SLOVENSKI STANDARD
SIST-TS CEN/TS 16800:2021

01-april-2021

Nadomešča:
SIST-TS CEN/TS 16800:2016

Smernica za validacijo fizikalno-kemijskih analiznih metod

Guideline for the validation of physico-chemical analytical methods

Anleitung zur Validierung physikalisch-chemischer Analysenverfahren

Lignes directrices pour la validation des méthodes d'analyse physico-chimiques

Ta slovenski standard je istoveten z: **CEN/TS 16800:2020**

ICS:

13.060.50	Preiskava vode na kemične snovi	Examination of water for chemical substances
13.080.10	Kemijske značilnosti tal	Chemical characteristics of soils

SIST-TS CEN/TS 16800:2021 **en**

TECHNICAL SPECIFICATION

SPÉCIFICATION TECHNIQUE

TECHNISCHE SPEZIFIKATION

CEN/TS 16800

December 2020

ICS 13.060.50

Supersedes CEN/TS 16800:2015

English Version

Guideline for the validation of physico-chemical analytical methods

Lignes directrices pour la validation des méthodes d'analyse physico-chimiques

Anleitung zur Validierung physikalisch-chemischer Analysenverfahren

This Technical Specification (CEN/TS) was approved by CEN on 9 November 2020 for provisional application.

The period of validity of this CEN/TS is limited initially to three years. After two years the members of CEN will be requested to submit their comments, particularly on the question whether the CEN/TS can be converted into a European Standard.

CEN members are required to announce the existence of this CEN/TS in the same way as for an EN and to make the CEN/TS available promptly at national level in an appropriate form. It is permissible to keep conflicting national standards in force (in parallel to the CEN/TS) until the final decision about the possible conversion of the CEN/TS into an EN is reached.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.

EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

Ref. No. CEN/TS 16800:2020 E

Contents

Page

European foreword

This document (CEN/TS 16800:2020) has been prepared by Technical Committee CEN/TC 444 “Environmental characterization of solid matrices”, the secretariat of which is held by NEN.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN shall not be held responsible for identifying any or all such patent rights.

This document supersedes CEN/TS 16800:2015.

The main changes compared to the previous edition are listed below:

— the scope has been extended from water only to water and environmental solid matrices, thus the document has been modified accordingly;

— a protocol for spiking of solid matrices has been added in an informative annex.

According to the CEN/CENELEC Internal Regulations, the national standards organisations of the following countries are bound to announce this Technical Specification: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Introduction

Environmental monitoring of chemical substances is increasingly carried out within a European framework, and there is concern about the comparability of data at the European level. Methods used for the monitoring of substances with recent interest have often not been properly validated either in-house (i.e. within a single laboratory) or at the international level.

These issues may be addressed by adopting a harmonized approach towards method development and validation. The main objective of this document is to provide a common European approach to the validation of chemical methods for the respective monitoring of chemical substances in a broad range of matrices. Although the development of this approach was triggered by the needs for monitoring of emerging pollutants, it is of general nature and can be applied to the measurement of the concentration of a wide range of substances in a variety of matrices.

This guidance considers the different requirements for the level of method maturity and validation at different stages of the investigation or regulation of chemical substances.

This protocol will guide the user through the following steps:

— classification of existing methods with respect to their status towards validation, and the selection of the appropriate validation approach;

— development of a method to extend its application; for example, if a method for determining a required target compound in a selected matrix is available, but is not suitable for the same compound in a different matrix of interest;

— the validation procedures to be undertaken to effectively demonstrate the validation status of a selected method according to the approach adopted.

To agree on the use of one method, or several similar methods, in a trans-border or a multi-metrological context, and allow comparison of the results reported by several data producers on the same location (water quality measured on both bank of the same river, or soil composition measured on both sides of a border, or continuity of quality assessment of waste after measurement provider, e.g.), the procedure of establishing the LOQ of the measurement method must be clearly published.

The LOQ may result of:

— statistical evaluation of repeated measurements of a blank sample or a sample with a low concentration of the compound of interest (LOQ);

— experimental verification with a spike matched matrix that the LOQ meets accuracy validation criteria (LOQ-V).

Many (national and international) standards currently contain in their scope a statement like “this method is applicable from a concentration level of xx µg/l or yy mg/kg dry matter”, without any statement how this concentration level was established. When the limit of quantification is evaluated (LOQ) or verified (LOQ-V) using the procedure of this guideline, there is a possibility that it does not meet the lower limit of the claimed range.

