### C.5.5 Acceptable bias range

Some methods that cover a wide range of sample matrices specify an acceptable range for the bias, within which it has to be demonstrated that the method performs when used in a particular laboratory for a particular application [e.g. ISO 15202 (all parts)][4][5][6]. In such instances, the relative standard uncertainty of the analytical bias (non-random) can be estimated from the acceptable range, assuming a rectangular probability distribution, using Formula (C.8):

$$u_{ab} = \frac{B_{\max,m}}{\sqrt{3}} \tag{C.8}$$

where

$u_{ab}$ is the relative standard uncertainty of the analytical bias, in per cent;

$B_{\max,m}$ is the maximum bias specified in the method, in per cent.

### C.5.6 Procedures that incorporate a design-based sample preparation method

The uncertainty of the analytical bias can be taken to be zero for measuring procedures that incorporate a design-based sample preparation method, such as procedures for soluble metals and metalloids in workplace air, since the analytical recovery is by definition 100 % (see A.1).

## C.6 Uncertainty associated with analytical variability

### C.6.1 General

The uncertainty associated with analytical variability can be estimated either from analytical precision data obtained under repeatability conditions (see C.6.3) or from analytical precision data obtained under reproducibility conditions (see C.6.4). In both cases, separate uncertainty estimates need to be made for any sources of systematic error, where applicable (e.g. non-random uncertainty associated with the concentration of the calibration standards) (see C.6.3.2 and C.6.4.2), calibration function (see C.6.3.3 and C.6.4.3), dilution of the sample solution (see C.6.3.4 and C.6.4.4) and instrument response drift (see C.6.3.5 and C.6.4.5).When the analytical precision is determined from laboratory reproducibility data (e.g. using quality control data, most random and randomized uncertainty components are included). See ISO 21748[8] for further guidance.

### C.6.2 Range of sample loadings at which the analytical variability has to be estimated

For each metal and metalloid of interest, the sample loadings for which the analytical variability has to be estimated should be calculated taking into consideration the measurement task for which the performance of the procedure is to be evaluated. These sample loadings should cover sufficient combinations of sampling time and concentration of metal or metalloid in air to provide enough data for the expanded uncertainty to be estimated for the relevant measuring ranges (see ISO 20581).

Tables C.3 and C.4 give the conditions under which analytical variability has to be known for a comprehensive evaluation of the performance of methods for making measurements for comparison with OELVs. However, an abbreviated test can be performed in many instances. In this case, a recommended procedure is to start by considering the two extreme loading levels (given in bold italics in Tables C.3 and C.4) and use the results to estimate the uncertainty of the measuring procedure. If the most stringent ISO 20581 uncertainty requirement is met for both the extreme loading levels then the requirements of ISO 20581 will be met in all cases and no further loading levels need to be considered.

If this is not the case, it will be necessary to test the performance of the measuring procedure at other loading levels until sufficient information is obtained to make a meaningful statement about the sampling times and measuring ranges for which the ISO 20581 requirements are met.

**Table C.3 — Conditions for calculating sample loadings for measurements for comparison with short-term OELVs**

| Sampling time | Concentration of metal or metalloid in air | |
|---|---|---|
| | Low | High |
| 15 min | **0,5 LV × 15 min** | **2 LV × 15 min** |

Sample loadings should be calculated for the nominal flow rate of the samplers used, i.e. the flow rate at which they are designed to collect the intended fraction of airborne particles.

NOTE Other intermediate sample loadings can also be tested, if desired, for example for a sampling time of 4 h or a concentration of 1 LV.

**Table C.4 — Conditions for calculating sample loadings for measurements for comparison with 8 h time-weighted average OELVs**

| Sampling time | Concentration of metal or metalloid in air | | |
|---|---|---|---|
| | Low | Medium | High |
| 30 min | **0,1 LV × 30 min** | 0,5 LV × 30 min | 2 LV × 30 min |
| 120 min | 0,1 LV × 120 min | 0,5 LV × 120 min | 2 LV × 120 min |
| 480 min | 0,1 LV × 480 min | 0,5 LV × 480 min | **2 LV × 480 min** |

## C.6.3 Estimation using repeatability data

### C.6.3.1 Analytical precision

#### C.6.3.1.1 Estimation from data obtained from the analysis of spiked collection substrates

For each of the sample loadings at which the analytical variability is to be determined (see C.6.2), analytical precision can be estimated by spiking six laboratory blanks with an appropriate volume of working standard solution containing a known mass of each metal and metalloid of interest, preparing and analysing the test samples as described in the measuring procedure and calculating the coefficient of variation.

