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Milk — Definition and evaluation of the overall accuracy of alternative methods of milk analysis —

Part 1: Analytical attributes of alternative methods

Lait — Définition et évaluation de la précision globale des méthodes alternatives d'analyse du lait —

Partie 1: Attributs analytiques des méthodes alternatives

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

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

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

ISO 8196-1|IDF 128-1 was prepared by Technical Committee ISO/TC 34, *Food products*, Subcommittee SC 5, *Milk and milk products*, and the International Dairy Federation (IDF). It is being published jointly by ISO and IDF.

This second edition of ISO 8196-1|IDF 128-1 cancels and replaces the first edition (ISO 8196-1:2000) which has been technically revised.

ISO 8196|IDF 128 consists of the following parts, under the general title *Milk — Definition and evaluation of the overall accuracy of alternative methods of milk analysis*:

— *Part 1: Analytical attributes of alternative methods*

— *Part 2: Calibration and quality control in the dairy laboratory*

— *Part 3: Protocol for the evaluation and validation of alternative quantitative methods of milk analysis*

Foreword

IDF (the International Dairy Federation) is a non-profit organization representing the dairy sector worldwide. IDF membership comprises National Committees in every member country as well as regional dairy associations having signed a formal agreement on cooperation with IDF. All members of IDF have the right to be represented at the IDF Standing Committees carrying out the technical work. IDF collaborates with ISO in the development of standard methods of analysis and sampling for milk and milk products.

The main task of Standing Committees is to prepare International Standards. Draft International Standards adopted by the Action Teams and Standing Committees are circulated to the National Committees for voting. Publication as an International Standard requires approval by at least 50 % of IDF National Committees casting a vote.

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All work was carried out by the Joint IDF-ISO Action Team on *Automated methods* of the Standing Committee on *Quality assurance, statistics of analytical data and sampling* under the aegis of its project leader, Mr. O. Leray (FR).

This edition of ISO 8196-1|IDF 128-1, together with ISO 8196-2|IDF 128-2 and ISO 8196-3|IDF 128-3, cancels and replaces IDF 128:1985, which has been technically revised.

ISO 8196|IDF 128 consists of the following parts, under the general title *Milk — Definition and evaluation of the overall accuracy of alternative methods of milk analysis*:

— *Part 1: Analytical attributes of alternative methods*

— *Part 2: Calibration and quality control in the dairy laboratory*

— *Part 3: Protocol for the evaluation and validation of alternative quantitative methods of milk analysis*

Introduction

The main purpose of this part of ISO 8196|IDF 128 is to provide definitions of the relevant performance characteristics for quantitatively evaluating the overall accuracy of an analytical method, through the application of proper experimental designs and recommended statistical procedures.

Performance characteristics of an analytical method can be defined as a set of quantitative and experimentally determined values, or criteria, of fundamental importance in assessing the suitability of a method for any given purpose. The general concepts apply to all analytical methods, but special emphasis is given to rapid physico-chemical methods which are currently in use for compositional testing of milk.

In analytical methods where measurements result from combinations of multiple output signals of measurement channels either in series or in parallel (e.g. methods in which multivariate mathematical models are applied), the process of combining the primary raw information is considered as a full part of the method itself. For the purpose of ISO 8196|IDF 128 (all parts), this process is considered as a closed device ("black box"). As such, this process is assumed to be optimized prior to the assessments and evaluations done within the scope of ISO 8196|IDF 128 (all parts).

ISO 8196-2|IDF 128-2 provides practical details and recommendations for the calibration of instruments and quality control in routine dairy laboratories including checking compliance with a specification value or limit.

ISO 8196-3|IDF 128-3 is intended to complement this part of ISO 8196|IDF 128 as an alternative to the evaluation of new methods to which this part of ISO 8196|IDF 128 cannot apply, e.g. when the organization of interlaboratory studies is hampered by the number of new instruments available, which is too small for such a protocol.

While this part of ISO 8196|IDF 128 and ISO 8196-3|IDF 128-3 are mainly intended for experts to assess new methods of analysis, ISO 8196-2|IDF 128-2 aims to be a guide for routine laboratories using these methods.

ISO 8196|IDF 128 (all parts) only specifies the single linear regression model as a simplified approach to allow users to determine equivalence of an alternative method with a reference method. However, the linear regression approach is valid as a determination of method equivalence only in limited circumstances or if a high correlation between the results of the reference method and the routine method is achieved. If a high correlation is not achieved, recourse should be made to other data handling and measurement error modelling techniques. Although these techniques are referred to, they are not specified in ISO 8196|IDF 128 (all parts).