Also, the LOQ and LOQ-V might be different depending on the analytical method. Therefore, if criteria are set to the LOQ of a method, it is necessary to clarify if LOQ or LOQ-V is meant.

1 Scope

This document describes an approach for the validation of physico-chemical analytical methods for environmental solid matrices and water.

The guidance in this document addresses the initial description of the method and two different validation approaches, in increasing order of complexity. These are:

a) method development, if the method is developed by the laboratory, or conditions of adoption, if the method is a standardized protocol adopted by the laboratory;

b) validation at the level of single laboratories (within-laboratory validation);

c) method validation at the level of several laboratories (between-laboratory or inter-laboratory validation), with a focus on methods that are sufficiently mature and robust to be applied not only by a few expert laboratories but by laboratories operating at the routine level.

The concept is strictly hierarchical, i.e. a method shall fulfil all criteria of within-laboratory validation before it can enter the validation protocol of the between-laboratory.

This document is applicable to the validation of a broad range of quantitative physico-chemical test methods for the analysis of water (including drinking water, surface water, groundwater, waste water, marine water), and of solid environmental matrices, such as soil, sludge, liquid and solid waste, sediment and biota. It is intended for standardized protocols adopted by a laboratory, and either for test methods aiming at substances that have recently become of interest or for test methods applying recently developed technologies.

The minimal requirements that are indispensable for the characterization of the fitness for the intended purpose of an analytical method are: selectivity, precision, trueness, performances characteristics and measurement uncertainty. The aim of validation is to prove that these requirements are met.

In this document after the definitions (Clause 3) and description of the principles (Clause 4) a toolbox is given describing the relevant performance characteristics in the validation process.

Clause 7 and 8 focus on the within laboratory validation process (V1) and Clause 9 on the interlaboratory validation process (V2). Clause 7 and 8 describe largely the same processes, but differ in approach for establishing the LOQ.

Reporting of the results of the validation studies is addressed in Clause 10.

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/IEC Guide 99:2007, *International vocabulary of metrology — Basic and general concepts and associated terms (VIM)*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO/IEC Guide 99:2007 (VIM) and the following apply.

3.1
accepted reference value
value that serves as an agreed-upon reference for comparison, and which is derived as:

a) a theoretical or established value, based on scientific principles;

b) an assigned or certified value, based on experimental work of some national or international organization;

c) a consensus or certified value, based on collaborative experimental work under the auspices of a scientific or engineering group;

d) when a), b) and c) are not available, the expectation of the (measurable) quantity, i.e. the mean of a specified population of measurements

[SOURCE: ISO 3534-2:2006, definition 3.2.7]

3.2
accuracy
closeness of agreement between a test result and the accepted reference value

Note 1 to entry: The term accuracy, when applied to a set of test results, involves a combination of random components (usually expressed by a precision measure) and a common systematic error or bias component (usually expressed by a measure for trueness).

Note 2 to entry: The technical term "accuracy" should not be confused with the term 'trueness' (see definition of "trueness").

[SOURCE: ISO 3534-2:2006, definition 3.3.1]

3.3
analyte
substance to be analysed (chemical species or physical parameter)

Note 1 to entry: The quantity of an analyte is the measurand (3.15).

3.4
bias
difference between the expectation of a test result or measurement result and a true value

Note 1 to entry: Bias is the total systematic error as contrasted to random error. There may be one or more systematic error components contributing to the bias. A larger systematic difference from the accepted reference value is reflected by a larger bias value.

Note 2 to entry: The bias of a measuring instrument is normally estimated by averaging the error of indication over an appropriate number of repeated measurements. The error of indication is the: "indication of a measuring instrument minus a true value of the corresponding input quantity".

Note 3 to entry: In practice, accepted reference value is substituted for the true value.

[SOURCE: ISO 3534-2:2006, definition 3.3.2]

3.5
blank
sample or test scheme without the analyte known to produce the measured signal

Note 1 to entry: Use of various types of blanks enable assessment of which proportion of the measured signal is attributable to the measurand and which proportion to other causes. Various types of blank are available (see definition of Reagent Blank and Sample Blank).

3.6
calibration
operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication

Note 1 to entry: A calibration may be expressed by a statement, calibration function, calibration diagram, calibration curve, or calibration table. In some cases, it may consist of an additive or multiplicative correction of the indication with associated measurement uncertainty.

Note 2 to entry: Calibration should not be confused with adjustment of a measuring system, often mistakenly called "self-calibration", nor with verification of calibration.

