codex alimentarius commission

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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Agenda Item 4 **CX/MAS 05/26/6**
March, 2005

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON METHODS OF ANALYSIS AND SAMPLING
Twenty-sixth Session
Budapest, Hungary, 4-8 April 2005

REVIEW OF THE *ANALYTICAL TERMINOLOGY FOR CODEX USE* IN THE PROCEDURAL MANUAL

GOVERNMENT COMMENTS AND RECOMMENDATIONS OF INTERSESSION WORKING GROUP

BACKGROUND

At the Twenty-fourth Session of the Codex Committee on Methods of Analysis and Sampling, it was agreed to initiate the revision of the definitions contained in the Codex Procedural Manual (Analytical Terminology for Codex Use) (ALINORM 03/23, para. 95). This was approved by the 26th Session of the Commission as new work (ALINORM 03/41, para. 138-140 and Appendix VIII).

At the Twenty-fifth Session of CCMAS, some delegations stressed the need to have only one set of clearly defined, harmonized definitions for Codex use and to establish different definitions only if they were necessary. It was indicated that international definitions contained in ISO or IUPAC documents were being revised; therefore, it was necessary to have cross references in order to ensure consistency. It was also proposed to add new definitions to the Codex Procedural Manual. The definitions for Result, Specificity, Selectivity, Accuracy, and Trueness were modified by the committee and their amended definitions are presented in Appendix II of the meeting summary (Alinorm 04/27/23).

The Twenty-fifth session of the Codex Committee on Methods of Analysis and Sampling (Alinorm 04/27/23) agreed to have an *ad hoc* intersession working group develop this paper on definitions of analytical terminology for use in the Codex Procedural Manual. This working group was chaired by the United States and consisted of representatives from Austria, Brazil, the European Community and the AOAC. A circular letter (CL 2004/37) was distributed to Codex members requesting their comments on both the current definitions of analytical terms and any suggestions for additional analytical terms that should be included in the Codex Procedural Manual. In order to facilitate the comments, a 2002 compendium entitled "Harmonization of analytical terminology in accordance with international standards", which includes Codex definitions and those from other international organizations was included in the CL. This compendium was originally prepared to facilitate discussions on the harmonization of analytical terminology by the chairman of the Inter-Agency Meeting on Methods of Analysis and Sampling. The IAM paper contained a comprehensive list of analytical terms with multiple comparative definitions for each term.

Comments in response to CL 2004/37 were received from Brazil, the European Community, Switzerland and the United States and are included in Appendix I. These comments were reviewed and a list of proposed new terms and revisions to the current analytical terminology in the Procedural Manual was prepared by the

intersession terminology working group. This proposed revised list of analytical terms for use in the Codex Procedural Manual is enclosed in Appendix II for discussion by CCMAS.

RECOMMENDATIONS

Because terms for Codex Procedural Manual use are normally applied directly to methods, criteria and standards for analysis, terms associated with quality assurance were considered inappropriate and were not recommended for inclusion in the Codex Procedural Manual. In most cases if an ISO or IUPAC definition was available for a specific term, this definition was recommended. However, because definitions for Codex purposes are not meant for as wide a variety of constituencies as those from ISO or IUPAC, discrepancies in specific ISO or IUPAC definitions that might otherwise have lead to disputes were corrected. Furthermore, since methods used by Codex are applied technically to specific products related to food for human consumption, it did not appear necessary to include in the Procedural Manual, highly theoretical analytical conceptualities meant for a very broad range of methods and materials. The references considered were included with each recommended term. New and revised terminology was also included for use in biomolecular and microbiological testing. In most cases the justification for inclusion of specific terms is self-explanatory; however, recommendations are given on a per term basis. It is recommended that the new and revised definitions proposed in Appendix II be discussed at the Twenty-sixth Session of CCMAS. It is also recommended that CCMAS not propose these changes for the Codex Procedural Manual until the Inter-Agency Meeting (IAM) members come to a consensus on what should be the internationally harmonized definitions or determine that this task is not achievable. Ultimately, if there is sufficient consensus within CCMAS, then the new list of definitions, as revised during this and perhaps the next meeting, should be proposed to the Codex Commission as amendments to the Codex Procedural Manual.

APPENDIX I

Country Comments
Comments from the Brazilian Delegation

BRAZIL COMMENTS ON CL2004/37 ANALYTICAL TERMINOLOGY FOR CODEX USE (PROCEDURAL MANUAL)

Comments about the Analytical Terminology for Codex Use

Annex I of the CL 2004/37

We ask for more time to present suggestions on the Annex I.

To maintain the current methodology of including, in the Procedural Manual, the definitions of the terms utilized and:

- To put the terms in alphabetical order;
- To include only the definitions without the inclusion of the procedure to obtain the data;
- To include all the terms used in the scope of Codex and, in minimum, of the CCMAS, for example: quality terms, sampling, statistics applied to assays, parameters of Codex standards;
- Whenever possible, to use definitions from international standards;
- The terminology document would be updated frequently, ON LINE, and could be available in electronic way (pdf document or a space, section in the Codex home page) with all the terms and definitions used in Codex documents, related to analytical terminology, with its respective bibliography references.

Comments from the European Community

European Community Comments on
Codex Circular Letter CL 2004/37-MAS
Requesting Comments on Analytical Terminology for Codex Use (Procedural Manual)

The European Community would like to favour the following definitions:

1. Limit of detection
Minimum concentration or amount of an analyte which can be detected with a given level of confidence.