Milk — Definition and evaluation of the overall accuracy of alternative methods of milk analysis —

Part 1: Analytical attributes of alternative methods

1 Scope

This part of ISO 8196|IDF 128 specifies various performance characteristics that constitute and serve to characterize the overall accuracy of an analytical method. It furthermore establishes general principles for the design of experiments and gives guidelines for the procedures to be used to evaluate these characteristics quantitatively.

2 Normative references

The following referenced documents are indispensable for the application 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 3534 (all parts), *Statistics — Vocabulary and symbols*

ISO 5725 (all parts), *Accuracy (trueness and precision) of measurement methods and results*

3 Terms and definitions

For the purposes of this part of ISO 8196|IDF 128, the terms and definitions given in ISO 3534 (all parts) and ISO 5725-1 apply, together with the following.

3.1 General terms and definitions

3.1.1
true quantity value
true value of a quantity
true value
quantity value consistent with the definition of a quantity

NOTE 1 In the Error Approach to describing measurement, a true quantity value is considered unique and, in practice, unknowable. The Uncertainty Approach is to recognize that, owing to the inherently incomplete amount of detail in the definition of a quantity, there is not a single true quantity value but rather a set of true quantity values consistent with the definition. However, this set of values is, in principle and in practice, unknowable. Other approaches dispense altogether with the concept of true quantity value and rely on the concept of metrological compatibility of measurement results for assessing their validity.

NOTE 2 In the special case of a fundamental constant, the quantity is considered to have a single true quantity value.

NOTE 3 When the definitional uncertainty associated with the measurand is considered to be negligible compared to the other components of the measurement uncertainty, the measurand may be considered to have an "essentially unique" true quantity value. This is the approach taken by ISO/IEC Guide 98-3:2008[3] and associated documents, where the word "true" is considered to be redundant.

[ISO/IEC Guide 99:2007[4], 2.11]

3.1.2
reference method
anchor method
method of analysis internationally recognized by experts or by agreement between the parties

NOTE 1 Adapted from ISO 21187|IDF 196:2004[1], 3.2.

NOTE 2 A reference method gives the "true value" or "assigned value" of the quantity of the measurand.

3.1.3
alternative method
routine method
method of analysis allowing quantification of the status of a test sample

NOTE 1 Adapted from ISO 21187|IDF 196:2004[1], 3.1.

NOTE 2 An alternative method demonstrates or estimates, for a given category of products, the same measurand as determined using the corresponding **reference method** (3.1.2).

NOTE 3 The alternative method can be either an indirect method — i.e. one not measuring directly the component or the characteristic that it is intended to quantify, but instead one or more quantities or properties which are functionally linked to that component — or a direct method. It can have specific adaptations for user convenience (e.g. speed, automation, miniaturization, cost) that can introduce deviation into the analytical process (e.g. incomplete component or characteristic measurement) and thus prevent direct estimation and give different accuracy.

3.2 Terms and definitions on precision

3.2.1
precision
closeness of agreement between independent test/measurement results obtained under stipulated conditions

[ISO 3534-2:2006, 3.3.4]

3.2.2
repeatability limit
r
value less than or equal to which the absolute difference between two final values, each of them representing a series of test results or measurement results obtained with the same method on identical test/measurement items in the same test or measuring facility by the same operator using the same equipment within short intervals of time, is expected to be for a specified probability of 95 %

NOTE Adapted from ISO 3534-2:2006, 3.3.6, 3.3.8, 3.3.9.

3.2.3
reproducibility limit
R
value less than or equal to which the absolute difference between two final values, each of them representing a series of test results or measurement results obtained with the same method on identical test/measurement items in different test or measuring facilities with different operators using different equipment, is expected to be for a specified probability of 95 %

NOTE Adapted from ISO 3534-2:2006, 3.3.11, 3.3.13, 3.3.14.

3.3 Terms and definitions on accuracy

The terms and definitions on accuracy apply specifically to indirect alternative methods for the purpose of this part of ISO 8196|IDF 128.

3.3.1
accuracy
closeness of agreement between a test result or measurement result and the **true value** (3.1.1)

NOTE 1 In practice, the accepted reference value is substituted for the true value.

NOTE 2 The term accuracy, when applied to a set of test or measurement results, involves a combination of random components and a common systematic error or bias component.

NOTE 3 Accuracy refers to a combination of **trueness** (3.3.2) and **precision** (3.2.1).

[ISO 3534-2:2006, 3.3.1]

3.3.2
trueness
closeness of agreement between the expectation of a test result or a measurement result and a **true value** (3.1.1)

NOTE 1 The measure of trueness is usually expressed in terms of bias.

NOTE 2 Trueness is sometimes referred to as "accuracy of the mean". This usage is not recommended.

