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Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood —

Part 2: Isolated genomic DNA

Analyses de diagnostic moléculaire in vitro — Spécifications relatives aux processus préanalytiques pour le sang total veineux —

Partie 2: ADN génomique extrait

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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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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 212, *Clinical laboratory testing and in vitro diagnostic test systems.*

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.

A list of all parts in the ISO 20186 series can be found on the ISO website.

Introduction

Molecular in vitro diagnostics has enabled significant progress in medicine. Further progress is expected by new technologies analysing profiles of nucleic acids, proteins, and metabolites in human tissues and body fluids. However, the profiles of these molecules can change drastically during the pre-examination process, including the specimen collection, transport, storage and processing. Consequently, this makes the outcome from diagnostics or research unreliable or even impossible, because the subsequent examination might not determine the real situation in the patient but an artificial profile generated during the pre-examination processes.

Genomic DNA can fragment or degrade after blood collection. Therefore, special measures need to be taken to secure good quality specimens for genomic DNA examination. This is particularly relevant for examination test procedures requiring high molecular weight DNA (HMW DNA).

Standardization of the entire workflow from specimen collection to the genomic DNA examination is needed due to genomic DNA degradation and fragmentation after blood collection. Studies have been undertaken to determine the important influencing factors. This document draws upon such work to codify and standardize the steps for venous whole blood genomic DNA examination in what is referred to as the pre-examination phase.

In this document, the following verbal forms are used:

— “shall” indicates a requirement;

— “should” indicates a recommendation;

— “may” indicates a permission;

— “can” indicates a possibility or a capability.

Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood —

Part 2: Isolated genomic DNA

1 Scope

This document gives guidelines on the handling, storage, processing and documentation of venous whole blood specimens intended for genomic DNA examination during the pre-examination phase before a molecular examination is performed. This document covers specimens collected in venous whole blood collection tubes.

This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities.

Different dedicated measures are taken for stabilizing blood cell free circulating DNA, which are not described in this document.

NOTE Circulating cell free DNA in blood is covered in ISO 20186-3.

Different dedicated measures are taken for collecting, stabilizing, transporting and storing capillary blood as well as for collecting and storing blood by paper based technologies or other technologies generating dried blood. These are not described in this document.

This document does not cover the isolation of specific blood cells and subsequent isolation of genomic DNA therefrom.

DNA in pathogens present in blood is not covered by this document.

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 15189:2012, *Medical laboratories — Requirements for quality and competence*

3 Terms and definitions

For the purposes of this document, the following terms and definitions 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
analyte
component represented in the name of a measurable quantity

[SOURCE: ISO 17511:2003, 3.2]

3.2
backflow
flow of a liquid opposite to the usual or desired direction

3.3
blood collection set
intravenous device specialized for venepuncture consisting of a stainless steel bevelled needle and tube (tubing) with attached plastic wings and fitting connector

Note 1 to entry: The connector attaches to an additional blood collection device, e.g. a *blood collection tube* (3.4).

3.4
blood collection tube
tube used for blood collection, usually in a vacuum which forces blood from the vein through the needle into the tube

3.5
blood genomic DNA stabilizers
compounds, solutions or mixtures that are designed to minimize degradation and fragmentation of *genomic DNA* (3.12) in blood

3.6
closed system
non-modifiable system provided by the vendor including all necessary components for the examination (i.e. hardware, software, procedures and reagents)

3.7
deoxyribonucleic acid
DNA
polymer of deoxyribonucleotides occurring in a double-stranded (dsDNA) or single-stranded (ssDNA) form

[SOURCE: ISO 22174:2005, 3.1.2]

3.8
DNase
deoxyribonuclease
enzyme that catalyses the degradation of DNA into smaller components

3.9
examination
analytical test
set of operations having the object of determining the value or characteristics of a property

Note 1 to entry: Processes that start with the isolated *analyte* (3.1) and include all kinds of parameter testing or chemical manipulation for quantitative or qualitative examination.