2. Limit of quantification
Minimum concentration or amount of an analyte for which specified requirements for a given set of relevant quality criteria are fulfilled (the choice of relevant quality criteria depends on the purpose and kind of analysis, but should include in all cases precision and selectivity).
Comments:
- The European Community is of the opinion that it is much better to speak of "limit of quantification" instead of "limit of determination" since determination is an ambiguous term which may mean "identification + quantification" or "detection" or "quantification".
- Quantitative determination includes the need to meet a given set of performance criteria. Up to now, precision was meant to be the parameter bearing the major dependency on concentration. As the need of sufficient selectivity has been recognised and mathematical models for quantifying selectivity have recently been developed, it is known now that selectivity is another parameter being highly dependent on the concentration of the analyte. Further parameters, e.g. linearity and ruggedness, may also be dependent on the concentration level.

3. Recovery
The ratio $R = c_{obs} / c_{ref}$ ***of the observed concentration or amount*** c_{obs} ***obtained by the application of an analytical procedure to a material containing analyte at a reference level*** c_{ref} **.**

c_{ref} ***will be: (a) a reference material certified value, (b) measured by an alternative definitive method, or (c) defined by a spike addition.*** [1]

4. Accuracy
The closeness of agreement between a test result and the accepted reference value (NOTE: The term accuracy, when applied to a set of test results, involves a combination of random components and a common systematic error or bias component).[2]
Comments: The proposed definition in the Codex document is indeed confusing. A distinction is made between accuracy "as a concept" and accuracy "as a statistic". Both terms are defined in the same way and the difference is explained by the relevant notes. The EC therefore supports the proposal made at the 25th session of CCMAS, i.e. to adopt the definition from ISO 3534-1.

5. Quality assurance/Quality assurance system
A single definition could be used to cover these two aspects. In fact, the first definition is general (referring to a product or service) and the second one has a limited scope (referring to laboratories and analysis), but apart from this difference of scope, the meaning is the same.
The European Community therefore proposes to only keep the first definition on Quality Assurance: ***All those planned and systematic actions to provide adequate confidence that a product or service will satisfy given requirements for quality.***

6. Repeatability/Reproducibility
The AOAC definitions are not in line with the other definitions, as these terms are used in the same meaning as given in the definitions of repeatability limit and reproducibility limit respectively. The AOAC definitions

[1] IUPAC, Pure Appl. Chem., 1999, **71**, 347-348
[2] ISO 3534-1

should be avoided, as the repeatability limit as well as the repeatability standard deviation are possibilities of expressing repeatability. The same applies to reproducibility. Only the "original" ISO definitions should be kept, that is from ISO 3534-1, identical to the ones of ISO 78-2 and Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003.

7. Specificity/Selectivity

As already agreed during the 25th session of CCMAS, the term specificity should be strictly avoided. Selectivity was agreed to be the term to be used instead. The Committee was informed about recently published statistical approaches for selectivity [Kapeller R (2003) Anal Bioanal Chem 377:1060-107] based on the IUPAC definition. The Committee agreed that the IUPAC definition [Vessman J et al (2001) Pure Appl Chem 73:1381-1386] should be used.

8. Standard reference solution

The current definition seems acceptable, since the notes under the definition appear to clarify what is a "reference solution".

Other terms, like 'standard solution' and 'standard matching solution' are defined in very similar terms and the European Community is of the opinion that these additional definitions are not needed.

9. True value

The term applies to any characteristic, not only to analytes. The European Community therefore suggests to adopt the definition of ISO 3534-1 : ***The value which characterizes a quantity perfectly defined in the conditions which exist when the quantity is considered. (NOTE: The true value of a quantity is a theoretical concept and, in general, cannot be known exactly)***

10. Trueness

The European Community proposes to strictly adhere to the definition of ISO 3534-1: ***The closeness of agreement between the average value obtained from a large series of test results and an accepted reference value (NOTES: 1-The measure of trueness is usually expressed in terms of bias; 2- Trueness has been referred to as "accuracy of the mean". This usage is not recommended).***

Comments from the Swiss Delegation

Swiss comments on CX 4/50 CL 2004/37-MAS
Analytical Terminology for Codex Use (Procedure Manual)

Dear Sir,

Switzerland welcomes the opportunity to submit comments on the Analytical terminology for Codex Use (Procedure Manual)

General Comments:
We believe that a standardization of the analytical terminology at a global level would be helpful for Codex purposes and more generally would facilitate communication between scientists of the analytical community worldwide.

For better consistency, we recommend that pre-existing definitions from recognized international organizations such as ISO should be adopted without change. For clarity, the source of these definitions may be quoted in {} in the final text.

Much attention should be given to a correct and unitary translation of these specific terms in other languages. Again, pre-existing norms should be taken into consideration at this point.

Specific comments:
The proposals from Switzerland regarding this matter are listed in the table in annex.

We thank you for considering our comments.
Yours sincerely,

Division of International Affairs
Codex Alimentarius,
International Food Safety Issues

Awilo Ochieng Pernet, lic. in law

ANNEX (Swiss Comments)