NOTE 3 In practice, the accepted reference value is substituted for the true value.

[ISO 3534-2:2006, 3.3.3]

3.3.3
exactness of calibration
closeness of agreement, at each level of the measurand, between an alternative method value and the estimated average true value for all individual samples at the corresponding level

3.3.4
accuracy of estimate
closeness of agreement between the average test result obtained by the reference method and an alternative method on identical materials, provided that the calibration of the alternative method is exact

NOTE Accuracy of estimate measures the part of the systematic error not due to error in calibration.

3.4 Other analytical characteristics

3.4.1
selectivity
property of a method to respond exclusively to the characteristic or analyte to be measured, or degree to which a method can quantify that characteristic or analyte accurately in the presence of interferents

NOTE As a general principle, selectivity is sufficiently good for any interference to be ignored. Selectivity contributes to trueness.

3.4.2
sensitivity
smallest change in concentration which can be measured by an analytical procedure

NOTE Sensitivity is calculated as the ratio of the variation of the method response to the variation of analyte concentration. As this is usually arbitrary, depending on instrumental settings, it is not useful in validation. However, it may be useful in quality assurance procedures to test whether an instrument is performing to a consistent and satisfactory standard.

3.4.3
limit of detection
LOD
minimum amount or concentration of the analyte in a test sample which can be detected reliably but not necessarily quantified, as demonstrated by a collaborative trial or other appropriate validation

[ISO 24276:2006[2], 3.1.6]

NOTE For instrumental methods, sensitivity and limit of detection are usually determined by the sensitivity of the detector and the signal/noise ratio.

3.4.4
limit of determination
limit of quantitation
LOQ
〈analytical procedure〉 lowest concentration or amount of the analyte in a test sample which can be quantitatively determined with an acceptable level of precision and accuracy, as demonstrated by a collaborative trial or other appropriate validation

[ISO 24276:2006[2], 3.1.7]

4 Explanation of the definitions

4.1 Accuracy — General description

The concept applies mainly to the test result of an alternative method calibrated against the accepted value of the reference method or standard material, or when the true value of the component concentration is known.

The accuracy is an index indicating a value of the amount of errors involved, and is ordinarily expressed as the error associated with the method used and calculated under appropriate conditions.

When a single quantitative measurement, x_i, of a specific measurand (or variable) is made with a given method of analysis, that measurement is always an estimate of its true value, μ. The error of the method is given by the difference, $x_i - \mu$. The accuracy is best when the difference, $x_i - \mu$ is the smallest.

Basically, the aforementioned difference depends on the following major analytical characteristics of the method:

a) precision;

b) trueness;

c) selectivity;

d) sensitivity;

e) limit of detection and limit of determination.

Only the precision and the trueness are considered in this part of ISO 8196|IDF 128.

4.2 Precision

4.2.1 General description

Precision is a general characteristic applicable to all analytical methods. Basically, it covers all types of fortuitous and random errors which cannot be completely avoided and whose main characteristics vary from one test to another (volume delivered by a pipette, environmental conditions, stability of an instrument, electronic noise, etc.). Mistakes, such as misreading or operational failings or, more generally, any value found as outlier with the appropriate tests but worth considering, are not included in precision data.

Obviously, the variability between test results is small when tests are performed within a laboratory under repeatability conditions. It is larger when tests are performed by different laboratories under reproducibility conditions. The latter may be expressed as interlaboratory reproducibility, when only variability is considered.

In order to give quantitative measures of the variability between results under these two extreme situations, precision is expressed in terms of repeatability and reproducibility. Many intermediate conditions are conceivable, e.g. day-to-day variations, between-instrument or operator variations within the same laboratory. Results obtained using different operators and different equipment within the same facility can be used to calculate intra-laboratory reproducibility. Repeatability and reproducibility have been found to deal with most practical cases.

In practice:

a) two single test results obtained within a laboratory under repeatability conditions should be considered suspect if they differ by more than the repeatability limit, r;

b) two single test results obtained by two laboratories under reproducibility conditions should be considered suspect if they differ by more than the reproducibility limit, R.

4.2.2 Mathematical expressions

Derived from the analysis of variance (ANOVA) for data obtained through an interlaboratory trial (see 5.2), the repeatability and reproducibility of a method are expressed for a given range of concentrations of the analyte by:

a) the standard deviation of repeatability, σ_r;

b) the standard deviation of reproducibility, σ_R.

Use of the coefficient of variation, C_V, expressed as a percentage, and given by

$$C_V = \frac{\sigma}{\mu} \times 100 \tag{1}$$

where

σ is the standard deviation;

μ is the mean;

is only recommended whenever the standard deviation varies proportionally with the level of the measurand.