#### C.6.3.1.2 Estimation from data obtained by interpolation of standard deviation

Alternatively, for each of the sample loadings at which the analytical variability is to be determined (see C.6.2), analytical precision can be estimated from data obtained at a particular sample loading or over a range of sample loadings using the interpolation method described in Annex D. This is particularly useful for estimating analytical precision in the case of published methods for which limited method performance data are available.

#### C.6.3.1.3 Estimation from theory

In some instances, it is possible to estimate analytical precision at each of the required sample loadings from theory (e.g. for an XRF method analytical precision can be estimated from counting statistics using experimentally determined sensitivity data).

### C.6.3.2 Calibration standards

#### C.6.3.2.1 Commercial stock standard solutions

**C.6.3.2.1.1** The non-random uncertainty component associated with the concentration of a commercial stock standard solution can be estimated from the range on the certified value provided by the manufacturer. Assuming a rectangular probability distribution, the relative standard uncertainty associated with the concentration of the standard solution is given by Formula (C.9):

$$u_{\mathrm{ss1}} = \frac{B_{\mathrm{max,ss1}}}{\sqrt{3}} \tag{C.9}$$

where

$u_{\mathrm{ss1}}$ is the relative uncertainty associated with the concentration of the commercial stock standard solution, in per cent;

$B_{\mathrm{max,ss1}}$ is the maximum bias of the concentration of the stock standard solution from the confidence interval given on the certificate provided by the manufacturer, in per cent.

**C.6.3.2.1.2** The non-random uncertainty component associated with the concentration of a commercial stock standard solution can be estimated from the 95 % confidence limit of the certified value and the coverage factor provided by the manufacturer. For example, for a stock standard solution of (1 000 ± 3) mg · $\mathrm{l}^{-1}$ the relative standard uncertainty is 0,3 divided by *k*, where *k* is the coverage factor.

#### C.6.3.2.2 Custom-made stock standard solutions

The non-random uncertainty component associated with the concentration of a custom-made stock standard solution can be estimated from the uncertainty of balance used for weighing of the pure compound from which the solution was prepared and the maximum bias of the volumetric flask in which it was prepared, assuming a rectangular probability distribution and that the effect of temperature on the solution volume and the contribution of the uncertainty of the pure compound used is negligible, using Formula (C.10):

$$u_{\mathrm{ss2}} = \sqrt{\frac{\left(K_{\mathrm{v,b}}\right)^2}{3} + \frac{\left(B_{\mathrm{max,f}}\right)^2}{3} + \left(u_{\mathrm{Vf}}\right)^2} \tag{C.10}$$

where

$u_{\mathrm{ss2}}$ is the relative uncertainty associated with the concentration of the custom-made stock standard solution, in per cent;

$K_{\mathrm{v,b}}$ is the coefficient of variation of the balance used to weigh the pure compound used for preparation of the stock standard solution, in per cent;

$B_{\mathrm{max,f}}$ is the maximum bias of the volumetric flask in which the stock standard solution was made from the confidence interval given on the certificate provided by the manufacturer, in per cent;

$u_{\mathrm{Vf}}$ is the relative uncertainty of the volume of volumetric flask, in per cent.

#### C.6.3.2.3 Reference air samples

If reference air samples (see 6.4) are used for calibration in procedures that do not involve sample dissolution, the non-random uncertainty component associated with the sample loadings needs to be taken into account.

### C.6.3.3 Calibration function

The random uncertainty component associated with the calibration function can be calculated from parameters obtained by the least-squares linear regression[16].

A reasonable estimate of the random uncertainty component associated with the calibration function is 2 % is and it may be used in most cases. This was the value used in the EU project BC/CEN/ENTR/000/2002-16, *Analytical methods for chemical agents*[19].

### C.6.3.4 Dilution of sample solutions (if applicable)

If sample solutions are diluted before analysis, it is necessary to take into consideration the random and non-random uncertainty components associated with the dilution process.