Title	Swiss comments
ACCURACY	WE RECOMMEND TO ENDORSE THE DEFINITION FROM ISO 3534-1, INCLUSIVE THE NOTE STARTING WITH "THE TERM ACCURACY....BIAS COMPONENT"
Analytical run	-
Analytical system	we agree with the proposed definition
Assigned value	we agree with the proposed definition
Applicability	we agree with the proposed definition and the Note, but we recommend to delete the word "codex" as this would prevent this definition of being used by other international organisations. The definition would then read: The analytes, matrices,....to determine compliance with a standard"
Bias	We recommend to endorse the definition from ISO 3534-1, inclusive the Note 1 starting with "Bias is the total...."
Bias of the measurement method	we agree with the proposed definition
Certified reference material	we agree with the proposed definition
Control material	we agree with the proposed definition
Coordinator	we agree with the proposed definition
Empirical method of analysis	we agree with the proposed definition
Error	we agree with the proposed definition
Fitness for purpose	we agree with the proposed definition
Internal quality control	we agree with the proposed definition
Interlaboratory study	we agree with the proposed definition
Interlaboratory test comparisons	we agree with the proposed definition
Laboratory bias	we agree with the proposed definition
Laboratory component of bias	we agree with the proposed definition
Laboratory-performance (proficiency) study	we agree with the proposed definition
Laboratory sample	we agree with the proposed definition
Limit of detection	We recommend to endorse the definition from Nordic Committee On Food Analysis starting with "the amount... allowing exact quantification". However, the choice of the correct way of estimation of the limit of detection should be left to the analyst as there is no agreement on this matter at the present time.
Limit of determination	We recommend to endorse the definition from Nordic Committee On Food Analysis starting with "the limit of quantification.... certain confidence". However, the choice of the correct way of estimation of the limit of determination should be left to the

	analyst as there is no agreement on this matter at the present time.
Linearity (new)	We propose to copy the definition from Alinorm 04/27/23, Appendix V, p 98. "Guidelines for evaluating acceptable methods of analysis": "The ability of a method of analysis, within a certain range, to provide an instrumental response or results proportional to the quantity of analyte to be determined in the laboratory sample. This proportionality is expressed by an a priori defined mathematical expression. The linearity limits are the experimental limits of concentrations between which a linear calibration model can be applied with a known confidence level (generally taken to be equal to 1%)"
Material-certification study	We recommend to endorse the definition from CAC
Measurement uncertainty (uncertainty of measurement)	we agree with the proposed definition
	we agree with the proposed definition
METHOD-PERFORMANCE STUDY	
Native analyte	we agree with the proposed definition
	we agree with the proposed definition
ONE-WAY ANALYSIS OF VARIANCE	
Precision	We recommend to endorse the definition from ISO 3534-1, inclusive the Notes 1-3
Proficiency testing scheme	we agree with the proposed definition
Quality assurance	we agree with the proposed definition
Rational method of analysis:	we agree with the proposed definition
Recovery	we agree with the proposed definition
Reference material	we agree with the proposed definition
Relative uncertainty	we agree with the proposed definition
	we agree with the proposed ISO definition
REPEATABILITY	
Repeatability conditions	We recommend to endorse the definition from ISO 3534-1
Repeatability limit	We recommend to endorse the definition from ISO 3534-1, inclusive note 1 from same reference and note 2 from ISO 5725-7.
Repeatability standard deviation	We recommend to endorse the definition from ISO 3534-1, inclusive note 1 and 2
Repeatability relative standard deviation	we agree with the proposed definition
Reproducibility	We recommend to endorse the definition from ISO 3534-1
Reproducibility conditions	We recommend to endorse the definition from ISO 3534-1
Reproducibility limit	We recommend to endorse the definition from ISO 3534-1, inclusive note 1 from same reference and note 2 from ISO 5725-7.

	We recommend to endorse the definition from ISO 3534-1
REPRODUCIBILITY STANDARD DEVIATION	
Reproducibility relative standard deviation	We recommend to endorse the definition from ISO 3534-1
Result	We recommend to endorse the definition from CAC
Ruggedness	We recommend to endorse the definition from CAC/IUPAC
Run (analytical run)	we agree with the proposed definition
Sample blank (new)	We propose to define this term as it is used in the CX 2/7 "Guidelines for evaluating acceptable methods of analysis" Proposal: translated from DIN 32645 (1994) "A sample blank is a sample witch does not contain the analyte, while being otherwise identical with it"
Selectivity	We propose to copy the definition from Alinorm 04/27/23, Appendix V, p 102. "Guidelines for evaluating acceptable methods of analysis" "Selectivity is the extent to which a method can determine particular analyte(s) in mixtures or matrices without interferences from other components"
Sensitivity	We recommend to endorse the definition from CAC inclusive both notes from IUPAC
~~Specificity~~	we recommend that this term be deleted in order to be compatible with the Alinorm 04/27/23, Appendix V "Guidelines for evaluating acceptable methods of analysis"
Standard matching solution	we agree with the proposed definition
Standard reference solution	we agree with the proposed definition
Standard solution	we agree with the proposed definition
Standard volumetric solution	we agree with the proposed definition
Surrogate	we agree with the proposed definition
Surrogate recovery	we agree with the proposed definition
Target value for standard deviation	
Test portion	we agree with the proposed definition
Test sample	we agree with the proposed definition
Testing laboratory	we agree with the proposed definition
Traceability	we agree with the proposed definition
True value	we agree with the proposed definition
Trueness	We recommend to endorse the definition from ISO 3534-1, inclusive the Notes 1 and 2
Validated range	we agree with the proposed definition

Comments from the United States Delegation

Secretary
Joint FAO/WHO Food Standards Programme
FAO
Viale delle Terme di Caracalla
00100 Rome, Italy

Dear Sir:

Currently twenty-four terms are defined in the chapter of the Codex Alimentarius Commission Procedural Manual (13th Edition) entitled "Guidelines for the Inclusion of Specific Provisions in the Codex Standards and Related Text (Analytical Terminology for Codex Use)." With the expanded use of statistical analysis in sampling and methods of analysis and increased demand for methods to detect and analyze products of modern biotechnology, the addition of new terms to the Procedural Manual is warranted.

