# **EESTI STANDARD**

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

#### NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 23118:2021 sisaldab Euroopa standardi EN ISO 23118:2021 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 23118:2021 consists of the English text of the European standard EN ISO 23118:2021.			
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 02.06.2021.	Date of Availability of the European standard is 02.06.2021.			
Standard on kättesaadav Eesti Standardimis- ja Akrediteerimiskeskusest.	The standard is available from the Estonian Centre for Standardisation and Accreditation.			
Fagasisidet standardi sisu kohta on võimalik edastad	da, kasutades EVS-i veebilehel asuvat tagasiside vorm			

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 autorikaitse 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 copyright, please contact Estonian Centre for Standardisation and Accreditation:

Homepage www.evs.ee; phone +372 605 5050; e-mail info@evs.ee

# **EUROPEAN STANDARD** NORME EUROPÉENNE **EUROPÄISCHE NORM**

## **EN ISO 23118**

June 2021

ICS 11.100.10

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.

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 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.

### Contents

Page

Fore	word			iv	
Intro	oduction			v	
1	Scope			1	
2	Normative references				
3	Terms and definitions				
4	General considerations				
5	Urine	Urine			
5	5.1	Outside the la 5.1.1 Urin 5.1.2 Tran	aboratory le collection isport requirements		
	5.2	Inside the lat   5.2.1 Spec   5.2.2 Stora   5.2.3 Urin   5.2.4 Long   5.2.5 Urin	soratory simen reception age requirements le sample processing g-term storage requirements for urine samples he thawing		
6	Blood			7	
	6.1	Outside the la 6.1.1 Prim	aboratory nary collection nsport of pre-processed specimens to laboratory	7 7 	
	6.2	Inside the lab 6.2.1 Spec 6.2.2 Sam 6.2.3 Tran or tr 6.2.4 Long 6.2.5 Seru	poratory cimen reception ple processing isport of processed samples to a laboratory for metabolomics analysis cansport to a biobank g-term storage requirements		
Ann	<b>ex A</b> (info	ormative) <b>Inst</b>	ability of the metabolome		
Rihl	iogranh	,		17	
BIDI	iography			17	

### 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 <a href="https://www.iso.org/directives">www.iso.org/directives</a>).

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 <a href="https://www.iso.org/patents">www.iso.org/patents</a>).

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 <a href="https://www.iso.org/iso/foreword.html">www.iso.org/iso/foreword.html</a>.

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 <u>www.iso.org/members.html</u>.

### 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<sup>[1]</sup>. The analyses are mainly performed via two major analytical techniques, namely mass spectrometry (MS) and nuclear magnetic resonance (NMR) <sup>[2][3][4]</sup>. 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  $\mu$ M 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 preexamination 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 <u>http://www.electropedia.org/</u>

#### 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