

Molecular in vitro diagnostic examinations -  
Specifications for pre-examination processes for frozen  
tissue - Part 2: Isolated proteins (ISO 20184-2:2018)

## EESTI STANDARDI EESSÕNA

## NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 20184-2:2018 sisaldab Euroopa standardi EN ISO 20184-2:2018 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 20184-2:2018 consists of the English text of the European standard EN ISO 20184-2:2018.
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.
Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 12.12.2018.	Date of Availability of the European standard is 12.12.2018.
Standard on kättesaadav Eesti Standardikeskusest.	The standard is available from the Estonian Centre for Standardisation.

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

ICS 11.100.10

Standardite reprodutseerimise ja levitamise õigus kuulub Eesti Standardikeskusele

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

Kui Teil on küsimusi standardite autorikaitse kohta, võtke palun ühendust Eesti Standardikeskusega:  
Koduleht [www.evs.ee](http://www.evs.ee); telefon 605 5050; e-post [info@evs.ee](mailto:info@evs.ee)

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

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.

If you have any questions about copyright, please contact Estonian Centre for Standardisation:

Homepage [www.evs.ee](http://www.evs.ee); phone +372 605 5050; e-mail [info@evs.ee](mailto:info@evs.ee)

English Version

**Molecular in vitro diagnostic examinations - Specifications  
for pre-examination processes for frozen tissue - Part 2:  
Isolated proteins (ISO 20184-2:2018)**

Analyses de diagnostic moléculaire in vitro -  
Spécifications relatives aux processus préanalytiques  
pour les tissus congelés - Partie 2: Protéines extraites  
(ISO 20184-2:2018)

Molekularanalytische in-vitro-diagnostische Verfahren  
- Spezifikationen für präanalytische Prozesse für  
schockgefrorene Gewebeproben - Teil 2: Isolierte  
Proteine (ISO 20184-2:2018)

This European Standard was approved by CEN on 30 September 2018.

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, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, 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 20184-2:2018) 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 June 2019, and conflicting national standards shall be withdrawn at the latest by December 2021.

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 16826-2:2015.

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, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

## Endorsement notice

The text of ISO 20184-2:2018 has been approved by CEN as EN ISO 20184-2:2018 without any modification.

# Contents

Page

<b>Foreword</b> .....	<b>iv</b>
<b>Introduction</b> .....	<b>v</b>
<b>1 Scope</b> .....	<b>1</b>
<b>2 Normative references</b> .....	<b>1</b>
<b>3 Terms and definitions</b> .....	<b>1</b>
<b>4 General considerations</b> .....	<b>4</b>
<b>5 Outside the laboratory</b> .....	<b>5</b>
5.1 Specimen collection.....	5
5.1.1 General.....	5
5.1.2 Information about the specimen donor/patient.....	5
5.1.3 Information about the specimen.....	6
5.1.4 Specimen processing.....	6
5.2 Fresh tissue transport requirements.....	6
5.2.1 General.....	6
5.2.2 Preparations for the transport.....	7
5.2.3 During transport.....	7
<b>6 Inside the laboratory</b> .....	<b>7</b>
6.1 Information about the reception of the specimen.....	7
6.2 Evaluation of the pathology of the specimen and selection of the sample(s).....	7
6.3 Freezing of the specimen or sample(s).....	8
6.4 Storage requirements.....	10
6.5 Isolation of total protein.....	10
6.5.1 General.....	10
6.5.2 Using commercial kits.....	11
6.5.3 Using the laboratories own protocols.....	11
6.6 Quantity and quality assessment of isolated proteins.....	11
6.7 Storage of isolated total protein.....	12
<b>Annex A (informative) Quantitative protein examination demonstrates changes of protein amounts during cold ischemia</b> .....	<b>13</b>
<b>Bibliography</b> .....	<b>17</b>

## 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](http://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](http://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](http://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*.

A list of all parts in the ISO 20184 series can be found on the ISO website.

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](http://www.iso.org/members.html).

## Introduction

Molecular in vitro diagnostics, including molecular pathology, has enabled a significant progress in medicine. Further progress is expected with new technologies analysing nucleic acids, proteins, and metabolites in human tissues and body fluids. However, the profiles and/or integrity 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 examination assay will not determine the situation in the patient but an artificial molecular pattern generated during the pre-examination process. Therefore, a standardization of the entire process from specimen collection to the protein examination is needed. Studies have been undertaken to determine the important influencing factors. This document draws upon such work to codify and standardize the steps for frozen tissue with regard to protein examination in what is referred to as the pre-examination phase.

Protein profiles and protein-protein interactions in tissues can change drastically before, during (e.g. due to warm ischemia) and after tissue collection (e.g. due to cold ischemia). The changes are caused by e.g. gene induction, gene down regulation, protein degradation. Protein species amounts can change differently in different donors'/patients' tissues. The expression of genes can be influenced by the given treatment or intervention (surgery, biopsy), or drugs administered for anaesthesia or even treatment of concomitant disease as well as by the different environmental conditions after the tissue removal from the body.

Therefore, it is essential to take special measures to minimize the described protein profile changes and modifications within the tissue for subsequent examination.

Tissues that have undergone chemical stabilization pre-treatment before freezing are not covered in this document. In addition this document is not applicable to protein examination by immunohistochemistry.

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 frozen tissue —

## Part 2: Isolated proteins

### 1 Scope

This document gives guidelines on the handling, documentation, storage and processing of frozen tissue specimens intended for the examination of isolated proteins during the pre-examination phase before a molecular assay is performed.

This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories and molecular pathology laboratories that evaluate proteins isolated from frozen tissue. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organisations 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 15189:2012, *Medical laboratories — Requirements for quality and competence*

### 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 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. Tissues are heterogeneous and therefore cannot be aliquoted.

Note 2 to entry: The definition is derived from the Compendium of Chemical Terminology Gold Book. International Union of Pure and Applied Chemistry. Version 2.3.3., 2014; the PAC, 1990, 62, 1193 (Nomenclature for sampling in analytical chemistry (Recommendations 1990)) p. 1206; and the PAC 1990, 62, 2167 [Glossary of atmospheric chemistry terms (Recommendations 1990)] p. 2173.