SLOVENSKI STANDARD
SIST-TS CEN/TS 17811:2022

01-september-2022

Molekularne diagnostične preiskave in vitro - Specifikacije za predpreiskovalne procese pregleda urina in drugih telesnih tekočin - Izolirana brezcelična DNK

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for urine and other body fluids - Isolated cell free DNA

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für Urin und andere Körperflüssigkeiten - Isolierte zellfreie DNA

Ta slovenski standard je istoveten z: **CEN/TS 17811:2022**

ICS:

11.100.10	Diagnostični preskusni sistemi in vitro	In vitro diagnostic test systems

SIST-TS CEN/TS 17811:2022 **en,fr,de**

TECHNICAL SPECIFICATION

SPÉCIFICATION TECHNIQUE

TECHNISCHE SPEZIFIKATION

CEN/TS 17811

June 2022

ICS 11.100.10

English Version

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for urine and other body fluids - Isolated cell free DNA

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für Urin und andere Körperflüssigkeiten - Isolierte zellfreie DNA

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EUROPEAN COMMITTEE FOR STANDARDIZATION
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Ref. No. CEN/TS 17811:2022 E

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European foreword

This document (CEN/TS 17811:2022) has been prepared by Technical Committee CEN/TC 140 “In vitro diagnostic medical devices”, the secretariat of which is held by DIN.

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Introduction

Molecular *in vitro* diagnostics has enabled a 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 specimen collection, transport, storage and processing thus making the outcome from diagnostics or research unreliable or even impossible because the subsequent analytical assay will not determine the situation in the patient but an artificial profile generated during the pre-examination process.

Most of the DNA in the body is located within cells, but a small amount of nucleic acids can also be found outside of cells, so called cell-free DNA (cfDNA). In case of circulating body fluids such as blood, this DNA is called circulating cell-free DNA (ccfDNA) and in case of non-circulating body fluids such as urine, saliva, cerebrospinal fluid, pleural effusion, ascites, and synovial fluid, the DNA is called cell-free DNA (cfDNA). cfDNA is of specific interest, as for example cfDNA in urine originates from cells from the genitourinary tract or from ccfDNA in circulation passing through glomerular filtration [1]. cfDNA from cancerous or malignant cells in urine have been associated with cancer specific sequences, epigenetic and structural changes [2], [3].

Standardization of the entire workflow from specimen collection to the cfDNA examination is needed to minimize release of DNA from cells into the fluid, and degradation of cfDNA in the specimen, which can change the original native cfDNA profile in the body fluid after specimen collection. Post collection microbial growth in the specimen can further enhance the degradation of the cfDNA, e.g. in urine and saliva. Studies have been undertaken to determine the important influencing factors as they can impact the sensitivity and reliability of cfDNA examination from urine and other body fluids.

This document draws upon such work to codify and standardize the steps for cfDNA examination from body fluids 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.

1 Scope

This document specifies requirements and gives recommendations on the handling, storage, processing and documentation of body fluids specimens intended for human cfDNA examination during the pre-examination phase before a molecular examination is performed.

This document is applicable to molecular *in vitro* diagnostic examinations performed by medical laboratories. It is also intended to be used by health institutions including facilities collecting and handling specimen, laboratory customers, *in vitro* diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities.

Dedicated measures that need to be taken for cytohistological analysis of body fluid derived nucleated cells are not described in this technical specification. Neither are measures for preserving and handling of pathogens, and other bacterial or whole microbiome DNA in body fluids described.

Different dedicated measures need to be taken for preserving ccfDNA from other body fluids such as blood, lymph and others. These are not described in this document. ccfDNA from blood is covered in EN ISO 20186-3.

NOTE 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.

EN ISO 15189, *Medical laboratories - Requirements for quality and competence (ISO 15189)*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in EN ISO 15189 and 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
aliquot
portion of a larger amount of homogenous material, assumed to be taken with negligible sampling error

Note 1 to entry: The term is usually applied to fluids. Tissues are heterogeneous and therefore cannot be aliquoted.

Note 2 to entry: The definition is derived from [4], [5] and [6].

3.2
ambient temperature
unregulated temperature of the surrounding air

3.3
analyte
component represented in the name of a measurable quantity

[SOURCE: EN ISO 17511:2021, 3.1 — Deleted example.]

3.4
analytical test performance
analytical performance
examination performance
accuracy, precision, and sensitivity of a test to measure the analyte of interest

Note 1 to entry: Other test performance characteristics such as robustness, repeatability can apply as well.