[SOURCE: ISO/IEC Guide 99:2007, definition 2.39]

3.7
certified reference material
CRM
reference material, accompanied by documentation issued by an authoritative body and providing one or more specified property values with associated uncertainties and traceabilities, using valid procedures

[SOURCE: ISO/IEC Guide 99:2007, definition 5.14]

3.8
fitness for purpose
degree to which data produced by a measurement process enables a user to make technically and administratively correct decisions for a stated purpose

3.9
intermediate precision
precision under intermediate precision conditions

[SOURCE: ISO 3534-2:2006, definition 3.3.15]

3.10
intermediate precision conditions
conditions where test results or measurement results are obtained with the same method, on identical test/measurement items in the same test or measurement facility, under some different operating conditions

Note 1 to entry: There are four elements to the operating condition: time, calibration, operator and equipment.

[SOURCE: ISO 3534-2:2006, definition 3.3.16 and ISO 11352:2012, definition 3.10]

3.11
limit of detection
LOD
measured quantity value, obtained by a given measurement procedure, for which the probability of falsely claiming the absence of a component in a material is β, given a probability α of falsely claiming its presence

Note 1 to entry: IUPAC recommends default values for α and β equal to 0,05.

Note 2 to entry: The abbreviation LOD is sometimes used.

Note 3 to entry: The term "sensitivity" is discouraged for 'detection limit'.

Note 4 to entry: The LOD is the lowest concentration of measurand in a sample that can be detected, but not necessarily quantitated under the stated conditions of the test.

[SOURCE: ISO/IEC Guide 99:2007, definition 4.18]

3.12
limit of quantification
LOQ
lowest concentration of a measurand that can be determined with acceptable precision under the stated conditions of the test

Note 1 to entry: as such defined, LOQ is based on evaluation of precision. This does not encompass neither any eventual bias, nor laboratory measurement uncertainty at LOQ level.

3.13
Verified LOQ
LOQ-V

lowest concentration of a measurand that can be determined with acceptable accuracy under the stated conditions of the test

Note 1 entry: LOQ-V is based on the check of a defined level of accuracy of the method at LOQ-V level. Bias and precision have been considered to verify LOQ-V

3.14
reporting limit
RL
specific concentration at or above the limit of quantification that is reported to the client with a certain degree of confidence

Note 1 to entry: The reporting limit is often defined on a project-specific basis. If the reporting limit is set below the limit of quantification by the client, method modification is required

[SOURCE: ISO/TS 13530:2009, 4.4.7]

3.15
linearity
ability of the method to obtain test results proportional to the concentration of measurand

Note 1 to entry: The linear range is by inference the range of measurand concentrations over which the method gives test results proportional to the concentration of the measurand.

[SOURCE: EURACHEM Guide]

3.16
measurand
quantity intended to be measured

Note 1 to entry: The specification of a measurand requires knowledge of the kind of quantity, description of the state of the phenomenon, body, or substance carrying the quantity, including any relevant component, and the chemical entities involved.

Note 2 to entry: In chemistry, "analyte", or the name of a substance or compound, are terms sometimes used for "measurand". This usage is erroneous because these terms do not refer to quantities.

[SOURCE: ISO/IEC Guide 99:2007, definition 2.3]

3.17
measurement
process of experimentally obtaining one or more quantity values that can reasonably be attributed to a quantity

[SOURCE: ISO/IEC Guide 99:2007, definition 2.1]

3.18
measurement uncertainty
non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used

[SOURCE: ISO/IEC Guide 99:2007, definition 2.26]

3.19
outlier
member of a set of values which is inconsistent with the other members of that set

Note 1 to entry: ISO 5725-2 specifies the statistical tests and the significance level to be used to identify outliers in trueness and precision experiments.

[SOURCE: ISO 5725-1:1994, definition 3.21]

3.20
precision
closeness of agreement between independent test results obtained under stipulated conditions

Note 1 to entry: Precision depends only on the distribution of random errors and does not relate to the true value or the specified value.

Note 2 to entry: The measure of precision is usually expressed in terms of imprecision and computed as a standard deviation of the test results. Less precision is reflected by a larger standard deviation.

Note 3 to entry: "Independent test results" means results obtained in a manner not influenced by any previous result on the same or similar test object. Quantitative measures of precision depend critically on the stipulated conditions. Repeatability and reproducibility conditions are particular sets of extreme conditions.