[SOURCE: ISO 15189:2012, 3.7, modified — Term and definition are used here without the original notes; an additional term was added.]

3.10
examination performance
analytical test performance
analytical performance
ability of an examination procedure to measure or detect a particular *analyte* (3.1)

Note 1 to entry: Analytical performance is determined from analytical performance studies used to assess the ability of an in vitro diagnostic examination procedure to measure or detect a particular analyte.

Note 2 to entry: Analytical performance includes such characteristics as analytical sensitivity, detection limit, analytical specificity (interference and cross-reactivity), trueness, precision and linearity.

[SOURCE: ISO/TS 17822-1:2014, 3.2, modified — Two terms have been added.]

3.11
examination provider
analytical test provider
entity that provides the specific analytical test

3.12
genomic DNA
DNA from the nuclear and mitochondrial genomes containing all coding (exon) and non-coding (intron and other) sequences

Note 1 to entry: In this document, reference is only made to genomic DNA present in cells in blood, excluding circulating cell free DNA.

3.13
high molecular weight DNA
HMW DNA
DNA with an average double strand size larger than 50 kb on a pulsed field electrophoresis gel for the purpose of this document

3.14
interfering substances
endogenous or exogenous substances in clinical *specimens* (3.17)/*samples* (3.23) that can alter an examination result

Note 1 to entry: Examples of endogenous substances are blood components and acidic polysaccharides.

Note 2 to entry: Examples of exogenous substances are talc and anticoagulant.

3.15
needle holder
barrel used in routine venepuncture procedures to hold the *blood collection tube* (3.4) in place and to protect the phlebotomist from direct contact with blood

3.16
pre-examination processes
preanalytical phase
preanalytical workflow
processes that start, in chronological order, from the clinician's request and include the examination request, preparation and identification of the patient, collection of the *primary sample(s)* (3.17), transportation to and within the medical laboratory, isolation of analytes, and end when the analytical examination begins

Note 1 to entry: The pre-examination phase includes preparative processes, e.g. DNA isolation procedures, which influence the outcome of the intended examination.

[SOURCE: ISO 15189:2012, 3.15, modified — An additional term has been added and more details have been included.]

3.17
primary sample
specimen
discrete portion of a body fluid, breath, hair or tissue taken for examination, study or analysis of one or more quantities or properties assumed to apply for the whole

[SOURCE: ISO 15189:2012, 3.16, modified — Notes to entry have been omitted.]

3.18
primary sample collection device
apparatus specifically intended by an IVD manufacturer to obtain, contain and preserve a body fluid or tissue for in vitro diagnostic examination

[SOURCE: ISO 18113-1:2009, 3.55]

Note 1 to entry: Includes devices intended to store a specimen prior to examination.

Note 2 to entry: Includes both vacuum and non-vacuum specimen collection devices.

3.19
proficiency testing
evaluation of participant performance against pre-established criteria by means of inter-laboratory comparisons

[SOURCE: ISO 17043:2010, 3.7, modified — Term and definition are used here without the original notes.]

3.20
RNA
ribonucleic acid
polymer of ribonucleotides occurring in a double-stranded or single-stranded form

[SOURCE: ISO 22174:2005, 3.1.3]

3.21
RNase
ribonuclease

enzyme that catalyses the degradation of RNA into smaller components

3.22
room temperature
temperature in the range of 18 °C to 25 °C

Note 1 to entry: Local or national regulations can have different definitions.

3.23
sample
one or more parts taken from a *primary sample* (3.17)

[SOURCE: ISO 15189:2012, 3.24, modified — The example has been omitted.]

3.24
stability
ability of a sample material, when stored under specified conditions, to maintain a stated property value within specified limits for a specified period of time

[SOURCE: ISO Guide 30:2015, 2.1.15, modified — The words “reference material” were replaced by “sample material”.]