[SOURCE: EN ISO 20184-1:2018, 3.4]

3.5
ascites
abnormal build-up of fluid in the abdomen that can cause swelling

Note 1 to entry: In late-stage cancer, tumour cells can be found in the fluid in the abdomen.

Note 2 to entry: Ascites also occurs in patients with liver disease.

Note 3 to entry: This definition was derived from [7].

3.6
body fluid collection device
tube or other container in which the body fluid (e.g. urine) specimen is collected

3.7
ccfDNA
circulating cell free DNA
extracellular human DNA present in blood and plasma

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

[SOURCE: EN ISO 20186-3:2019, 3.5]

3.8
cfDNA
cell free DNA
extracellular human DNA present in body liquids such as urine

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

3.9
cfDNA profile
cell free DNA profile
amount of different cfDNA molecules, that are present in a body liquid, that can be measured in the absence of any losses, inhibition and interference

3.10
closed system
non-modifiable system provided by the vendor including all necessary components for the analysis (i.e., hardware, software, procedures and reagents)

3.11
CSF
cerebrospinal fluid
fluid that flows in and around the hollow spaces of the brain and spinal cord, and between two of the meninges (the thin layers of tissue that cover and protect the brain and spinal cord)

Note 1 to entry: Cerebrospinal fluid is made by tissue called the choroid plexus in the ventricles (hollow spaces) in the brain.

Note 2 to entry: This definition was derived from [7].

3.12
DNA
deoxyribonucleic acid
polymer of deoxyribonucleotides occurring in a double-stranded (dsDNA) or single-stranded (ssDNA) form

[SOURCE: EN ISO 22174:2005, 3.1.2]

3.13
DNA stabilizers
compounds, solutions or mixtures that are designed to minimize degradation and fragmentation of cfDNA as well as release of genomic DNA from nucleated cells

3.14
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 measurand and include all kinds of parameter testing or chemical manipulation for quantitative or qualitative examination.

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

3.15
examination manufacturer
analytical test manufacturer
entity that manufactures and/or produces a specific analytical test

[SOURCE: CEN/TS 17747:2021, 3.9 — Deleted Note.]

3.16
examination performance
analytical test performance
analytical performance
accuracy, precision, and sensitivity of a test to measure the analyte of interest

Note 1 to entry: Other test performance characteristics such as robustness, repeatability can apply as well.

[SOURCE: EN ISO 20184-1:2018, 3.4]

3.17
genomic DNA
gDNA
genomic DNA present in nucleated cells

3.18
homogenous
uniform in structure and composition

3.19
interfering substances
endogenous or exogenous substances (e.g. stabilization solution) that can be present in specimens and that can alter an examination result

3.20
microorganisms
entity of microscopic size, encompassing bacteria, fungi, protozoa and viruses

[SOURCE: ISO 18362:2016, 3.18]

3.21
pleural effusion
abnormal collection of fluid between the thin layers of tissue (pleura) lining the lung and the wall of the chest cavity

Note 1 to entry: This definition was derived from [7].

3.22
pre-examination processes
pre-analytical phase
pre-analytical workflow
pre-examination phase

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), transportation to and within the analytical laboratory, storage, isolation of analytes, and end when the analytical examination begins

Note 1 to entry: The pre-examination phase includes preparative processes that influence the outcome of the intended examination.

[SOURCE: EN ISO 15189:2012, 3.15, modified — An additional term was added and more detail was included.]

3.23
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: EN ISO 15189:2012, 3.16, modified — The term and definition are used here without the original notes.]

3.24
proficiency test
evaluation of participant performance against pre-established criteria by means of inter-laboratory comparisons

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

3.25
room temperature
temperature in the range of 18 °C to 25 °C

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

[SOURCE: EN ISO 20166-1:2018, 3.22]

3.26
sample
one or more parts taken from a primary sample

[SOURCE: EN ISO 15189:2012, 3.24, modified — Example has been removed.]

3.27
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

Note 1 to entry: The measurand constituent for the purpose of this document is isolated DNA.

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

3.28
storage
prolonged interruption of the pre-analytical workflow of a sample or analyte respectively, or of their derivatives, under appropriate conditions in order to preserve their properties

Note 1 to entry: Long-term storage typically occurs in laboratory archives or in biobanks.

[SOURCE: EN ISO 20184-1:2018, 3.21, modified — Example has been removed.]

3.29
synovial fluid
transparent, sticky liquid produced in joints (i.e. places where two bones are connected) that allows the bones and tendons to move smoothly

Note 1 to entry: In pathological situations the collected synovial fluid can have a different colour.

Note 2 to entry: This definition was derived from [9].