



International Standard

ISO 18704

Molecular in vitro diagnostic examinations — Requirements and recommendations for pre-examination processes for urine and other body fluids — Isolated cell-free DNA (<https://standards.iteh.ai>)

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](#)

<https://standards.iteh.ai/catalog/standards/iso/357b96c0-766c-46f7-b7d6-89b01406d13f/iso-18704-2026>

**First edition
2026-02**

iTeh Standards
(<https://standards.iteh.ai>)
Document Preview

[ISO 18704:2026](#)

<https://standards.iteh.ai/catalog/standards/iso/357b96c0-766c-46f7-b7d6-89b01406d13f/iso-18704-2026>



COPYRIGHT PROTECTED DOCUMENT

© ISO 2026

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

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

Contents

Page

Foreword	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 General requirements	6
5 Outside the laboratory	7
5.1 Specimen collection	7
5.1.1 Information about the patient or specimen donor	7
5.1.2 Selection of the body fluid collection device by the laboratory	7
5.1.3 Urine and other body fluid specimen collection from the patient or donor and stabilization procedures	8
5.1.4 Information about the specimen storage requirements at the body fluid collection facility	9
5.2 Transport requirements	11
5.2.1 General	11
5.2.2 Transport using urine and other body fluid collection devices with cfDNA stabilizers	11
5.2.3 Transport using urine and other body fluid collection devices without cfDNA stabilizers	12
6 Inside the laboratory	12
6.1 Specimen or sample reception	12
6.2 Specimen or sample storage after transport and reception	12
6.3 Urine and other body fluid specimen or sample processing prior to cfDNA isolation	13
6.4 Storage requirements for urine and other body fluid samples after processing	13
6.5 Isolation of urine and other body fluid cfDNA	14
6.5.1 General	14
6.5.2 Using a commercial cfDNA isolation kit approved for diagnostic use	14
6.5.3 Using a laboratory developed cfDNA isolation procedure	14
6.6 Quantity and quality assessment of isolated cfDNA	15
6.6.1 General	15
6.6.2 Quantity assessment of cfDNA	15
6.6.3 Quality assessment of cfDNA	15
6.7 Storage of isolated urine and other body fluid cfDNA	16
6.7.1 General	16
6.7.2 Storage of isolated urine and other body fluid cfDNA, isolated with a commercially available kit	16
6.7.3 Storage of isolated urine and other body fluid cfDNA, isolated with the laboratory's own procedure	17
Annex A (informative) Effects of pre-examination storage of unstabilized urine on cfDNA	18
Annex B (informative) Effects of pre-examination storage of unstabilized and stabilized urine on the amount of a specific cfDNA target sequence	22
Bibliography	24

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).

ISO draws attention to the possibility that the implementation of this document may involve the use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents. ISO shall not be held responsible for identifying any or all such patent rights.

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, 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 www.iso.org/iso/foreword.html.

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).

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

<https://standards.iteh.ai/catalog/standards/iso/357b96c0-766c-46f7-b7d6-89b01406d13f/iso-18704-2026>

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.