SLOVENSKI STANDARD
oSIST prEN ISO 20186-3:2018

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Molekularne diagnostične preiskave in vitro - Specifikacije za predpreiskovalne procese za vensko polno kri - Celična RNA - 3. del: Iz plazme izolirani cirkulirajoči brezcelični DNA (ISO/DIS 20186-3:2018)

Molecular in-vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Cellular RNA - Part 3: Isolated circulating cell free DNA from plasma (ISO/DIS 20186-3:2018)

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für venöse Vollblutproben - Teil 3: Aus Plasma isolierte zirkulierende zellfreie DNS (ISO/DIS 20186-3:2018)

Tests de diagnostic moléculaire in vitro - Spécifications relatives aux processus pré-analytiques pour le sang - ARN cellulaire - Partie 3: ADN libre circulant extrait du plasma (ISO/DIS 20186-3:2018)

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

Part 3:
Isolated circulating cell free DNA from plasma

Tests de diagnostic moléculaire in vitro - Spécifications relatives aux processus pré-analytiques pour le sang - ARN cellulaire —

Partie 3: ADN libre circulant extrait du plasma

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ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

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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 on 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 the following URL: www.iso.org/iso/foreword.html.

The committee responsible for this document is ISO/TC 212, *Clinical laboratory testing and in vitro diagnostic test systems*.

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

Introduction

Molecular *in vitro* diagnostics has enabled a significant progress in medicine. Further progress is expected by new technologies analyzing 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 makesthe outcome from diagnostics or research unreliable or even impossible because the subsequent examination might not determine real the situation in the patient but an artificial profile generated during the pre-examination processes.

CcfDNA profiles can change significantly after blood collection (e.g., release of genomic DNA from cells in blood, ccfDNA fragmentation and ccfDNA quantity change). Therefore, special measures have to be taken to secure good quality specimens for ccfDNA examination.

Standardization of the entire workflow from specimen collection to the circulating cell free DNA (ccfDNA) examination is needed due to release of DNA from cells in blood, thus changing the original native ccfDNA profile in the body, but also ccfDNA 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 circulating cell free DNA examination from plasma prepared from human venous whole blood 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 — Cellular RNA —

Part 3: Isolated circulating cell free DNA from plasma

1 Scope

This document recommends the handling, storage, processing and documentation of venous whole blood specimens intended for circulating cell free DNA (ccfDNA) examination during the pre-examination phase before a molecular assay 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 need to be taken for stabilizing blood genomic DNA, which are not described in this document. Blood genomic DNA is covered in ISO 20186-2, *Molecular in vitro diagnostic examinations — specifications for pre-examination processes for venous whole blood — Part 2: Isolated genomic DNA*.

Different dedicated measures need to be taken for preserving DNA in circulating exosomes, which are not described in this document.

NOTE 1 CcfDNA obtained from blood by the procedures suggested in this document can contain DNA present in exosomes[8][9].

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

NOTE 2 International, national or regional regulations or requirements can also apply to specific topics covered in 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 (ISO 15189:2012, Corrected version 2014-08-15)*

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 http://www.iso.org/obp

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

3.1
ambient temperature
unregulated temperature of the surrounding air

3.2
analyte
component represented in the name of a measurable quantity

[SOURCE: ISO 17511:2013, 3.2]

3.3
backflow
flow of a liquid opposite to the usual or desired direction

3.4
blood collection set
intravenous device specialized for venipuncture consisting of a stainless steel beveled 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.

3.5
blood collection tube
tube used for blood collection, usually in a vacuum which forces blood from the vein through the needle into the tube

3.6
ccfDNA
circulating cell free DNA
extracellular human DNA present in blood, serum and plasma

Note 1 to entry: ccfDNA can include DNA present in vesicles such as exosomes[8][9].

3.7
ccfDNA profile/s
circulating cell free DNA profile/s
amounts of different ccfDNA molecules, that are present in blood and plasma that can be measured in the absence of any losses, inhibition and interference

3.8
ccfDNA proficiency testing program
proficiency testing for ccfDNA based examinations

3.9
closed system
non-modifiable system provided by the vendor including all necessary components for the examination (i.e., hardware, software, procedures and reagents)

3.10
cryo-precipitates
for the purpose of this document an insoluble residue when frozen plasma is thawed

3.11
DNA
deoxyribonucleic acid
polymer of deoxyribonucleotides occurring in a double-stranded (dsDNA) or single-stranded (ssDNA) form

[SOURCE: ISO 22174:2005, 3.1.2]