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BSI Standards Publication

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

bsi.

National foreword

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

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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.]