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Molecular biomarker analysis — Vocabulary for molecular biomarker analytical methods in agriculture and food production

Analyse de biomarqueurs moléculaires — Vocabulaire pour les méthodes d'analyse de biomarqueurs moléculaires dans l'agriculture et la production agroalimentaire

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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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

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

This second edition cancels and replaces the first edition (ISO 16577:2016), which has been technically revised.

The main changes are as follows:

— definitions have been updated, and new definitions have been added;

— typographical errors have been corrected.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Molecular biomarker analytical testing methods in agriculture and food production cover a broad spectrum of molecular technologies including but not limited to the analysis of nucleic acids, proteins, lipids and glycosides for biomarker identification and quantification, variety identification and detection of plant pathogens. This document includes terminology for biomolecular methods and processes in the food chain from primary production to consumption, as well as animal and vegetable propagation materials, in particular, as applied to sampling, methods of test and analysis, product specifications, food and feed safety, quality management, and requirements for packaging, storage and transportation. It includes terms that are useful metrologically in biomarker analysis of food and food products such as those from Codex Alimentarius and those applied to genetically modified organism (GMO) testing. It is important that a harmonized compendium of terms is available so that terms are used accurately and consistently throughout this field of standardization.

The terms in this document conform to the foundational FAIR principles: findability, accessibility, interoperability and reusability. They serve as a basis for terminology applied to horizontal methods for molecular biomarker analysis of food products.

Molecular biomarker analysis — Vocabulary for molecular biomarker analytical methods in agriculture and food production

1 Scope

This document defines terms for horizontal methods for molecular biomarker analysis in agriculture and food production.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1 Bioinformatics

3.1.1
bioinformatic analysis
bioinformatics
multidisciplinary examination of life sciences data using information technology as part of the methodology, as well as a reference to specific analytical "pipelines" to understand and interpret these biological data

Note 1 to entry: Life sciences data include genomics (including sequencing, massively parallel sequencing, metagenomics, epigenomics and functional genomics), transcriptomics, translatomics, proteomics, metabolomics, lipidomics, glycomics, enzymology, immunochemistry, life science imaging, synthetic biology, systems biology, systems medicine and related fields.

3.1.2
FASTA format
text-based format for representing either nucleotide sequences or amino acid (protein) sequences, in which nucleotides or amino acids are represented using single-letter codes

Note 1 to entry: A sequence in FASTA format begins with a single-line description, followed by lines of sequence data. The description line (defline) is distinguished from the sequence data by a greater-than (">") symbol at the beginning. It is recommended that all lines of text be shorter than 80 characters in length.

Note 2 to entry: An example sequence in FASTA format is:

>P01013 GENE X PROTEIN (OVALBUMIN-RELATED)
QIKDLLVSSSTDLDTTLVLVNAIYFKGMWKTAFNAEDTREMPFHVTKQESKPVQMMCMNNSFNVATLPAEKMKILELP-
FASGDLSMLVLLPDEVSDLERIEKTINFEKLTEWTNPNTMEKRRVKVYLPQMKIEEKYNLTSVLMALGMTDLFIPSANLT-
GISSAESLKISQAVHGAFMELSEDGIEMAGSTGVIEDIKHSPESEQFRADHPFLFLIKHNPTNTIVYFGRYWSP*

Note 3 to entry: Blank lines are not allowed in the middle of FASTA input. Sequences are represented in the standard IUB/IUPAC amino acid and nucleic acid codes, with these exceptions:

— lower-case letters are accepted and are mapped into upper-case;

— a single hyphen or dash can be used to represent a gap of indeterminate length;

— in amino acid sequences, U and * are acceptable letters.

It is common to end the sequence with an "*" (asterisk) character and to leave a blank line between the description and the sequence.

3.1.3
FASTQ format
FASTQ files
text based format for nucleic acid sequence files that includes the sequence and per base Phred or Q quality scores

Note 1 to entry: FASTQ files consist of a definition line that contains a read identifier and possibly other information, nucleotide base calls, a second description line (definition line), and per-base quality scores, all in text form.

Note 2 to entry: There are many variations of FASTQ formats.

Note 3 to entry: The following terms and formats are defined in general:

— Decimal-encoding, space-delimited: [0-9]+ | <quality>\s[0-9]+

— Phred-33 ASCII: [\!\"\#\$\%\&\'\(\)*\+,\-\.\/0-9:;<=>\?\@A-I]+

— Phred-64 ASCII: [\@A-Z\[\\\]\^_`a-h]+

Note 4 to entry: Quality string length should be equal to sequence length.