The random uncertainty component is the relative uncertainty of the solution volume dispensed by the micropipette used in dilution of the sample solutions, see Formula (C.11):

$$u_{\mathrm{di,r}} = \sqrt{\left(u_{\mathrm{p2}}\right)^2 + \left(u_{\mathrm{Vf}}\right)^2} \tag{C.11}$$

where

$u_{\mathrm{di,r}}$ is the random uncertainty component (of the relative uncertainty) associated with dilution of the sample solutions, in per cent;

$u_{\mathrm{p2}}$ is the relative uncertainty of the solution volume dispensed by the micropipette used in dilution of the sample solutions, in per cent;

$u_{\mathrm{Vf}}$ is the relative uncertainty of the volume of volumetric flask, in per cent.

Assuming rectangular probability distributions for the bias of the micropipette and the volumetric flasks used in dilution of the sample solutions, the non-random uncertainty component associated with dilution of the sample solutions, $u_{\mathrm{di,nr}}$, in per cent, is given by Formula (C.12):

$$u_{\mathrm{di,nr}} = \sqrt{\frac{\left(B_{\mathrm{max,s}}\right)^2}{3} + \frac{\left(B_{\mathrm{max,f}}\right)^2}{3}} \tag{C.12}$$

where

$B_{\mathrm{max,s}}$ is the maximum bias of the solution volume dispensed by the micropipette used in dilution of the sample solutions, in per cent;

$B_{\mathrm{max,f}}$ is the maximum bias of the volumetric flasks used in dilution of the sample solutions according to the manufacturer's specification, in per cent.

### C.6.3.5 Instrument response drift

Methods and laboratory operating procedures generally specify a maximum instrument response drift that is permitted before recalibration (often monitored by repeat analysis of a calibration solution). It is necessary to take this non-random uncertainty component into consideration. Assuming a rectangular probability distribution, the relative standard uncertainty associated with instrument response drift, $u_{\mathrm{dr}}$, in per cent, is given by Formula (C.13):

$$u_{\mathrm{dr}} = \frac{d_{\mathrm{max}}}{\sqrt{3}} \tag{C.13}$$

where $d_{\mathrm{max}}$ is the maximum instrument response drift permitted in the method or laboratory operating procedure, in per cent.

## C.6.4 Estimation using laboratory reproducibility data

### C.6.4.1 Analytical precision

The uncertainty associated with analytical variability can be estimated from laboratory reproducibility data obtained from the analysis of stable quality control samples, normally laboratory blanks spiked with low and high masses of the metals and metalloids of interest (e.g. masses equivalent to 10 % and 90 % of the working range of the measuring procedure). It is important to cover long-term random variations, so the data used should be from the analysis of quality control samples over a period of several months.

The relative standard uncertainty associated with analytical precision is given by Formula (C.14):

$$u_{\mathrm{ap}} = \sqrt{\frac{\left[(n_1 - 1)\times(K_{\mathrm{v,q1}})^2\right] + \left[(n_2 - 1)\times(K_{\mathrm{v,q2}})^2\right]}{(n_1 - 1) + (n_2 - 1)}} \tag{C.14}$$

where

$u_{\mathrm{ap}}$ is the relative standard uncertainty associated with analytical precision, in per cent;

$K_{\mathrm{v,q1}}$ is the coefficient of variation of the results for the first quality control sample, in per cent;

$n_1$ is the number of results for the first quality control sample;

$K_{\mathrm{v,q2}}$ is the coefficient of variation of the results for the second quality control sample, in per cent;

$n_2$ is the number of results for the second quality control sample.

### C.6.4.2 Concentration of calibration standards

See C.6.3.2.

### C.6.4.3 Calibration function

Under reproducibility conditions, the random uncertainty component associated with the calibration function is included in the estimate of analytical precision (see C.6.4.1) and no separate uncertainty estimate is required.

### C.6.4.4 Dilution of the sample solutions (if applicable)

See C.6.3.4.

### C.6.4.5 Instrument response drift

See C.6.3.5.

## C.6.5 Blank subtraction

### C.6.5.1 General

The random uncertainty associated with blank subtraction needs to be included in the uncertainty budget if sample results are blank corrected; or a non-random uncertainty component needs to be included if blank correction is not performed.

#### C.6.5.2 Recalculating of analytical precision to include the random uncertainty associated with blank subtraction

For each of the sample loadings at which the analytical variability is to be determined (see C.6.2), the estimated coefficient of variation (see C.6.3.1 and C.6.4.1) is converted to a standard deviation and combined with the standard deviation of the laboratory blank using Formula (C.15):

$$s'_{\mathrm{x}} = \sqrt{(s_{\mathrm{x}})^2 + \frac{(s_0)^2}{n}} \qquad \text{(C.15)}$$

where

$s'_{\mathrm{x}}$ is the standard deviation of a blank corrected measurement for a mass of analyte, $m_{\mathrm{x}}$;

$s_{\mathrm{x}}$ is the standard deviation of a measurement for a mass of analyte, $m_{\mathrm{x}}$;

$s_0$ is the standard deviation of $n$ blank measurements for a mass of analyte, $m_0$.

