

Molecular in vitro diagnostic examinations -
Specifications for pre-examination processes in
metabolomics in urine, venous blood serum and
plasma (ISO 23118:2021)

EESTI STANDARDI EESSÕNA

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ICS 11.100.10

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EUROPEAN STANDARD

EN ISO 23118

NORME EUROPÉENNE

EUROPÄISCHE NORM

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Supersedes CEN/TS 16945:2016

English Version

**Molecular in vitro diagnostic examinations - Specifications
for pre-examination processes in metabolomics in urine,
venous blood serum and plasma (ISO 23118:2021)**

Analyses de diagnostic moléculaire in vitro -
Spécifications relatives aux processus préanalytiques
pour l'analyse du métabolome dans l'urine et le sang
veineux (sérum et plasma) (ISO 23118:2021)

Molekularanalytische in-vitro-diagnostische Verfahren
- Spezifikationen für präanalytische Prozesse für
Metabolomuntersuchungen in Urin, venösem
Blutserum und -plasma (ISO 23118:2021)

This European Standard was approved by CEN on 20 May 2021.

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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 23118:2021) 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of an identical text or by endorsement, at the latest by December 2021, and conflicting national standards shall be withdrawn at the latest by June 2024.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 16945:2016.

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 23118:2021 has been approved by CEN as EN ISO 23118:2021 without any modification.

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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).

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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).

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Introduction

Metabolomics is the "-omic" science that deals with the characterization of the metabolome, in turn defined as the whole set of small molecules (molecular mass <2 000 Da) in a certain biological system such as a cell, a tissue, an organ, or an entire organism^[1]. The analyses are mainly performed via two major analytical techniques, namely mass spectrometry (MS) and nuclear magnetic resonance (NMR)^{[2][3][4]}. The former has a sensitivity that can be as low as picomolar, requires sample separation and multiple experimental runs targeted to specific classes of compounds. The latter measures metabolites present at concentration above 1 µM and is mainly used for untargeted analyses, where all metabolites above the detection limit are observed simultaneously, independent of their chemical nature, without any separation procedure.

The metabolome is dynamic and quite sensitive to perturbations. The metabolome can change drastically during primary sample collection, transport, storage, and processing. As a result, the outcome from the diagnostic and research measurements could become an unreliable representation of the specific targeted physiological state or point in time, but instead describes an artificial profile generated during the pre-examination process. Pre-analytical variations have been identified to originate from two main sources:

- a) enzymatic activity in the samples, mainly related to the presence of cells;
- b) chemical reactions (e.g. redox reactions) among metabolites or between metabolites and oxygen, see References ^[5] to ^[11].

Moreover, the analyses can be influenced by the use of additives or by the introduction of contaminants, and therefore the selection of appropriate collection tubes and plasticware is also a critical aspect of the pre-examination phase.

Studies have been undertaken to establish the best pre-examination procedures in terms of maintenance of the original sample metabolome by identifying the critical steps and parameters affecting the metabolome composition. Additionally, standardization of the entire pre-examination workflow is needed to ensure comparability in multicentre studies. At the present state of the art, there are no defined pre-examination procedures for metabolomic samples. As a consequence, the procedures adopted by the various centres differentially influence the metabolome of the samples, making their comparison unreliable. The adoption of the present requirements for the pre-examination phase make it possible to compare and evaluate the results obtained from metabolic analysis.

This document draws upon such studies to codify and standardize the steps for urine, serum and plasma metabolomics analysis in what is referred to as the pre-analytical phase.

Molecular in vitro diagnostic examinations — Specifications for pre-examination processes in metabolomics in urine, venous blood serum and plasma

1 Scope

This document specifies requirements and gives recommendations for the handling, documentation and processing of urine, venous blood plasma and serum intended for metabolomics analysis in the pre-examination processes. This document is applicable to metabolomics examinations and can be used by biomedical laboratories, customers of laboratories, in vitro diagnostics developers and manufacturers, institutions and companies performing biomedical research, biobanks, and regulatory authorities.

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

biofluid

biological fluid which can be excreted (such as urine or sweat), secreted (such as breast milk, saliva or bile), obtained with a needle (such as blood or cerebrospinal fluid), or produced as a result of a pathological process (such as blister or cyst fluid)

3.2

examination

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

Note 2 to entry: For metabolomic analysis, analyte isolation is not necessarily required.

[SOURCE: ISO 20166-1:2018, 3.10, modified — admitted term “analytical test” has been deleted and Note 2 entry has been added.]

3.3

fasting

abstinence from any solid or liquid food excluding water for at least 8 hours