Note 5 to entry: In a limited set of cases, log odds or non-ASCII numerical quality values will succeed during a sequence read archive (SRA) submission. Files from various platforms employing this format are acceptable:

@<identifier and expected information>; <sequence>; +<identifier and other information OR empty string>; <quality>

Note 6 to entry: Where each instance of Identifier, Bases and Qualities are newline-separated, extra information added beyond the < identifier and expected information > examples is likely to be discarded/ignored. As indicated above, the Qualities string can be space-separated numeric Phred scores or an ASCII string of the Phred scores with the ASCII character value = Phred score plus an offset constant used to place the ASCII characters in the printable character range. There are two predominant offsets: 33 (0 = !) and 64 (0=@).

3.1.4
metadata
data providing information about one or more aspects of the datasets ("data about data")

EXAMPLE Means of creation of the data, purpose of the data, file size, data quality, source of the data.

Note 1 to entry: Metadata are used to summarize basic information about data which can make tracking and working with specific data easier.

3.2 Immunology

3.2.1
antibody
Ab
host proteins produced in response to the presence of foreign molecules, organisms or other agents in the organism

Note 1 to entry: Antibodies are useful reagents that can bind with high affinity to chosen antigens.

Note 2 to entry: In animals, antibodies are synthesized predominantly by plasma cells, terminally differentiated cells of the B-lymphocyte lineage, and circulate throughout the blood and lymph where they bind to antigens.

3.2.2
antibody specificity
ability of an antibody to specifically bind to an antigenic determinant (epitope) but not to other similar structures on that or other antigens

3.2.3
antigen
Ag
molecule, macromolecule or molecular structure, containing epitopes that can be bound by an antibodies (Ab), B-cells or T-cells

Note 1 to entry: The presence of antigens in vertebrates can trigger an immune response.

Note 2 to entry: The antigen binding site of an antibody is formed by the variable regions of the heavy and light chains.

3.2.4
blocking reagent
compound used to saturate the residual unspecific binding sites

Note 1 to entry: Blocking agents are typically used in preparation of an ELISA plate: blocking the plate with a non-reactive protein is used to prevent non-specific adsorption of proteins added in subsequent steps and storage of the ELISA plates.

Note 2 to entry: A blocking reagent can be used to decrease the background in protein or nucleic acid hybridization methods.

3.2.5
conjugate
material produced by attaching two or more substances together by a covalent bond via chemical groups

Note 1 to entry: Conjugates of antibodies with fluorochromes (e.g. a chemical entity, such as a molecule or group that emits light in response to excitation by absorbed incident light, radiolabelled substances, gold or enzymes) are often used in immunoassays.

3.2.6
enzyme-linked immunosorbent assay
ELISA
in vitro assay used for qualitative, semi-quantitative or quantitative purposes that combines enzyme-linked antibodies and a substrate to form a coloured or a fluorescence emitting reaction product

3.2.7
epitope
antigenic determinant
spatially localized components of an antigen to which an antibody binds that can be formed by contiguous or non-contiguous amino acid sequences and haptens

Note 1 to entry: The association between an Ab and an Ag involves myriad of non-covalent interactions between the epitope (the binding site on the Ag) and the paratopes (the binding site on the Ab).

3.2.8
lateral flow device
LFD
lateral flow membrane assay
lateral flow strip
LFS
immunoassay in which antibodies are bound in specific zones on a porous membrane of one or more layers, and where a liquid sample is applied to one end of the membrane and drawn through the reagent zones by capillary action, usually assisted by an absorbent at the opposite end of the membrane

Note 1 to entry: Typically, a coloured "control line" furthest from the end of the strip that is inserted into the sample indicates whether the test performed successfully. Results of the test are indicated by the presence or absence of one or more additional test lines that are expected between the point of sample application and the "control line".

Note 2 to entry: Immunoassay is the most common form of LFD but other biorecognition systems, e.g. nucleic acid hybridization, are also used.

3.2.9
monoclonal antibody
mAb
population of antibody molecules that share the same amino acid sequence, bind the same epitope, and are produced by a cell line derived from a single clonal cell or are produced recombinantly

3.2.10
polyclonal antibody
population of antibody molecules secreted by different B-cell lineages that react against a specific antigen, each potentially identifying a different epitope

3.3 Metrology

3.3.1
absolute error
result of a measurement minus the true value of the measurand

3.3.2
accordance
similarity of consistent results from a qualitative method (i.e. both positive or both negative) from identical test items analysed in the same laboratory under repeatability conditions

3.3.3
accuracy
closeness of agreement between a test result or measurement result and a reference value

Note 1 to entry: 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 2 to entry: When applied to a test method, the term "accuracy" refers to a combination of trueness and precision.

3.3.4
analyte
component of a system to be analysed

Note 1 to entry: This definition can be applied to molecular biological analytical methods, e.g. protein, lipid, RNA or DNA.

