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## Molecular biomarker analysis — Terms and definitions

*Analyse moléculaire de biomarqueurs — Termes et définitions*

ICS: 67.050

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## Foreword

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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.

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ISO 16577 was prepared by Technical Committee ISO/TC 34, *Food products*, Subcommittee SC 16, *Horizontal methods for molecular biomarker analysis*.

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## Molecular Biomarker Analysis — Terms and definitions

### 1 Scope

This Standard gives the definition of terms used in the International Standards published in the frame of ISO/TC 34/SC 16. It may also be useful for other methods.

### 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 3534-2: 2006, Statistics -- Vocabulary and symbols -- Part 2: Applied statistics

ISO 21572:2013, Foodstuffs -- Molecular biomarker analysis -- Protein-based methods

ISO 13495:2013, Foodstuffs – Molecular biomarker analysis -- Principles of selection and criteria of validation for varietal identification methods using specific nucleic acid

### 3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

#### 3.1

##### **absolute error**

result of a measurement minus a true value of the measurand

#### 3.2

##### **accordance**

similarity of consistent results (i.e. both positive or both negative) from identical samples analyzed in the same laboratory in repeatability conditions in terms of qualitative method

#### 3.3

##### **accuracy**

closeness of agreement between a test result or measurement result and a reference value

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

NOTE When applied to a test method, the term accuracy refers to a combination of trueness and precision.

#### 3.4

##### **allele**

competitive phenomenon that results in the preferential amplification of one allelic sequence over another in a heterozygous or mixed sample during the application of nucleic acid amplification technologies such as PCR

**3.5**  
**allele competition**

competitive phenomenon that results in the preferential amplification of one allelic sequence over another in a heterozygous or mixed sample during the application of nucleic acid amplification technologies such as PCR

NOTE Adapted from ISO 13495:2013

**3.6**  
**allele frequency**

frequency at which an allele appears on a specific locus in a population

NOTE Adapted from ISO 13495:2013

**3.7**  
**amplicon**

DNA sequence produced by a DNA-amplification technology, such as the PCR technique.

NOTE Adapted from ISO 13495:2013

**3.8**  
**analyte**

component of a system to be analyzed

**3.9**  
**annealing**

pairing of complementary single strands of nucleic acids to form a double stranded molecule

**3.10**  
**antibody**

protein produced by B lymphocytes that recognizes a particular foreign 'antigen', and thus triggers an immune response

NOTE Immunoglobulin is the common synonym for antibody

**3.11**  
**antibody selectivity**

ability of an antibody to specifically bind to an antigenic determinant but not to other similar structures on that or other antigens

**3.12**  
**antigen**

substance that is recognized as foreign by the immune system and elicits an immune response through stimulating antibody production

**3.13**  
**applicability**

analytes, matrices, and concentrations for which an analytical approach may be used satisfactorily

**3.14**  
**applicability range**  
**range of quantification**  
**range of linearity**  
**dynamic range**

upper and lower limits of quantification as expressed by a set of reference materials (or dilutions) with a suitable level of precision and accuracy

**3.15**  
**background**

intrinsic level of signal resulting from the instruments, reagents and consumables used in the reaction

**3.16****baseline**

level of detection or the point at which a reaction reaches fluorescence or signal intensity above the background level

**3.17****bias**

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

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

**3.18****biotechnology-derived trait**

see genetically engineered organism

**3.19****blocking reagent**

compound used to saturate the residual unspecific binding sites

**3.20****calibration**

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

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

**3.21****certified reference material****CRM**

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

NOTE Documentation is given in the form of a "certificate" (see ISO guide 30:1992). Procedures for the production and certification of certified reference materials are given, e.g. in ISO Guide 34 and ISO Guide 35. "Uncertainty" covers both measurement uncertainty and uncertainty associated with the value of the nominal property, such as for identity and sequence. Traceability covers both metrological traceability of a value and traceability of a nominal property value.

**3.22****clone**

population of cells, generated by asexual reproduction, that are genetically identical and direct descendants of a parent cell, derived from a single cell

**3.23****collaborative trial**

see inter-laboratory study

**3.24****complementary sequence**

complementarity is a property shared between two nucleic acid sequences, such that when they are aligned antiparallel to each other, the nucleotide bases at each position will be complementary



**3.25****concordance**

similarity or agreement of results (i.e. both positive or both negative) from identical samples that are analyzed in two different laboratories in terms of qualitative analysis

**EXAMPLE** Conjugates of antibodies with fluorochromes (or fluorophores; chemical entity, such as a molecule or group, that emits light that is in response to being stimulated by absorption of incident light), radiolabelled substances, gold or enzymes are often used in immunoassays.

**3.26****construct-specific detection method**

method which targets a combination of inserted DNA sequences (such as genes, promoters, terminators or other genetic elements of interest) unique to biotechnology-derived organisms

**3.27****conventional quantity value**

quantity value attributed by agreement to a quantity for a given purpose

**NOTE** Sometimes a conventional quantity value is an estimate of a true quantity value. The term “conventional true quantity value” is sometimes used for this concept. A conventional quantity value is generally accepted as being associated with a suitably small measurement uncertainty, which might be effectively considered to be zero.

**3.28****copy number**

number of molecules (copies) of a DNA sequence.

**3.29****critical value**

value of the net concentration or amount, the exceeding of which leads, for a given error probability,  $\alpha$ , to the decision that the concentration or amount of the analyte in the analyzed material is larger than that in the blank material:

$$\Pr(\hat{L} > L_c | L = 0) \leq \alpha$$

Where  $\hat{L}$  is the estimated value,  $L$  is the expectation or true value and  $L_c$  is the critical value.

