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Biotechnology — Biobanking — General requirements for the validation and verification of processing methods for biological material in biobanks

Biotechnologie — Biobanques — Exigences générales pour la validation et la vérification des méthodes de traitement du matériel biologique dans les biobanques

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Foreword

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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).

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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 276, *Biotechnology*.

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

Biobanks, producing viable and non-viable biological materials (human, animal, plant, microbial) for research purposes, within biotechnology, use processing methods. Many biobanks include processing laboratories where processing methods are performed and biological materials are produced as an output. Examples of widely used processing methods, applied by biobank laboratories, include DNA, RNA and protein extractions from blood, tissue, seeds, bacteria, or other biological material, or primary cell cultures. An example for the validation of a processing method is provided in Reference [27]. Biobank laboratories are not always equipped to perform testing methods, which are required for annotation or qualification of the biological material output.

This document sets out specific requirements for validation of processing methods. It is intended to help biobank laboratories who perform processing of biological materials, whether they perform themselves testing activities on the biological materials they have produced, or not. It enables validation of processing methods, complements the quality management system of any biobank laboratory performing processing of biological materials and gives more credibility to such an organization. It is understood that while the term "method" used in ISO/IEC 17025 corresponds to "testing method" or "calibration method", a fundamental distinction exists between "processing methods" where the output is a biological material and "testing methods" where the output is a test result (see Annex A). It is understood that validation of processing methods performed by accredited testing laboratories, who test the biological material output themselves, is already included in their accreditation scope.

Validation of a processing method encompasses confirmation of the fitness for purpose of the output biological material, assessment of the homogeneity and stability of the biological material, and assessment of the reproducibility and robustness of the processing method. This validation requires testing in order to assess/measure the qualitative or quantitative properties of the biological material. This testing will lead to the assessment of the fitness for purpose, the reproducibility, and the robustness of the processing method. Examples of such properties are: viability, purity, pluripotency, molecular integrity, concentration, growth capacity, etc.

Biotechnology — Biobanking — General requirements for the validation and verification of processing methods for biological material in biobanks

1 Scope

This document specifies the validation and verification requirements applicable to a biobank to be able to demonstrate that it operates its processing of biological materials with validated and/or verified methods that are fit for purpose.

This document is intended for use in the implementation and validation of processing methods for biological materials.

This document covers method validation and verification for the production of all biological materials. This document does not apply to biological material intended for food/feed production, laboratories undertaking food/feed analysis, and/or therapeutic use.

Reference material production is not covered in this document. For the production requirements for reference materials, see ISO 17034.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 20387, *Biotechnology — Biobanking — General requirements for biobanking*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 20387 and the following apply.

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

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

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

3.1
aliquot
portion of a quantity of biological material which has been divided into separate parts at the same time under identical conditions

Note 1 to entry: The aliquot is representative of the biological material with respect to the property or properties being investigated.

Note 2 to entry: The term aliquot most commonly refers to liquid or semi-liquid biological materials.

3.2
biobank laboratory
processing (3.15) laboratory under the control of a biobank where *processing methods* (3.16) are performed for the output/production of biological materials

3.3
exploratory processing method
processing method (3.16) or adaptation/modification of a processing method, at an early stage of development by the *biobank laboratory* (3.2) and for which further assessment is needed to determine if it is useful for a specified application

3.4
external provider
body that undertakes aspects of the collection, transportation, *preparation* (3.14), handling, *homogeneity* (3.7) and *stability* (3.21) assessment, testing or storage of the biological materials under its own management system, on behalf of the biobank, on a contractual basis, or in the context of the *validation* (3.25) of a *processing method* (3.16)

Note 1 to entry: A body can be an organization or a company, public or private.

3.5
feasibility
assessment of whether the *processing method* (3.16) can be applied to produce the desired type of biological material output, independently from the properties of interest of this output biological material

3.6
fit for purpose
fitness for the intended purpose
in-line with prearranged requirements for an intended use

Note 1 to entry: The definition of such requirements can take place within the biobank itself and/or in collaboration with users and should consider analytical and other relevant criteria.

Note 2 to entry: These requirements correspond to the *feasibility* (3.5) of the downstream intended use and the satisfaction of predefined *performance* (3.12) criteria of the intended use.

[SOURCE: ISO 20387:2018, 3.24, modified — Note 2 to entry has been added.]

3.7
homogeneity
uniformity of a specified, quantitative or qualitative, property value throughout a defined portion [or among different *aliquots* (3.1)] of a biological material

3.8
installation qualification
IQ
process of establishing by objective evidence that all key aspects of the process equipment and ancillary system installation comply with the approved specification

[SOURCE: ISO 11139:2018, 3.220.2]

3.9
measurand
quantity intended to be measured

[SOURCE: ISO/IEC Guide 99:2007, 2.3, modified — Notes to entry and examples were deleted.]

3.10
measurement
process of experimentally obtaining one or more quantity values that can reasonably be attributed to a quantity

Note 1 to entry: Measurement does not apply to nominal properties.

Note 2 to entry: Measurement implies comparison of quantities or counting of entities.

