



Annex 9: Glossary of Terms Used in ISTA Method Validation Studies

A

Accuracy

B

Bias

C

Certification Mark
Comparative Test
Critical Control Point
Cross Reactivity

E

Error

- Error of Measurement
- Random Error
- Systematic Error

F

Fitness for Purpose

L

Limit of Detection
Limit of Quantitation
Linearity

M

Measurand
Measurement
Method (of a measurement)
Multi-laboratory Study

P

Peer Review

Peer Validation

Performance Approved Method

Performance Based Method

Performance Validated Method

Precision

- Intermediate Precision
- Measurement Precision

Proficiency Testing

Q

Quality

- Quality Assurance
- Quality Control
- Internal Quality Control

R

Recovery

Reference Material

- Certified Reference Material

Repeatability

Reproducibility

Result of a Measurement

Ruggedness Test

S

Specified Traits

Sponsor

Standard Deviation

T

Test Kit

Test Organiser

Test Plan

Test Report

Traceability

Trueness

U

Uncertainty (of Measurement)

V

Validation

- Method Validation

Value

- Accepted Reference Value
- True Value

Verification

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.* [ISO 3534-1].

Accuracy (of Measurement):

'Closeness of the agreement between the result of a measurement and a true value of the measurand.'

Accuracy (of a Measuring Instrument):

'Ability of a measuring instrument to give responses close to a true value.'

Note: *In these contexts accuracy is a qualitative concept.* [IUPAC 'Orange' Book]. The term 'precision' should not be used for 'accuracy'. [VIM, 1993].

Bias:

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

Note: *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.* [ISO 3534-1]

Bias (of a Measuring Instrument):

'Systematic error of the indication of a measuring instrument.'

Note: *The bias of a measuring instrument is normally estimated by averaging the error of indication over an appropriate number of repeated measurements.* [VIM, 1993].

Certification Mark:

'Identifier given by ISTA to a test kit manufacturer which signifies that the test kit has been granted Performance Validated Method status.'

Comparative Test:

1. 'A comparison of different test methods to determine which one of these tests should be adopted as a validated test method.'
2. 'A multi-laboratory study of a test method used in method validation studies.'

Critical Control Point (CCP):

In the HACCP (Hazard Analysis and Critical Control Point) approach, CCP is 'a point, step or procedure in a process at which control can be applied, and an adverse event can, as a result, be prevented, eliminated or reduced to acceptable levels.'

Cross Reactivity:

'Response (of method) to analogues, metabolites, or other non-target components that may be present in the matrix(es).' [AOAC - PVMC].

Error (of Measurement):

'The value of a result minus the true value.' [IUPAC Compendium of Chemical Technology, 1985].

'Result of a measurement minus a true value of the measurand.' [VIM, 1993].

Note: *Since a true value cannot be determined, in practice a conventional true value is used.*

Random Error:

'Result of a measurement minus the mean that would result from an infinite number of measurements of the same measurand carried out under repeatability conditions.'

Note: Random error is equal to error minus systematic error. Because only a finite number of measurements can be made, it is possible to determine only an estimate of random error. [VIM 1993].

Systematic Error:

'Mean that would result from an infinite number of measurements of the same measurand carried out under repeatability conditions minus a true value of the measurand.'

Note: Systematic error is equal to error minus random error. Like true value, systematic error and its causes cannot be known. [VIM 1993].

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.' [IUPAC 'Orange' Book].

Limit of Detection:

'The lowest content that can be measured with reasonable statistical certainty.' [AOAC - PVMC].

Limit of Quantitation:

'The lowest concentration of an analyte that can be determined with acceptable precision (repeatability) and accuracy under the stated conditions of the test.' [NATA Tech Note #13].

Linearity:

'Defines the ability of the method to obtain test results proportional to the concentration of analyte.'

Note: The Linear Range is by inference the range of analyte concentrations over which the method gives test results proportional to the concentration of the analyte. ' [AOAC - PVMC].

Measurand:

'Particular quantity subject to measurement.'

Note: Specification of a measurand may require statements about quantities such as time, temperature and pressure. [VIM 1993].