The United States proposes that CCMAS consider expanding the current list of definitions for analytical terms to include an additional twenty-one terms as listed in the 2002 compendium entitled "Harmonization of Analytical Terminology in Accordance with International Standards." This document includes Codex Alimentarius definitions as well as definitions from other international organizations, and was included as an annex to CL2004/37-MAS (July, 2004). Ideally, pre-existing definitions from international organizations should be adopted as is and the source noted at the end of the definition. These additional analytical terms should not be proposed for addition to the Codex Procedural Manual until after the Inter-Agency Meeting (IAM) members come to a consensus on what should be the internationally harmonized definitions. In addition, the United States suggests the revision of several definitions of terms to make them more consistent with the definitions from other international organizations.

Term	**Suggested Definition**
Expectation	The expected value of a random variable, e.g. assigned value or long term average.
Certified Reference Material	A reference material, accompanied by a certificate, one or more of whose property values and their accompanying uncertainty are assured by a competent authority.
Control Material	A stable material with an assigned value that is used as the basis for comparison of the results of the measurement method
Error	Result of a measurement minus the true or assigned value of the measurand.
Fitness for Purpose	The degree [or extent] to which data produced by a measurement process enable a user to make technical or administrative decisions for a stated purpose.
Internal Quality Control	The set of procedures for the continuous monitoring of operations through the results of measurements in order to ensure a process operates within predetermined limits.
Interlaboratory Test Comparisons	Organization, performance, and evaluation of tests on identical portions of an effectively homogeneous material or on identical items by two or more laboratories in accordance with predetermined conditions.
Laboratory Bias	The expected value of a random variable, e.g. assigned value or long term average.

Limit of Detection (LD)	
LD: Quantitative determinations	The amount or content of an analyte corresponding to the lowest measurement signal that may be interpreted with acceptable certainty as indicating the presence of the analyte in the solution/analytical sample, but not necessarily allowing exact quantification. LD = 3*Sa/b where LD is the limit of detection, Sa is the standard deviation of x blank results (x > 20) and b is the slope of the calibration curve/regression line.
LD: Qualitative determinations	The threshold concentration below which positive identification is unreliable.
Limit of Quantitation	The lowest amount of analyte in a sample which can be quantitatively determined with a certain confidence. LQ = 10*Sa/b where LQ is the limit of quantification, Sa is the standard deviation of x blank results (x > 20) and b is the slope of the calibration curve/regression line.
Material	A specific combination of analyte matrix at specific concentrations
Measurement Uncertainty	The range of values within which the value of the quantity being measured is expected to lie with a stated level of confidence.
Quality Assurance	All laboratory activities aimed at achieving a required standard of analysis, including internal quality control, proficiency testing, staff training, administrative procedures, management structure, auditing, supplies, cleanliness, and waste disposal.
Recovery	The proportion or fraction of the amount of an analyte initially present that is finally measured.
Ruggedness	The ability of a chemical measurement process to resist changes in results when subjected to minor changes in environmental and procedural variables.

The terms s_r, RSD_r, s_R, RSD_R and R should be standardized to either the AOAC or the ISO terminology.

The definition of "Repeatability Limit" contains the variable 's' which is not explicitly defined. It should be defined within the definition as the estimated standard deviation.

The term HORRAT, the relative interlaboratory standard deviation normalized with respect to concentration, is indicative of method performance and should be included in the Procedural Manual.

One-Way Analysis of Variance is an important statistical method, and a definition should be included into the Procedural Manual. A suggested source is the Steiner portion of the Statistical Manual of AOAC and in Wernimont, Use of Statistics to Develop and Evaluate Analytical Methods.

Thank you for the opportunity to provide comments on CL 2004/37-MAS.
Sincerely,

F.Edward Scarbrough, Ph.D.
U.S. Manager for Codex
Office of the Under Secretary
Food Safety

APPENDIX II:

NEW OR REVISED DEFINTIONS THAT ARE RECOMMENDED FOR INCLUSION IN THE PROCEDURAL MANUAL

ACCURACY

RECOMMENDATION: CCMAS(25th Session) recommended that only one definition, ISO 3534-1, be used in order to prevent confusion. The following will be acceptable for Codex use.

{ISO 3534-1}

The closeness of agreement between a test result and the accepted reference value.

Note:

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

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *ISO Standard 78-2: Chemistry – Layouts for Standards – Part 2: Methods of Chemical Analysis,1999*
3. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
4. Codex Alimentarius Commission, Alinorm 04/27/23, 2004

APPLICABILITY

RECOMMENDATION: This term should remain in the Codex Procedural Manual and should only be used in application of a Codex Standard.

The analytes, matrices, and concentrations for which a method of analysis may be used satisfactorily to determine compliance with a Codex standard.

REFERENCE:

Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003

BIAS

RECOMMENDATION: The ISO 3534-1 definition, with a definition of expectation included as note three, should be adopted in the Codex Procedural Manual. To avoid disputes and discrepancies with the definition of the terms for accuracy and error, there should be only one accepted reference value. Thus, in the definition, the article "an" should be replaced with "the." Note #3, refers to a long term average which at a theoretical level may be considered a practical approximation to an infinite series. Because Codex requires the practical application this term is used.

{ISO 3534-1}

The difference between the expectation of the test results and the accepted reference value.

Notes:

1. Bias is the total systematic error as contrasted to random error. There may be one or more systematic error components contributing to bias. A larger systematic difference from the accepted reference value is reflected by a larger bias value. {ISO 3534-1}

2. When the systematic error component(s) must be arrived at by a process that includes random error, the random error component is increased by propagation of error considerations and reduced by replication.