For each of the sample loadings, the resulting standard deviation is then converted back into a coefficient of variation to obtain the analytical precision of the blank corrected measurement.

#### C.6.5.3 Non-random uncertainty component associated with no blank subtraction

For each of the sample loadings at which the analytical variability is to be determined (see C.6.2), the estimated coefficient of variation (see C.6.3.1 and C.6.4.1) is converted to a standard deviation and combined with uncertainty of the laboratory blank using Formula (C.16):

$$s''_{\mathrm{x}} = \sqrt{(s_{\mathrm{x}})^2 + \left(\frac{b_{\max}}{\sqrt{3}}\right)^2} \qquad \text{(C.16)}$$

where

$s''_{\mathrm{x}}$ is the standard deviation of a non-blank corrected measurement for a mass of analyte, $m_{\mathrm{x}}$;

$s_{\mathrm{x}}$ is the standard deviation of a measurement for a mass of analyte, $m_{\mathrm{x}}$;

$b_{\max}$ is the maximum value for the laboratory blank permitted in the method or estimated from previous data.

For each of the sample loadings, the resulting standard deviation is then converted back into a coefficient of variation to obtain the analytical precision of the non-blank corrected measurement.

## C.7 Calculation of combined uncertainty

### C.7.1 Random and non-random components of sampling and analytical uncertainty

To calculate the random and non-random components of sampling uncertainty and analytical uncertainty, the relevant individual uncertainty components are combined according to Formulae (C.17) to (C.20):

$$u_{s_{\mathrm{r}}} = \sqrt{\sum_{i=1}^{j_{s_{\mathrm{r}}}} u_{s_{\mathrm{r}i}}{}^2} \qquad \text{(C.17)}$$

$$u_{s_{nr}} = \sqrt{\sum_{i=1}^{j_{s_{nr}}} u_{s_{nri}}{}^2} \qquad (C.18)$$

$$u_{a_r} = \sqrt{\sum_{i=1}^{j_{a_r}} u_{a_{ri}}{}^2} \qquad (C.19)$$

$$u_{a_{nr}} = \sqrt{\sum_{i=1}^{j_{a_{nr}}} u_{a_{nri}}{}^2} \qquad (C.20)$$

where

| | |
|---|---|
| $u_{s_r}$, $u_{s_{nr}}$, $u_{a_r}$ and $u_{a_{nr}}$ | are the random uncertainty associated with sampling, the non-random uncertainty associated with sampling, the random uncertainty associated with analysis and the non-random uncertainty associated with analysis, respectively; |
| $u_{s_{ri}}$, $u_{s_{nri}}$, $u_{a_{ri}}$ and $u_{a_{nri}}$ | are the corresponding relevant individual uncertainty components; |
| $j_{s_r}$, $j_{s_{nr}}$, $j_{a_r}$ and $j_{a_{nr}}$ | are the corresponding numbers of relevant individual uncertainty components. |

### C.7.2 Random and non-random uncertainty of the measuring procedure

The random uncertainty of the measuring procedure as a whole $\left(u_{c_r}\right)$ is calculated according to Formula (C.21):

$$u_{c_r} = \sqrt{u_{s_r}{}^2 + u_{a_r}{}^2} \qquad (C.21)$$

The non-random uncertainty of the measuring procedure as a whole $\left(u_{c_{nr}}\right)$ is calculated according to Formula (C.22):

$$u_{c_{nr}} = \sqrt{u_{s_{nr}}{}^2 + u_{a_{nr}}{}^2} \qquad (C.22)$$

### C.7.3 Combined standard uncertainty of the measuring procedure

The combined standard uncertainty of the measuring procedure ($u_c$) is calculated according to Formula (C.23):

$$u_c = \sqrt{u_{c_r}{}^2 + u_{c_{nr}}{}^2} \qquad (C.23)$$

## C.8 Calculation of expanded uncertainty

The expanded uncertainty of the measuring procedure, $U$, is calculated, using a coverage factor $k = 2$, according to Formula (C.24):

$$U = 2 \times u_c \qquad (C.24)$$