# Molecular in vitro diagnostic examinations - Requirements and recommendations for pre-examination processes for urine and other body fluids - Isolated cell-free DNA (ISO 18704:2026)

EESTI STANDARDIMIS- JA AKREDITEERIMISKESKUS
ESTONIAN CENTRE FOR STANDARDISATION AND ACCREDITATION

## EESTI STANDARDI EESSÕNA

## NATIONAL FOREWORD



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|---|---|
| See Eesti standard EVS-EN ISO 18704:2026 sisaldab Euroopa standardi EN ISO 18704:2026 ingliskeelset teksti. | This Estonian standard EVS-EN ISO 18704:2026 consists of the English text of the European standard EN ISO 18704:2026. |
| Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas. | This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation. |
| Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 25.02.2026. | Date of Availability of the European standard is 25.02.2026. |
| Standard on kättesaadav Eesti Standardimis-ja Akrediteerimiskeskusest. | The standard is available from the Estonian Centre for Standardisation and Accreditation. |

Tagasisidet standardi sisu kohta on võimalik edastada, kasutades EVS-i veebilehel asuvat tagasiside vormi või saates e-kirja meiliaadressile standardiosakond@evs.ee.

ICS 11.100.10

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

# EN ISO 18704

February 2026

ICS 11.100.10

Supersedes CEN/TS 17811:2022

English Version

# Molecular in vitro diagnostic examinations - Requirements and recommendations for pre-examination processes for urine and other body fluids - Isolated cell-free DNA (ISO 18704:2026)

Analyses de diagnostic moléculaire in vitro - Exigences et recommandations relatives aux processus préanalytiques pour l'urine et d'autres liquides corporels - ADN libre extrait (ISO 18704:2026)

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für Urin und andere Körperflüssigkeiten - Isolierte zellfreie DNA (ISO 18704:2026)

This European Standard was approved by CEN on 13 February 2026.



EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

**CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels**



Ref. No. EN ISO 18704:2026 E

## European foreword

This document (EN ISO 18704:2026) has been prepared by Technical Committee ISO/TC 212 "Medical laboratories and in vitro diagnostic systems" in collaboration with Technical Committee CEN/TC 140 “In vitro diagnostic medical devices” the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by August 2026, and conflicting national standards shall be withdrawn at the latest by February 2029.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN shall not be held responsible for identifying any or all such patent rights.

This document supersedes CEN/TS 17811:2022.

Any feedback and questions on this document should be directed to the users’ national standards body/national committee. A complete listing of these bodies can be found on the CEN website.

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## Endorsement notice

The text of ISO 18704:2026 has been approved by CEN as EN ISO 18704:2026 without any modification.

International Standard

ISO 18704

First edition
2026-02

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

*Analyses de diagnostic moléculaire in vitro — Exigences et recommandations relatives aux processus préanalytiques pour l'urine et d'autres liquides corporels — ADN libre extrait*



Reference number
ISO 18704:2026(en)

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

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# Foreword

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This document was prepared by Technical Committee ISO/TC 212, *Medical laboratories and in vitro diagnostic systems*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 140, *In vitro diagnostic medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

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# Introduction

Molecular in vitro diagnostics has enabled significant progress in medicine. Further progress has been achieved and is still expected by new technologies used to examine profiles of nucleic acids, proteins, and metabolites in human tissues and body fluids (e.g. genomic, epigenomic, transcriptomic, proteomic and metabolomic profiling). However, the profiles of these molecules can change drastically during specimen collection, transport, storage and processing. This can make the outcome from diagnostics or research unreliable or even result in failure because the subsequent examination will not measure the genuine profile of nucleic acids, proteins or metabolites as it was in the patient, but a profile altered by the pre-examination process. Therefore, specifying, developing, verifying and validating preanalytical workflows has become an essential part of examination development.[21]

Most of the DNA in the body is located within cells, but small amounts of DNA originating from cells can also be found outside of cells (extracellular DNA). 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 passing through glomerular filtration.[22] cfDNA from cancerous or malignant cells in urine have been associated with cancer specific sequences, epigenetic and structural changes.[23],[24] Urine is currently the most frequently used non-circulating body fluid for cfDNA examination because it is easily obtained from patients. Although urine is often described as the major specimen type, in this document the term body fluid is used for urine and other body fluids as defined in Clause 3.

Standardization of the entire workflow from specimen collection to the cfDNA examination is needed to minimize post-collection 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. Post collection microbial growth in the specimen can further enhance the degradation of the cfDNA, e.g. in urine and saliva. Furthermore, the isolation of cfDNA can lead to a cfDNA profile bias. Different methods to determine cfDNA yield and quality can lead to additional variations and impacts.

Studies have been undertaken to determine the pre-examination sources of these and other variables, as they can impact the cfDNA examination. The variables can compromise the specified examination performance characteristics, such as sensitivity, specificity, linearity and reproducibility. They can also impact the examination reliability which could lead to an erroneous examination result and misdiagnosis.

This document draws upon such work to codify and standardize the steps prior to cfDNA examination from body fluids in what is referred to as the pre-examination process.

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 — Requirements and recommendations for pre-examination processes for urine and other body fluids — Isolated cell-free DNA



## 1 Scope

This document specifies requirements and provides recommendations for the pre-examination process of cell-free DNA (cfDNA) from body fluid specimens other than blood, including but not limited to the collection, handling, storage, transport, processing and documentation of human body fluids, such as urine, pleural effusions, ascites, cerebrospinal fluid (CSF), and saliva, intended for cfDNA examination. Processing includes multiple steps, such as centrifugation for specimen purification and isolation of cfDNA.

This document does not cover dedicated measures for cytohistological analysis of nucleated cells derived from body fluid, nor measures for preserving and handling of pathogens, and other bacterial or whole microbiome DNA in body fluids described.

Dedicated measures for preserving circulating cell-free DNA (ccfDNA) from blood are covered in ISO 20186-3.

This document is applicable to medical laboratories, health institutions including facilities collecting and handling specimens, laboratory customers, in vitro diagnostic examination developers and manufacturers, biobanks, institutions and organizations performing biomedical research, and regulatory authorities.

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.

ISO 15189, *Medical laboratories — Requirements for quality and competence*

ISO 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

## 3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 15189, ISO 13485 and the following apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://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 that are uniform in structure and composition. Tissues are heterogeneous and therefore cannot be aliquoted.