3. Expectation is the expected value of a random variable, e.g. assigned value or long term average

REFERENCES:

1. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
2. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
3. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*

CERTIFIED REFERENCE MATERIAL

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual.

Reference material, accompanied by a certificate, one or more of whose property values are certified by a procedure which establishes its traceability to an accurate realization of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence. {VIM}

REFERENCES:

1. *VIM, International vocabulary for basic and general terms in metrology, 2nd Edition, 1993, ISO, Geneva*
2. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1993*
3. *International harmonised protocol for the proficiency testing of (chemical) analytical laboratories, 1993*

EMPIRICAL METHOD OF ANALYSIS

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual.

A method which determines a value that can be arrived at only in terms of the method *per se* and serves by definition as the only method for establishing the measurand. (Sometimes called "defining method of analysis.")

REFERENCE:

Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995

ERROR

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual. To avoid disputes and be consistent with the definition of the terms for accuracy and bias, there should be only one accepted reference value. Thus, in the definition, the article "an" should be replaced with "the."

Result of a measurement minus the true value of the measurand. {VIM}

REFERENCES:

1. *VIM, International vocabulary for basic and general terms in metrology, 2nd Edition, 1993, ISO, Geneva*
2. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*

FITNESS FOR PURPOSE

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual. It is expected that this term will be important as the question of fitness for purpose evolves.

Degree to which data produced by a measurement process enables a user to make technically and administratively correct decisions for a stated purpose.

REFERENCE:

Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995

HorRat

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual. The Horrat is an internationally recognized term that is appropriate for Codex use. It should be included.

The relative interlaboratory standard deviation normalized with respect to concentration that is indicative of method performance for a large majority of methods in chemistry. It is the ratio of the interlaboratory relative standard deviation found to that calculated from the Horwitz equation, $PRSD_R = 2C^{-0.15}$:

$$HORRAT(R) = RSD_R/PRSD_R ,$$
$$HORRAT(r) = RSD_r/PRSD_R ,$$

where C is concentration expressed as a mass fraction (both numerator and denominator expressed in the same units). Acceptable values lie between 0.5 and 2. (To check proper calculation of $PRSD_R$, a C of 10^(-6) should give a $PRSD_R$ of 16%.)

If applied to within-laboratory studies, the acceptable range of HORRAT(r) is 0.3-1.3.

REFERENCE:

A simple method for evaluating data from an interlaboratory study, *1998.*

LIMIT OF DETECTION

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual. This term should replace the term detection limit. The quantitative definition of the Nordic Committee should be used with the following modifications. The assignment of a limit to a qualitative method makes it a quantitative method. The first note provides specificity for the method. The second note is important for methods in molecular biology and possibly microbiology that do not produce negative results.

The amount or the content of an analyte corresponding to the lowest measurement signal which with a certain statistical confidence may be interpreted as indicating that the analyte is present in the solution/analytical sample, but not necessarily allowing quantification.

Notes:

1. LD = $3*S_a/b$ where LD is the limit of detection, S_a is the standard deviation of x blank results (x > 20) and b is the slope of the calibration curve/regression line.

2. For quantitative tests using the polymerase chain reaction (PCR), the distribution of blank values is typically truncated and thus not normally distributed (non-Gaussian) around zero. Thus, the LD needs to be experimentally determined unless the targeted concentrations are well above the LD and the LD, therefore, becomes irrelevant.

REFERENCES:

1. Nordic Committee on Food Analysis, 1996
2. Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003,
3. Polymerase chain reaction technology as an analytical tool in agricultural biotechnology, 2005

LIMIT OF QUANTITATION

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual. The term "Determination Limit" should be replaced and explicitly stated as the "Limit of Quantitation." The Nordic Committee Definition should be used with modification as follows. The first note provides specificity for the method. The second note is important for methods in molecular biology and possibly microbiology that do not produce negative results.

The limit of quantification (LQ) (also called limit of determination) of an analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with a certain confidence.

Notes:

1. LQ = $10*S_a/b$ where LQ is the limit of quantification, S_a is the standard deviation of x blank results (x > 20) and b is the slope of the calibration curve/regression line.

2. For quantitative tests using the polymerase chain reaction (PCR), the distribution of blank values is typically truncated and thus not normally distributed (non-Gaussian) around zero. Thus, the LD needs to be experimentally determined unless the targeted concentrations are well above the LD and the LD, therefore, becomes irrelevant.

REFERENCES:

1. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
2. *Nordic Committee on Food Analysis, 1996*
3. *Polymerase chain reaction technology as an analytical tool in agricultural biotechnology, 2005*

LINEARITY

RECOMMENDATION: This definition defines the ability of the method to produce test results that are directly proportional to the concentration of the analyte.

The ability of a method of analysis, within a certain range, to provide an instrumental response or results proportional to the quantity of analyte to be determined in the laboratory sample. This proportionality is expressed by an a priori defined mathematical expression. The linearity limits are the experimental limits of concentrations between which a linear calibration model can be applied with a known confidence level (generally taken to be equal to 1%).

REFERENCE:

Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003

MEASUREMENT UNCERTAINTY

RECOMMENDATION: This definition from GUM should be adopted for use in the Codex Procedural Manual.

Parameter, associated with the result of a measurement that characterises the dispersion of the values that could reasonably be attributed to the measurand. {GUM}

Notes:

1. The parameter may be, for example, a standard deviation (or a given multiple of it), or the half-width of an interval having a stated level of confidence. {GUM}
2. Uncertainty of measurement comprises, in general, many components. Some of these components may be evaluated from the statistical distribution of results of a series of measurements and can be characterised by experimental standard deviations. The other components, which can also be characterised by standard deviations, are evaluated from assumed probability distributions based on experience or other information. {GUM}
3. It is understood that the result of a measurement is the best estimate of the value of a measurand, and that all components of uncertainty, including those arising from systematic effects, such as components associated with corrections and reference standards, contribute to the dispersion. {GUM}
4. For Codex purposes measurement uncertainty is usually expressed as RSD_R.

