

Molecular in vitro diagnostic examinations -
Specifications for pre-examination processes for saliva
- Isolated human DNA (ISO 4307:2021)

This document is a preview generated by EVS

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 4307:2021 sisaldab Euroopa standardi EN ISO 4307:2021 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 4307:2021 consists of the English text of the European standard EN ISO 4307:2021.
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 03.11.2021.	Date of Availability of the European standard is 03.11.2021.
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

Standardite reprodutseerimise ja levitamise õigus kuulub Eesti Standardimis- ja Akrediteerimiskeskusele

Andmete paljundamine, taastekitamine, kopeerimine, salvestamine elektroonsesse süsteemi või edastamine ükskõik millises vormis või millisel teel ilma Eesti Standardimis- ja Akrediteerimiskeskuse kirjaliku loata on keelatud.

Kui Teil on küsimusi standardite autoriõiguse kaitse kohta, võtke palun ühendust Eesti Standardimis- ja Akrediteerimiskeskusega: Koduleht www.evs.ee; telefon 605 5050; e-post info@evs.ee

The right to reproduce and distribute standards belongs to the Estonian Centre for Standardisation and Accreditation

No part of this publication may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, without a written permission from the Estonian Centre for Standardisation and Accreditation.

If you have any questions about standards copyright protection, please contact the Estonian Centre for Standardisation and Accreditation: Homepage www.evs.ee; phone +372 605 5050; e-mail info@evs.ee

EUROPEAN STANDARD

EN ISO 4307

NORME EUROPÉENNE

EUROPÄISCHE NORM

November 2021

ICS 11.100.10

Supersedes CEN/TS 17305:2019

English Version

**Molecular in vitro diagnostic examinations - Specifications
for pre-examination processes for saliva - Isolated human
DNA (ISO 4307:2021)**

Analyse de diagnostic moléculaire in vitro -
Spécifications relatives aux processus préanalytiques
pour la salive - ADN humain extrait (ISO 4307:2021)

Molekularanalytische in-vitro-diagnostische Verfahren
- Spezifikationen für präanalytische Prozesse für
Speichel - Isolierte DNA (ISO 4307:2021)

This European Standard was approved by CEN on 18 October 2021.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.



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

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

European foreword

This document (EN ISO 4307:2021) has been prepared by Technical Committee ISO/TC 212 "Clinical laboratory testing and in vitro diagnostic test 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 May 2022, and conflicting national standards shall be withdrawn at the latest by November 2024.

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 17305:2019.

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.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 4307:2021 has been approved by CEN as EN ISO 4307:2021 without any modification.

Contents

Page

Foreword	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 General considerations	4
5 Activities outside the laboratory	5
5.1 Specimen collection.....	5
5.1.1 Information about the specimen donor/patient.....	5
5.1.2 Selection of the saliva collection device by the laboratory.....	5
5.1.3 Saliva specimen collection from the donor/patient and stabilization procedures.....	6
5.1.4 Information on the specimen and storage requirements at saliva collection facility/site.....	7
5.2 Transport requirements.....	8
5.2.1 General.....	8
5.2.2 Using saliva collection devices with DNA stabilizers.....	8
5.2.3 Using saliva collection devices without DNA stabilizers.....	8
6 Activities inside the laboratory	9
6.1 Specimen reception.....	9
6.2 Storage requirements.....	9
6.3 Isolation of the saliva DNA.....	9
6.3.1 General.....	9
6.3.2 Using a commercial kit.....	10
6.3.3 Using the laboratory's own protocol.....	10
6.4 Quantity and quality assessment of isolated DNA.....	10
6.5 Storage of isolated saliva DNA.....	11
6.5.1 General.....	11
6.5.2 Saliva DNA isolated with commercially available kits.....	11
6.5.3 Saliva DNA isolated with the laboratory's own protocols.....	11
Bibliography	12

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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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, *Clinical laboratory testing and in vitro diagnostic test 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.

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.

Genetic examination of DNA is commonly used in clinical practice. This includes, for example, predisposition testing, pharmacogenomics and analysis of genetic disorders with the perspective used in precision medicine. This is a fast-growing field in molecular diagnostics.

Saliva is increasingly used as a non-invasive alternative specimen to blood for the examination of human DNA. Saliva naturally contains microorganisms and extraneous substances (e.g. food debris), which make the composition of saliva more complex and unique among patients/donors. Dedicated measures are therefore needed for informing and preparing patients/donors for the collection and to check compliance with the instructions, in order to reduce the specimen variability. In contrast to invasive specimen collection, saliva collection does not require trained and educated professionals or dedicated facilities. By good instruction and verified collection device safety claims, saliva specimens can be self-collected at home; however, home collection also contributes to high variability in specimen quality. Similarly, medical laboratories/in vitro manufacturers need to be aware of specimen variability when performing design verification and validation.

DNA in saliva can fragment or degrade after collection. In addition, bacteria present in the saliva specimen can continue to grow, thus diluting the human DNA. DNases secreted by these bacteria can also accelerate the DNA degradation. This can impact the sensitivity and reliability of DNA examination.

Standardization of the entire process from specimen collection to the DNA examination is needed to minimize pre-examination impacts such as DNA degradation and fragmentation after saliva collection. This document describes special measures which need to be taken to obtain good quality saliva specimen/samples and isolated DNA therefrom for human DNA examination.

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 — Specifications for pre-examination processes for saliva — Isolated human DNA

1 Scope

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

This document is applicable to molecular in vitro diagnostic examination including laboratory developed tests performed by medical laboratories. It can also be used by 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 saliva collected on absorbing material or by mouth washes are not described in this document. Neither are measures for preserving and handling of native saliva cell-free DNA, pathogens, and other bacterial or whole microbiome DNA in saliva described.

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 15190, *Medical laboratories — Requirements for safety*

3 Terms and definitions

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

ambient temperature

unregulated temperature of the surrounding air

[SOURCE: ISO 20184-1:2018, 3.2]

3.2

analyte

component represented in the name of a measurable quantity

[SOURCE: ISO 17511:2003, 3.2, modified — The examples were not taken over.]