3.3.5
applicability
fitness for purpose
scope of application of the method identifying the matrix, analyte or species being measured, its concentration range and the type of study or monitoring, or both, efforts for which the procedure is suited, as judged from its performance characteristics

Note 1 to entry: In addition to a statement of the range of capability of satisfactory performance for each factor, the statement of applicability (scope) may also include warnings as to known interference by other analytes, or inapplicability to certain matrices and situations.

3.3.6
applicability range
range of quantification
dynamic range
quantity interval within which the analytical procedure has been demonstrated by a collaborative trial or other appropriate validation (e.g. reference materials or dilutions) to have a suitable level of precision and accuracy

3.3.7
background
intrinsic level of signal resulting from the instruments, reagents and consumables used in the reaction

3.3.8
baseline
level of detection or the point at which a reaction reaches a signal intensity above the background level

Note 1 to entry: The baseline is used in quantitative polymerase chain reaction analyses and can be automatically set by the instrument or manually determined.

3.3.9
bias
measurement bias
difference between the expectation of the test result or measurement result and the true value or conventional quantity value

Note 1 to entry: Bias is the total systematic error as contrasted to random error. There can 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.

Note 2 to entry: 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".

Note 3 to entry: Expectation is the expected value of a random variable, e.g. assigned value or long-term average estimate of a systematic measurement error.

3.3.10
binary result
qualitative result
result from a method of analysis where there are only two possible outcomes

3.3.11
calibration
operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties, and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication

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

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

Note 3 to entry: Often the first step in the above definition is perceived as being calibration.

3.3.12
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 1 to entry: Documentation is given in the form of a "certificate".

Note 2 to entry: Procedures for the production and certification of CRMs are given in, for example, ISO 17034 and ISO Guide 35.

Note 3 to entry: In this definition, "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".

Note 4 to entry: Specified values of CRMs require metrological traceability with associated measurement uncertainty.

3.3.13
coefficient of variation
C_v
DEPRECATED: relative standard deviation
standard variation divided by the mean

Note 1 to entry: The coefficient of variation is commonly reported as a percentage.

3.3.14
colorimetric detection
method of detecting an analyte by measuring a colorimetric signal, usually by using a spectrophotometer

EXAMPLE A method for detecting hybridization using immobilized probe DNA measuring a colorimetric signal.

Note 1 to entry: A fluorophore such as SYBR® Green[1)] may also be used.

Note 2 to entry: An enzyme-linked detection system (conjugated with an enzyme) is often used to measure the signal in an ELISA assay colorimetrically.

Note 3 to entry: Colloidal gold is also used for this purpose in lateral flow devices.

Note 4 to entry: Colorimetry may be used qualitatively or quantitatively.

3.3.15
concordance
similarity or agreement of results (i.e. both positive or both negative) from identical test items that are analysed in two different laboratories in terms of qualitative analysis

3.3.16
conventional quantity value
DEPRECATED: conventional true quantity
number and reference together expressing magnitude of a quantity attributed by agreement to a quantity for a given purpose

Note 1 to entry: Sometimes a conventional quantity value is an estimate of a true quantity value.

1) SYBR® Green is an example of a suitable product available commercially. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of the product named.

Note 2 to entry: A conventional quantity value is generally accepted as being associated with a suitably small measurement uncertainty, which can be effectively considered to be zero.

3.3.17
critical value
value of the net concentration or amount, the exceeding of which leads, for a given error probability, α, to the decision that the concentration or amount of the analyte in the analysed material is larger than that in the blank material:

$$P_r\left(\hat{L} > L_C \,\middle|\, L = 0\right) \leq \alpha$$

where

P_r is the probability function

$\hat{L}$ is the estimated value

L_C is the critical value

L is the expectation or true value

Note 1 to entry: The definition of critical value is important for defining the limit of detection (LOD). The critical value L_C is estimated by:

$$L_C = t_{1-\alpha\nu} s_o$$

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

Note 2 to entry: If L is normally distributed with known variance, i.e. $\nu = \infty$ with the default α of 0,05, then $L_C = 1{,}645 s_o$.

Note 3 to entry: A result falling below the L_C triggering the decision "not detected" should not be construed as demonstrating analyte absence. Reporting such a result as "zero" or as < LOD is not recommended.

Note 4 to entry: The estimated value and its uncertainty should always be reported.

3.3.18
defining method of analysis
empirical method of analysis
conventional method of analysis
method in which the quantity measured is defined by the result found upon following the stated procedure

Note 1 to entry: Defining methods of analysis are used for purposes that cannot be covered by rational methods.