REFERENCES:

1. *GUM, Guide to the expression of uncertainty in measurement,* ISO, Geneva, 1993
2. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*

METHOD-PERFORMANCE STUDY

RECOMMENDATION: The current Codex definition should continue to be used in the Codex Procedural Manual.

An interlaboratory study in which all laboratories follow the same written protocol and use the same test method to measure a quantity in sets of identical test samples. The reported results are used to estimate the performance characteristics of the method. Usually these characteristics are within-laboratory and among-laboratories precision, and when necessary and possible, other pertinent characteristics such as systematic error, recovery, internal quality control parameters, sensitivity, limit of quantitation, and applicability.

Notes

1. The materials used in such a study of analytical quantities are usually representative of materials to be analysed in actual practice with respect to matrices, amount of test component (concentration), and interfering components and effects. Usually the analyst is not aware of the actual composition of the test samples but is aware of the matrix.
2. The number of laboratories, number of test samples, number of determinations, and other details of the study are specified in the study protocol. Part of the study protocol is the procedure which provides the written directions for performing the analysis.
3. The main distinguishing feature of this type of study is the necessity to follow the same written protocol and test method exactly.
4. Several methods may be compared using the same test materials. If all laboratories use the same set of directions for each method and if the statistical analysis is conducted separately for each method, the study is a set of method-performance studies. Such a study may also be designated as a method-comparison study.

REFERENCE:

Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003

PRECISION

RECOMMENDATION: The ISO 3534-1 definition should be used, thus preserving the current Codex Procedural Manual definition.

{ISO 3534-1}

The closeness of agreement between independent test results obtained under stipulated conditions.

Notes:

1. Precision depends only on the distribution of random errors and does not relate to the true value or to the specified value.
2. 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.
3. “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.

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *ISO Standard 78-2: Chemistry – Layouts for Standards – Part 2: Methods of Chemical Analysis, 1999*
3. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
4. *Terms and definitions used in connections with reference materials, ISO Guide 30, 1992*
5. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*

6. *The international harmonised protocol for the proficiency testing of (chemical) analytical laboratories, 1993*

QUALITY ASSURANCE

RECOMMENDATION: This versatile definition is general (referring to a product or service). This definition should be adopted for use in the Codex Procedural Manual. It may also be applied to a quality assurance system.

All those planned and systematic actions necessary to provide adequate confidence that a product or service will satisfy given requirements for quality.

REFERENCES:

1. *Quality assurance and quality management - vocabulary, ISO 840, 1994*
2. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*
3. *International harmonised protocol for the proficiency testing of (chemical) analytical laboratories, 1993*

RATIONAL METHOD OF ANALYSIS

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural manual.

A method which determines an identifiable chemical(s) or analytes(s) for which there may be several equivalent methods of analysis available.

REFERENCE:

Harmonised guidelines for the use of recovery information in analytical measurement, 1998

RECOVERY

RECOMMENDATION: This definition should be kept in the Codex Procedural Manual as written with modification and notes added as follows.

Proportion of the amount of analyte, present in or added to the analytical portion of the test material, which is extracted and presented for measurement.

Notes:

1. Recovery is assessed by the ratio $R = c_{obs} / c_{ref}$ of the observed concentration or amount c_{obs} obtained by the application of an analytical procedure to a material containing analyte at a reference level c_{ref}.

2. c_{ref} will be: (a) a reference material certified value, (b) measured by an alternative definitive method, or (c) defined by a spike addition.

REFERENCE:

Harmonised guidelines for the use of recovery information in analytical measurement, 1998

REFERENCE MATERIAL

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual.

Material or substance whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials.

REFERENCES:

1. *International vocabulary for basic and general terms in metrology, 2nd Edition, ISO, Geneva, 1993*
2. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*

3. *International harmonised protocol for the proficiency testing of (chemical) analytical laboratories, 1993*

RELATIVE UNCERTAINTY

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual.

Uncertainty derived from a relative standard deviation.

REFERENCE:

Harmonised guidelines for single-laboratory validation of methods of analysis, 2002

REPEATABILITY [REPRODUCIBILITY]

RECOMMENDATION: The current Codex Procedural Manual definition {ISO 3534-1} should be used. We have also included the editorial combining of Repeatability and Reproducibility since this reduces copy. However, it is possible that this might be confusing for some readers.

{ISO 3534-1}

Precision under repeatability [reproducibility] conditions.

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *ISO Standard 78-2: Chemistry – Layouts for Standards – Part 2: Methods of Chemical Analysis, 1999)*
3. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
4. *AOAC International methods committee guidelines for validation of qualitative and quantitative food microbiological official methods of analysis, 2002.*

REPEATABILITY CONDITIONS

RECOMMENDATION: The current Codex Procedural Manual definition should be used.

{ISO 3534-1}

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.

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *ISO Standard 78-2: Chemistry – Layouts for Standards – Part 2: Methods of Chemical Analysis, 1999*
3. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
4. *"Statistics, vocabulary and symbols - Part 1: Probability and general statistical terms", ISO 3534 - 1, 1993*
5. *Harmonised guidelines for internal quality control in analytical chemistry laboratories*

REPEATABILITY [REPRODUCIBILITY] LIMIT

RECOMMENDATION: The current Codex Procedural Manual definition should be used, except the third note should be deleted. We have also included the editorial combining of Repeatability and Reproducibility since this reduces copy. However, it is possible that this might be confusing for some readers.