Measurement:

'Set of operations having the object of determining a value of a quantity.' [VIM 1993].

Method (of a Measurement):

'Generic description of a logical sequence of operations used in a measurement.'

Multi-Laboratory Study:

'A comparative test conducted by six or more laboratories during the method validation process.'

Peer Review:

'A critical review of a document (e.g. test plan/test report) by an experienced researcher/statistician other than the author(s).'

Peer Validation:

'A test method validation study conducted by a small (one to three) number of laboratories (c.f. multi-laboratory study).'

Performance Approved Method:

'Method evaluated and approved according to the principles of the performance based approach for quality testing; usually restricted to bio-molecular tests and bioassays for testing for the presence of specified traits.'

Performance Based Method:

'Synonym for Performance Approved Method.'

Performance Validated Method:

'A performance approved/based method which has had its performance claims verified.'

Precision:

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

Note: Precision depends only on the distribution of random errors and does not relate to the true value or specified value. The measure of precision is usually expressed in terms of imprecision and computed as a standard deviation of the test results. 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 are particular sets of extreme conditions. [ISO 3534-1].

Intermediate Precision:

'Intermediate precision expresses within laboratories variation: different days, different analysts, different equipment, etc.' [ICH Q2A, CPMP/ICH/381/95].

Measurement Precision:

'Closeness of agreement between quantity values obtained by replicate measurements of a quantity, under specified conditions.'

Note: Measurement precision is usually expressed numerically by measures of impression such as standard deviation, variance, or co-efficient of variation under the specified conditions of measurement. [VIM, 2004].

Proficiency Testing:

'A periodic assessment of the performance of individual laboratories and groups of laboratories that is achieved by the distribution by an independent testing body of typical materials for unsupervised analysis by the participants.' [IUPAC 'Orange' Book]

Quality:

'The totality of features and characteristics of a product or service that bear on its ability to satisfy stated or implied needs.' [ISO 9000:2000].

'Degree to which a set of inherent characteristics fulfils requirements.' [ISO/DIS 19011:2002].

Quality Assurance:

'All those planned and systematic activities implemented within the quality system, and demonstrated as needed, to provide adequate confidence that an entity will fulfil requirements for quality.' [ISO 8402:1994].

'Part of quality management focused on providing confidence that quality requirements will be fulfilled.' [ISO 9000:2000].

Quality Control:

'The operational techniques and activities that are used to fulfil requirements of quality.' [ISO 8402:1994].

'Part of quality management focussed on fulfilling quality requirements [ISO 9000:2000].

Internal Quality Control:

'Set of procedures undertaken by laboratory staff for the continuous monitoring of operations and the results of measurements in order to decide whether results are reliable enough to be released.' [IUPAC 'Orange' Book].

Recovery:

'The fraction of analyte added to a test sample (fortified or spiked sample) prior to analysis of the unfortified and fortified samples; percentage recovery (%R) is calculated as follows:

$$\%R = [(CF-CU)/CA] \times 100$$

Where CF is the concentration of analyte measured in the fortified sample; CU is the concentration of analyte measured in the unfortified sample; CA is the concentration of analyte added (measured value, not determined by method) in fortified sample.' [AOAC-PVMC].

Reference Material (RM):

'Material or substance one or more of 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.'

Note: The term reference material describes materials which are often also called measurement standards, e.g. chemical substances used for calibration or identification purposes. Care is necessary when using the term 'standard' as it is commonly used in two different contexts. The term may refer to 'measurement standards' in the reference material sense, or it may refer to written standards, such as standard methods. It is important to ensure the distinction is always clear. [ISO/IEC Guide 30 - 1992, 2.1].

Certified Reference Material (CRM):

'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 realisation 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.' [ISO/IEC Guide 30 - 1992, 2.2].

Repeatability:

Closeness of the agreement between the results of successive measurement of the same measurand carried out in the same conditions of measurement.' [IUPAC 'Orange' Book].

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.

Note: A valid statement of reproducibility requires specification of the conditions changed. Reproducibility may be expressed quantitatively in terms of the dispersion of the results.' [ISO 3534-1].