Note 3 to entry: Measurement presupposes a description of the quantity commensurate with the intended use of a measurement result, a measurement procedure, and a calibrated measuring system operating according to the specified measurement procedure, including the measurement conditions

[SOURCE: ISO/IEC Guide 99:2007, 2.1]

3.11
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO 11139:2018, 3.220.3]

3.12
performance
set of properties of interest of a biological material, produced by a *processing method* (3.16), e.g. yield, purity, integrity, viability, functionality

3.13
performance qualification
PQ
process of establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements

[SOURCE: ISO 11139:2018, 3.220.4]

3.14
preparation
activities, taking place in a laboratory after acquisitioning, to make biological material ready for further use in the life cycle, storage or distribution

Note 1 to entry: These activities can include, e.g., determination of volume or weight, centrifugation, homogenization, purification, isolation, fixation, stabilization, filtration, sorting, culture, vacuum drying, freeze drying, fractionation, aliquoting, removing tissues, cutting / milling / shaping, washing / soaking with antibiotic or antimicrobial solutions, volume reduction / concentration, demineralization, glycerolisation, sterilization, controlled or uncontrolled freezing, vitrification, cryopreservation.

[SOURCE: ISO 20387:2018, 3.37, modified — Note 1 to entry was modified by adding more details.]

3.15
processing
performing any activity on biological material and associated data during all stages of the life cycle

[SOURCE: ISO 20387:2018, 3.36]

3.16
processing method
procedure, applied to biological material and/or associated data during *processing* (3.15), with potential to impact the intrinsic properties of the biological material and/or associated data produced as output

Note 1 to entry: A processing method can include, but is not limited to, activities belonging to: collection, *preparation* (3.14), preservation, storage.

Note 2 to entry: The whole or part of a processing method can be a standard method.

Note 3 to entry: The term “standard” in this instance refers to the broader definition of “standard” — i.e., an agreed-upon set of requirements.

Note 4 to entry: A simple processing method is a processing method that requires a simple laboratory manipulation (e.g. centrifugation of collection tubes or mechanical disruption of tissues) without the addition of chemical substances by the *biobank laboratory* (3.2) operator, and without cell disruption or cell selection as part of a multi-step process (e.g. preparation of plasma, serum, buffy coat).

Note 5 to entry: A complex processing method is a processing method that requires usage of multiple steps and/or addition of chemical substances by the biobank laboratory operator (e.g. preparation of DNA, RNA, proteins, nuclei and other organelles, cell lines).

Note 6 to entry: Qualitative or quantitative tests for the examination of properties/quality/quantity attributes of the produced biological material are outside of the scope of the "processing method" itself. However, a qualitative or quantitative test can be part of a "processing method" if it is necessary as an "in-process control" step during the processing method.

[SOURCE: ISO 20387:2018, 3.38, modified — The notes to entry were added.]

3.17
proficiency testing
evaluation of participant *performance* (3.12) against pre-established criteria by means of interlaboratory comparisons

[SOURCE: ISO/IEC 17043:2010, 3.7, modified — Notes to entry have been deleted.]

3.18
property of interest
physical, chemical, biological, or microbiological property or characteristic that describes or is an indicator of quality

3.19
reproducibility
<processing method> coefficient of variation (CV %) of a property value being measured in biological materials which are the *processing* (3.15) output from *aliquots* (3.1) of the same input biological material (e.g. volume, weight, concentration)

Note 1 to entry: The reproducibility of a *processing method* (3.16) includes components arising from the processing method itself and from the analytical uncertainty of the testing method used to assess the reproducibility.

Note 2 to entry: In general, for a given set of information, it is understood that the reproducibility of a processing method is associated with a stated *measurand* (3.9). A modification of this measurand and the testing method results in a modification of the associated reproducibility.

3.20
robustness
<processing method> capacity of a *processing method* (3.16) to produce biological materials whose properties remain within defined limits despite deviations from the experimental conditions that are described in the *standard operating procedure (SOP)* (3.22) of the processing method

3.21
stability
ability of a biological material, when stored under specified conditions, to maintain a specified property value within specified limits for a specified period of time

[SOURCE: ISO Guide 30:2015, 2.1.15, modified — The words "reference material" have been replaced by "biological material" and Note 1 to entry has been deleted.]

3.22
standard operating procedure
SOP
written procedure prescribed for repetitive use as a practice, in accordance with agreed-upon specifications aimed at obtaining a desired outcome

3.23
standard processing method
method officially accepted and recognized described in unambiguous details and validated for a stated purpose

Note 1 to entry: Standard processing methods include e.g. methods published by a standardization body or approved by regulatory authorities or published in peer-reviewed scientific literature, dedicated, at least partly, to the *validation* (3.25) of the method.

Note 2 to entry: The term “standard” in this instance refers to the broader definition of “standard”—i.e., an agreed-upon set of requirements.

3.24
stress
intentional exposure of biological material to conditions that are different from the predefined routine conditions or procedures and that can affect the properties of the biological material

3.25
validation
confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled

Note 1 to entry: The objective evidence needed for a validation is the result of a test or other form of determination such as performing alternative calculations or reviewing documents.

Note 2 to entry: The word "validated" is used to designate the corresponding status.

Note 3 to entry: The use conditions for validation can be real or simulated.

Note 4 to entry: Validation is the confirmation that the specifications announced by the *biobank laboratory* (3.2) are met.

[SOURCE: ISO 9000:2015, 3.8.13, modified — Note 4 to entry was added.]

3.26
verification
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

Note 1 to entry: Verification is the confirmation that the specifications announced by a supplier, a publication or another external source are met.

Note 2 to entry: The objective evidence needed for a verification can be the result of an inspection or of other forms of determination such as performing alternative calculations or reviewing documents.

Note 3 to entry: The activities carried out for verification are sometimes called a qualification process.

Note 4 to entry: The word “verified” is used to designate the corresponding status.

[SOURCE: ISO 9000:2015, 3.8.12, modified — Note 1 to entry was added.]

4 Abbreviated terms

Abbreviated term	Explanation
CPT	cell preparation tube
CV	coefficient of variation
Hly	hemolysin
n	number of samples
M	mean square
OD	optical density