

SLOVENSKI STANDARD
oSIST prEN ISO 20186-3:2018
01-marec-2018

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)

Ta slovenski standard je istoveten z: prEN ISO 20186-3

ICS:

11.100.10	Diagnostični preskusni sistemi in vitro	In vitro diagnostic test systems
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oSIST prEN ISO 20186-3:2018

en

DRAFT INTERNATIONAL STANDARD

ISO/DIS 20186-3

ISO/TC 212

Secretariat: ANSI

Voting begins on:
2018-01-03Voting terminates on:
2018-03-28

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

ICS: 11.100.10

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Reference number
ISO/DIS 20186-3:2018(E)

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Foreword

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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.

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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 makes the 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;
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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

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/>

ISO/DIS 20186-3:2018(E)

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]