Result of a Measurement:

'Value attributed to a measurand, obtained by measurement.'

Note: When the term result of a measurement is used, it should be made clear whether it refers to: the indication; the uncorrected result; the corrected result, and whether several values are averaged. A complete statement of the result of a measurement includes information about the uncertainty of measurement.' [VIM 1993].

Ruggedness Test:

'Intra-laboratory study to study the behaviour of an analytical process when small changes in the environmental and/or operating conditions are made, akin to those likely to arise in different test environments. Ruggedness testing allows information to be obtained on effects of minor changes in a quick and systematic manner.' [AOAC - PVMC].

Specified Traits

'A named characteristic which may be present in a seed lot.'

Sponsor

'Any method developer or test kit manufacturer who submits a test method for validation.'

Standard Deviation:

'A measure of how values are dispersed about a mean in a distribution of values.'

Test Kit

'A commercially packaged system of the principal or key components of a testing method. Test kits include directions for use and are often self-contained, complete analytical systems; however they may also require supporting equipment and supplies. The key components frequently represent proprietary elements or reagents that may be readily prepared only by the producer of the kit.'

Test Organiser

'A person designated by the test sponsor or appointed by the ISTA Technical Committee to develop and organise the validation test.'

Test Plan

'Detailed plan for execution of a comparative test by several laboratories on one or more test methods.'

Test Report

'Standard technical report of the results of a comparative test, with discussion of results, conclusions and recommendations prepared by the test organiser.'

'ISTA Method Validation Report.'

Traceability:

'Property of the result of a measurement or the value of a standard whereby it can be related with a stated uncertainty, to stated references, usually national or international standards (i.e. through an unbroken chain of comparisons).'

Note: The standards referred to here are measurement standards rather than written standards. [ISO/IEC Guide 30 - 1992, 3.8].

'Ability to trace the history, application or location of that which is under consideration.' [ISO 9000:2000].

'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.'

Note: The concept is often expressed by the adjective traceable. The unbroken chain of comparisons is called a traceability chain. [VIM,].

Trueness:

'Closeness of agreement between the average that would ensue from an infinite number of quantity values obtained under specified measurement conditions and the true value of the measurand.'

Note: Trueness cannot be expressed as a numerical value.

Trueness is inversely related to systematic error only.

The term 'trueness of measurement' should not be used for accuracy of measurement. [Draft International Vocabulary of Basic and General Terms in Metrology, VIM, April 2004].

Uncertainty (of Measurement) i.e. Measurement Uncertainty:

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

Note: The parameter may be, for example, a standard deviation (or a given multiple of it), or the width of a confidence interval. Uncertainty of measurement comprises, in general, many components. Some of these components may be evaluated from the statistical distribution of the 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. It is understood that the result of the measurement is the best estimate of the value of the 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. ' [VIM 1993].

Validation:

'Confirmation by examination and provision of objective evidence that the particular requirements for a specified intended use are fulfilled.' [ISO 8402:1994].

Method Validation:

1. 'The process of establishing the performance characteristics and limitations of a method and the identification of influences which may change these characteristics and to what extent. Which analytes can it determine in which matrices in the presence of which interferences?

Within these conditions what levels of precision and accuracy can be achieved?'

2. 'The process of verifying that a method is fit for purpose, i.e. for use for solving a particular analytical problem.'

[Eurachem guide: The Fitness for Purpose of Analytical Methods]

Value:

Accepted Reference Value:

'A 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 organisation;
- 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 experimentation of the (measurable) quantity, i.e. the mean of a specified population of measurements.' [ISO 3534-1].

True Value:

'Value consistent with the definition of a given particular quantity.'

Note: This is a value that would be obtained by a perfect measurement. True values are by nature indeterminate. The indefinite article a rather than the definite article the is used in conjunction with true value because there may be many values consistent with the definition of a particular quantity. [VIM 1993].

Verification:

'Confirmation by examination and provision of objective evidence that specified requirements have been fulfilled.' [ISO 8402:1994].

'Confirmation, through provision of objective evidence, that specified requirements have been fulfilled.' [ISO 9000:2000].