**NOTE** The definition of critical value is important for defining the Limit of Detection (LOD). The critical value  $L_c$  is estimated by  $L_c = t_{1-\alpha, \nu} s_0$ ,

Where  $t_{1-\alpha, \nu}$  is Student's-t, based on  $\nu$  degrees of freedom for a one-sided confidence interval of  $1-\alpha$  and  $s_0$  is the sample standard deviation.

If  $L$  is normally distributed with known variance, i.e.  $\nu = \infty$  with the default  $\alpha$  of 0.05,  $L_c = 1.645s_0$ . A result falling below the  $L_c$  triggering the decision “not detected” should not be construed as demonstrating analyte absence.

**3.30****cross-reactivity**

degree to which binding occurs between an antibody and antigenic determinants which are not the analyte of primary interest

**3.31****cry proteins**

class of proteins produced by *Bacillus thuringiensis* (*B.t.*) bacteria (or plants into which a *Bt* gene has been inserted) that are toxic to certain categories of insects such as corn borers (e.g., *Ostrinia nubilalis*), corn rootworms (*Diabrotica virgifera virgifera*), armyworms (e.g., *Spodoptera frugiperda*), black cutworms (*Agrostis ipsilon*), velvetbean caterpillar (*Anticarsia gemmatalis*), mosquitoes, black flies, tobacco hornworm, some types of beetles, etc.), but harmless to mammals and most beneficial insects

**3.32****cultivar**

group of cultivated plants which may be clearly defined by morphological, physical, cytological, chemical or other characteristics and which, after sexual or asexual reproduction keeps its distinct character

NOTE The concept of "cultivar" is essentially different from the concept of the botanical variety "varietas", in that – "cultivar" is an infraspecific division resulting from controlled selection, even if empirical; – "varietas" is an infraspecific division resulting from natural selection. The terms "cultivar" and "variety" (in the sense of cultivated variety) are equivalent. In translations or adaptations of botanical nomenclature for particular uses, the terms "cultivar" or "variety" (or their equivalents in other languages) may be used in text.

NOTE The names of botanical varieties and species are always in Latin form and are governed by botanical nomenclature.

**3.33****cycle threshold****C<sub>t</sub>**

in real-time quantitative PCR, the cycle at which the fluorescence from the reaction crosses a specified threshold level at which the signal can be distinguished from background levels

**3.34****denaturation**

process of partial or total alteration of the native structure of a macromolecule resulting from the loss of tertiary and/or secondary structure that is a consequence of the disruption of stabilizing weak bonds

EXAMPLE Denaturation can occur when proteins and nucleic acids are subjected to elevated temperature, extremes of pH, non-physiological concentrations of salt, organic solvents, urea or other chemical agents.

**3.35****denatured DNA**

DNA that has been converted from double-stranded to a single-stranded form by a denaturation process such as heating

**3.36****denaturation of protein**

physical and/or chemical treatment which destroys or modifies the structural, functional, enzymatic, or antigenic properties of the protein of interest

**3.37****deoxyribonuclease/ribonuclease**

enzyme of the hydrolase class that catalyzes the hydrolytic cleavage of deoxyribonucleic acid/ribonucleic acid that may produce a single nucleotide residue by cleavage at the end of the chain or a polynucleotide by cleavage at a position within the chain, also referred to as *DNase/RNase*

**3.38****deoxyribonuclease/ribonuclease inhibitor**

substance that either fully or partially blocks deoxyribonuclease/ribonuclease activity

**3.39****deoxyribonucleic acid****DNA**

polymer of deoxyribonucleotides occurring in double strand (dsDNA) or single strand (ssDNA) form that is the carrier of genetic information, encoded in the sequence of bases (nitrogen containing ring compounds that are either purines or pyrimidines); and is present in chromosomes and chromosomal material of cell organelles as well as in plasmids and in viruses

**3.40**  
**deoxyribonucleotide triphosphate**  
**dNTP**

generic term referring to the four deoxyribonucleotides: deoxyadenosine nucleotide triphosphate (dATP), deoxycytidine nucleotide triphosphate (dCTP), deoxyguanosine nucleotide triphosphate (dGTP), and deoxythymidine nucleotide triphosphate (dTTP)

**3.41**  
**detection assay**

procedure or method that is used to identify the presence of traits, microorganisms, pests or other analytes in a biological sample, conducted at a specified taxonomic level

**3.42**  
**detection of PCR product**

act of noting or discovering the existence of a PCR product by visualizing a fluorescent band (i.e., ethidium bromide staining) on an agarose gel or with fluorescent probes in real-time PCR applications or other approaches

**3.43**  
**dip stick test**

see lateral flow membrane assay

**3.44**  
**DNA extraction**

procedure used for separating DNA from other cellular components (protein, lipids, carbohydrates, RNA etc.) and other impurities in a test sample

**3.45**  
**DNA polymerase**

enzyme that synthesizes DNA by catalyzing the addition of deoxyribonucleotide residues to the free 3'-hydroxyl end of a DNA molecular chain, starting from a mixture of the appropriate triphosphorylated bases

NOTE Taq DNA polymerase (3.205) is a thermostable DNA polymerase.

**3.46**  
**DNA probe**

short sequence of DNA labelled isotopically or chemically that is used for the detection of a complementary nucleotide sequence

NOTE Adapted from ISO 13495:2013

**3.47**  
**DNA purification**

see nucleic acid purification

**3.48**  
**DNA sequencer**  
**gene sequencer**  
**genetic analyzer**

apparatus used for determining the arrangement of the nucleotide bases (adenine, guanine, cytosine, and thymine) in a molecule of DNA

**3.49**  
**DNA target**

see target sequence