{ISO 3534-1}

The value less than or equal to which the absolute difference between two test results obtained under repeatability [reproducibility] conditions may be expected to be with a probability of 95%.

Notes:

1. The symbol used is r [R]. {ISO 3534-1}

2. When examining two single test results obtained under repeatability [reproducibility] conditions, the comparison should be made with the repeatability [reproducibility] limit, r [R] = 2.8sr [R]. {ISO 5725-6, 4.1.4}

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *ISO 5725-6 "Accuracy (trueness and precision) of a measurement methods and results—Part 6: Use in practice of accuracy values", ISO, 1994*
3. *ISO Standard 78-2: Chemistry – Layouts for Standards – Part 2: Methods of Chemical Analysis (Second Edition, 1999)*
4. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*

REPEATABILITY [REPRODUCIBILITY] STANDARD DEVIATION

RECOMMENDATION: The current Codex Procedural Manual definition {ISO 3534-1} should be used. We have also included the editorial combining of Repeatability and Reproducibility since this reduces copy. However, it is possible that this might be confusing for some readers.

{ISO 3534-1}

The standard deviation of test results obtained under repeatability [reproducibility] conditions.

Notes:

1. It is a measure of the dispersion of the distribution of test results under repeatability [reproducibility] conditions.

2. Similarly "repeatability [reproducibility] variance" and "repeatability [reproducibility] coefficient of variation" could be defined and used as measures of the dispersion of test results under repeatability [reproducibility] conditions.

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *CODEX ALIMENTARIUS COMMISSION, PROCEDURAL MANUAL, 13TH EDITION, 2003*
3. *AOAC International methods committee guidelines for validation of qualitative and quantitative food microbiological official methods of analysis, 2002.*

REPEATABILITY [REPRODUCIBILITY] RELATIVE STANDARD DEVIATION

RECOMMENDATION: This definition should be added to the Codex Procedural Manual. We have also included the editorial combining of Repeatability and Reproducibility since this reduces copy. However, it is possible that this might be confusing for some readers.

Relative standard deviation (RSD) is a useful measure of precision in quantitative studies. RSD is computed by dividing s_R and s_r by the mean. This is done so that one can compare variability of sets with different means. RSD values are independent of the amount of analyte over a reasonable range and facilitate comparison of variabilities at different concentrations. The result of a collaborative test may be summarized by giving the RSD for repeatability (RSD_r) and RSD for reproducibility (RSD_R).

REFERENCE:

1. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
2. *AOAC International methods committee guidelines for validation of qualitative and quantitative food microbiological official methods of analysis, 2002.*

REPRODUCIBILITY CONDITIONS

RECOMMENDATION: The current Codex Procedural Manual {ISO 3534-1} definition should be used.

{ISO 3534-1}

Conditions where test results are obtained with the same method on identical test items in different laboratories with different operators using different equipment.

Note:

When different methods give test results that do not differ significantly, or when different methods are permitted by the design of the experiment, as in a proficiency study or a material-certification study for the establishment of a consensus value of a reference material, the term "reproducibility" may be applied to the resulting parameters. The conditions must be explicitly stated.

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *ISO Standard 78-2: Chemistry – Layouts for Standards – Part 2: Methods of Chemical Analysis (Second Edition, 1999)*
3. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
4. *AOAC International*

RESULT

RECOMMENDATION: CCMAS has recommended that this definition remain unchanged as written below. The notes are given in an informative form in this definition, therefore, a result with uncertainty information is not necessarily incomplete.

The final value reported for a measured or computed quantity, after performing a measuring procedure including all sub-procedures and evaluations. {IUPAC, 1994}

Notes: {VIM}

1 When a result is given, it should be made clear whether it refers to:
-- the indication [signal]
-- the uncorrected result
-- the corrected result
and whether several values were averaged.

2 A complete statement of the result of a measurement includes information about the uncertainty of measurement.

REFERENCES:

1. *IUPAC, Nomenclature for the presentation of results of chemical analysis, 1994.*
2. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003, Alinorm 04/27/03, Appendix V "Guidelines for evaluating acceptable methods of analysis"*

ROBUSTNESS

RECOMMENDATION: Suggested by the delegation from Brazil

A measure of the capacity of an analytical procedure to remain unaffected by small but deliberate variations in method parameters providing an indication of its reliability during normal usage

REFERENCE

ICH Topic Q2 Validation of Analytical Methods, The European Agency for the Evaluation of Medicinal Products: ICH Topic Q 2 A - Definitions and Terminology (CPMP/ICH/381/95), 1995

SELECTIVITY

RECOMMENDATION: CCMAS has recommended that this definition replace specificity with modifications as follows.

Selectivity is the extent to which a method can determine particular analyte(s) in a mixture(s) or matrice(s) without interferences from other components of similar behaviour.

Note:

Selectivity is the recommended term in analytical chemistry to express the extent to which a particular method can determine analyte(s) in the presence other components. Selectivity can be graded. The use of the term specificity for the same concept is to be discouraged as this often leads to confusion.

REFERENCES:

1. Selectivity in analytical chemistry, Pure Appl Chem, 2001

2. Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003

3. Codex Alimentarius Commission, Alinorm 04/27/23, 2004

SENSITIVITY

RECOMMENDATION: This definition should remain unchanged in the Codex Procedural Manual.

Change in the response divided by the corresponding change in the concentration of a standard (calibration) curve; i.e., the slope, s_i, of the analytical calibration curve.