[SOURCE: ISO 3534-2:2006, definition 3.3.4]

3.21
proficiency testing
evaluation of participant performance against pre-established criteria by means of interlaboratory comparisons

[SOURCE: EN ISO/IEC 17043:2010, definition 3.7]

3.22
quality assurance
part of quality management focused on providing confidence that quality requirements will be fulfilled

Note 1 to entry: A major part of quality assurance is quality control.

[SOURCE: EN ISO 9000:2015, definition 3.3.6]

3.23
quality control
part of quality management focused on fulfilling quality requirements

[SOURCE: EN ISO 9000:2015, definition 3.3.7]

3.24
quantity
property of a phenomenon, body, or substance, where the property has a magnitude that can be expressed as a number and a reference

[SOURCE: ISO/IEC Guide 99:2007, definition 1.1]

3.25
working range
interval, being experimentally established and statistically proved by the calibration of the method, between the lowest and highest quantity possibly measured by the method

Note 1 to entry: The lowest possible limit of a working range is the limit of quantification of an analytical method.

3.26
reagent blank
all reagents used during the analytical process (including solvents used for extraction or dissolution) are analysed in isolation in order to check whether they contribute to the measurement signal

Note 1 to entry: The measurement signal arising from the measurand can then be corrected accordingly.

3.27
Analytical recovery
extent to which a known, added quantity of analyte (3.3) in a sample can be measured by an analytical system

Note 1 to entry: Recovery is calculated from the difference between results obtained from a spiked and an unspiked aliquot of sample and is usually expressed as a percentage.

[SOURCE: Adapted from ISO 5667-14:2014, definition 3.8]

3.28
reference material
RM
material, sufficiently homogeneous and stable with respect to one or more specified properties, which has been established to be fit for its intended use in a measurement process

Note 1 to entry: RM is a generic term.

Note 2 to entry: Properties can be quantitative or qualitative, e.g. identity of substances or species.

Note 3 to entry: Uses may include the calibration of a measurement system, assessment of a measurement procedure, assigning values to other materials, and quality control.

Note 4 to entry: ISO/IEC Guide 99:2007[1] has an analogous definition (5.13), but restricts the term "measurement" to apply to quantitative values. However, Note 3 of ISO/IEC Guide 99:2007, 5.13 (VIM), specifically includes qualitative properties, called "nominal properties".

[SOURCE: ISO Guide 30:2015, definition 2.1]

3.29
repeatability
precision under repeatability conditions, i.e. conditions where independent test results are obtained with the same method on identical test items in the same laboratory by the same operator using the same equipment within short intervals of time

[SOURCE: ISO 3534-2:2006, combination of definition 3.3.5 and definition 3.3.6]

3.30
reproducibility

precision under reproducibility conditions, i.e. conditions where test results are obtained with the same method on identical test items in different laboratories with different operators using different equipment

[SOURCE: ISO 3534-2:2006, combination of definition 3.3.10 and definition 3.3.11]

3.31
residual
difference between the observed response and that predicted by a calibration function

3.32
robustness
measure of capacity of a procedure to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage

3.33
sample
totality of a homogeneous analysis material with an identical composition or quality (similar to term batch)

[SOURCE: ISO/TS 20612:2007, definition 3.3]

3.34
blank sample
matrix with no measurand

Note 1 to entry: They are difficult to obtain but such materials are necessary to give a realistic estimate of interferences that would be encountered in the analysis of test samples.

3.35
selectivity
ability of a method to determine accurately and specifically the measurand of interest in the presence of other components in a sample matrix under the stated conditions of the test

3.36
sensitivity
change in the response of a measurand divided by the corresponding change in the stimulus

3.37
traceability
property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty

[SOURCE: ISO/IEC Guide 99:2007, definition 2.41]

3.38
trueness
closeness of agreement between the average value obtained from a large series of test results and an accepted reference value

Note 1 to entry: In the present document, trueness will be expressed in terms of bias.

Note 2 to entry: Trueness should not be confused with the term 'accuracy' (see definition of "accuracy").

3.39
validation
verification, where the specified requirements are adequate for an intended use

Note 1 to entry: This process is used to asses that a method is fit for its intended purpose. It includes:

— establishing the performance characteristics, advantages and limitations of a method and the identification of the influences which may change these characteristics, and the extent of such changes;

— a comprehensive evaluation of the outcome of this process with respect to the fitness for purpose of the method.

[SOURCE: ISO/IEC Guide 99:2007, definition 2.45]