Note 2 to entry: Bias in defining methods of analysis is conventionally zero.

3.3.19
error
measured quantity value minus a reference quantity value

Note 1 to entry: The concept of measurement "error" can be used: a) when there is a single reference quantity value to refer to, which occurs if a calibration is made by means of a measurement standard with a measured quantity value having a negligible measurement uncertainty or if a conventional quantity value is given, in which case the measurement error is known; and b) if a measurand is supposed to be represented by a unique true quantity value or a set of true quantity values of negligible range, in which case the measurement error is not known.

3.3.20
expanded measurement uncertainty
product of a combined standard measurement uncertainty and a factor larger than the number one

Note 1 to entry: The factor depends upon the type of probability distribution of the output quantity in a measurement model and on the selected coverage probability.

Note 2 to entry: The term "factor" in this definition refers to a coverage factor.

Note 3 to entry: Expanded measurement uncertainty is termed "expanded uncertainty".

3.3.21
false negative
error of failing to reject a null hypothesis when it is in fact not true

Note 1 to entry: A false negative is the result for a positive sample that has been classified as negative by the method/analysis.

3.3.22
false negative rate
probability that a known positive test sample has been classified as negative by the method

Note 1 to entry: The false negative rate is the number of misclassified known positives divided by the total number of positive test samples.

3.3.23
false positive
error of rejecting a null hypothesis when it is actually true

Note 1 to entry: A false positive is the result for a negative sample that has been classified as positive by the method/analysis.

3.3.24
false positive rate
probability that a known negative test sample has been classified as positive by the method

Note 1 to entry: The false positive rate is the number of misclassified known negatives divided by the total number of negative test samples.

3.3.25
good laboratory practice
GLP
set of rules and regulations issued by an authoritative body or standards organization, or generally agreed upon best practices for laboratory operation, that establishes broad methodological guidelines for laboratory procedures and record keeping

Note 1 to entry: GLP in the regulatory environment is a set of requirements that guide how laboratory studies are planned, performed, monitored, recorded, reported and archived in order to ensure the credibility and traceability of data submitted to regulatory bodies. Requirements can differ between countries.

3.3.26
HorRat
normalized performance parameter indicating the acceptability of methods of analysis with respect to interlaboratory precision (reproducibility)

Note 1 to entry: The HorRat is the ratio of the observed reproducibility coefficient of variation among laboratories calculated from the actual performance data ($C_{V,R}$) to the corresponding predicted $C_{V,R}$ calculated from the Horwitz equation:

$$C_{V,R\_\text{predicted}} = 2C^{-0,15}$$

where C is concentration expressed as a mass fraction (both numerator and denominator expressed in the same units).

Note 2 to entry: Normal values lie within 0,5 to 2. (To check the proper calculation of predicted $C_{V,R}$, a C of 10^{-6} should give a predicted $C_{V,R}$ of 16 %.)

Note 3 to entry: If applied to within-laboratory studies, the normal range of HorRat(r) is 0,30 to 1,30.

Note 4 to entry: For concentrations less than 0,12 mg/kg, the predicted standard deviation 22 % should be used.

3.3.27
identical test item
identical measurement item
prepared sample that is presumed to be identical for the intended purpose of measurement of the measurand

3.3.28
identity preservation
process or system of maintaining the segregation and documenting the identity of a product

3.3.29
intraclass correlation coefficient
ICC
measure of the reliability of measurements as performed by different groups

Note 1 to entry: Groups in this context equates to different laboratories with two or more results measured on identical test items (e.g. DNA copy number, % mass, seed count).

Note 2 to entry: This coefficient represents agreements between two or more results measured on identical test items.

3.3.30
item
entity
anything that can be described and considered separately

3.3.31
laboratory performance study
proficiency test
study consisting of one or more measurements performed independently by a group of laboratories on one or more homogeneous, stable, test samples by the method selected or used by each laboratory in the group where the reported results are compared with those from other laboratories or with the known or assigned reference value, usually with the objective of improving laboratory performance

Note 1 to entry: Laboratory performance studies can be used to support laboratory accreditation of laboratories or to audit performance. If a study is conducted by an organization with some type of management control over the participating laboratories (organizational, accreditation, regulatory or contractual), the method can be specified or the selection may be limited to a list of approved or equivalent methods. In such situations, a single test sample is insufficient to judge performance.

Note 2 to entry: A laboratory performance study can be used to select a method of analysis that will be used in a method performance study. If all laboratories or a sufficiently large subgroup of laboratories use the same method, the study may also be interpreted as a method performance study, provided that the test samples cover the range of concentration of the analyte.

Note 3 to entry: Laboratories of a single organization with independent facilities, instruments and calibration materials are treated as different laboratories.