Notes:

1. This term has been used for several other analytical applications, often referring to capability of detection, to the concentration giving 1% absorption in atomic absorption spectroscopy, and to ratio of found positives to known, true positives in immunological and microbiological tests. Such applications to analytical chemistry should be discouraged.

2. A method is said to be sensitive if a small change in concentration, c, or quantity, q, causes a large change in the measure, x; that is, when the derivative dx/dc or dx/dq is large.

3. Although the signal s_i may vary with the magnitude of c_i or q_i, the slope, s_i, is usually constant over a reasonable range of concentrations. s_i may also be a function of the c or q of other analytes present in the sample.

REFERENCE:

Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003

SURROGATE

RECOMMENDATION: As recommended by the Brazilian delegate

Pure compound or element added to the test material, the chemical and physical behaviour of which is taken to be representative of the native analyte.

REFERENCE:

Harmonised guidelines for the use of recovery information in analytical measurement, 1998

TRACEABILITY

RECOMMENDATION: This definition should be adopted for use in the Codex Procedural Manual.

Property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties.

REFERENCES:

1. International vocabulary for basic and general terms in metrology, 2nd Edition, ISO, Geneva, 1993
2. Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995

TRUE VALUE

RECOMMENDATION: The term applies to any characteristic, not only to analytes. The ISO 3534-1 definition should be adopted for use in the Codex Procedural Manual.

{ISO 3534-1}

The value which characterizes a quantity perfectly defined in the conditions which exist when the quantity is considered.

Note:

The true value of a quantity is a theoretical concept and, in general, cannot be known exactly

REFERENCES:

1. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
2. *International Harmonised Protocol for the Proficiency Testing of (Chemical) Analytical Laboratories, 1993*

TRUENESS

RECOMMENDATION: CCMAS (25th Session) has recommended the following definition for trueness

{ISO 3534-1}

The closeness of agreement between the average value obtained from a series of test results and an accepted reference value.

Notes:

1. The measure of trueness is usually expressed in terms of bias.
2. Trueness has been referred to as “accuracy of the mean”. This usage is not recommended.

REFERENCES:

1. *Codex Alimentarius Commission, Procedural Manual, 13th edition, 2003*
2. *ISO 3534-1 Statistics, vocabulary and symbols-Part 1:Probability and general statistical terms, ISO, 1993*
3. *Harmonised guidelines for internal quality control in analytical chemistry laboratories, 1995*
4. *International harmonised protocol for the proficiency testing of (chemical) analytical laboratories,1993*
5. Codex Alimentarius Commission, Alinorm 04/27/23, 2004

VALIDATED RANGE

RECOMMENDATION: There is definite interest in including this term in the Procedural manual.

That part of the concentration range of an analytical method which has been subjected to validation.

REFERENCE

Harmonised guidelines for single-laboratory validation of methods of analysis, 2002

APPENDIX III

REFERENCES

1. Terms and definitions used in connections with reference materials, ISO Guide 30:1992
2. GUM, Guide to the expression of uncertainty in measurement, ISO, Geneva, 1993.
3. The international harmonised protocol for the proficiency testing of (chemical) analytical laboratories, Pure Appl. Chem., 65, 2123-2144, 1993.-
4. International vocabulary for basic and general terms in metrology, ISO, Geneva, 2nd Edition, 1993.
5. Statistics, vocabulary and symbols - Part 1: Probability and general statistical terms, ISO 3534 -1: 1993.
6. VIM, International vocabulary for basic and general terms in metrology, 2nd Edition, ISO, Geneva, 1993.
7. IUPAC, Nomenclature for the presentation of results of chemical analysis, Pure and Applied Chemistry, 66(3):595-608, 1994.
8. NMKL Secretariat Finland, NMKL Procedures, 1994-1999
9. Quality management and quality assurance-vocabulary ISO 8402, second edition, 1994.
10. The harmonised guidelines for internal quality control in analytical chemistry laboratories, Pure Appl. Chem, 67:649–666, 1995.
11. ICH Topic Q2 Validation of Analytical Methods, The European Agency for the Evaluation of Medicinal Products: ICH Topic Q 2 A - Definitions and Terminology (CPMP/ICH/381/95), 1995
12. Protocol for the design, conduct and interpretation of method-performance studies, Pure Appl. Chem. 67(2):331-343, 1995.
13. Harmonized guidelines for the use of recovery information in analytical measurement, IUPAC/ISO/AOAC International/Eurachem technical report, 1998.
14. A simple method for evaluating data from an interlaboratory study, J AOAC, 81(6):1257-1265, 1998.
15. ISO Standard 78-2: Chemistry – layouts for standards – Part 2: Methods of chemical analysis, ISO, second edition, 1999.
16. Selectivity in Analytical Chemistry, Pure Appl. Chem., 73(8):1381-1386, 2001.
17. AOAC International Methods committee guidelines for validation of qualitative and quantitative food microbiological methods of analysis, J AOAC, 85(5):1187-1200, 2002
18. Harmonised guidelines for single-laboratory validation of methods of analysis, Pure Appl. Chem, 74(5):835-855, 2002.
19. Codex Alimentarius Commission, Procedural Manual, 13th edition, Food and Agriculture Organization of the United Nations, World Health Organization, 2003.
20. Codex Alimentarius Commission, Food and Agriculture Organization of the United Nations, World Health Organization, Alinorm 04/27/23, Report of the twenty-fifth session of the Codex committee on methods analysis and sampling, 2004
21. Polymerase chain reaction technology as an analytical tool in agricultural biotechnology, J AOAC, 88(1):128-135, 2005.