

ICS 11.100.10

English Version

**Molecular in vitro diagnostic examinations - Specifications for
pre-examination processes for venous whole blood - Part 1:
Isolated cellular RNA**

Tests de diagnostic moléculaire in vitro - Spécifications
relatives aux processus préanalytiques pour le sang
veineux total - Partie 1 : ARN cellulaire isolé

Molekularanalytische in-vitro-diagnostische Verfahren -
Spezifikationen für präanalytische Prozesse für venöse
Vollblutproben - Teil 1: Isolierte zelluläre RNS

This Technical Specification (CEN/TS) was approved by CEN on 30 May 2015 for provisional application.

The period of validity of this CEN/TS is limited initially to three years. After two years the members of CEN will be requested to submit their comments, particularly on the question whether the CEN/TS can be converted into a European Standard.

CEN members are required to announce the existence of this CEN/TS in the same way as for an EN and to make the CEN/TS available promptly at national level in an appropriate form. It is permissible to keep conflicting national standards in force (in parallel to the CEN/TS) until the final decision about the possible conversion of the CEN/TS into an EN is reached.

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, 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: Avenue Marnix 17, B-1000 Brussels

| Contents | Page |
|--|-------------|
| Foreword..... | 3 |
| Introduction..... | 4 |
| 1 Scope | 5 |
| 2 Normative references | 5 |
| 3 Terms and definitions | 5 |
| 4 General considerations..... | 6 |
| 5 Outside the laboratory | 7 |
| 5.1 Primary venous whole blood collection manual..... | 7 |
| 5.1.1 Information about the primary sample donor..... | 7 |
| 5.1.2 Selection of the venous blood collection tube by the laboratory..... | 7 |
| 5.1.3 Primary venous whole blood collection from the patient and stabilization procedures | 7 |
| 5.1.4 Information on the primary blood sample and storage requirements at the blood collection facility..... | 8 |
| 5.2 Transport requirements | 9 |
| 6 Inside the laboratory | 9 |
| 6.1 Sample reception..... | 9 |
| 6.2 Storage requirements..... | 9 |
| 6.3 Isolation of the cellular RNA..... | 10 |
| 6.4 Quality assessment of isolated cellular RNA | 11 |
| 6.5 Storage of isolated cellular RNA..... | 11 |
| Annex A (informative) Impact of preanalytical workflow steps on venous whole blood cellular RNA profiles | 12 |
| A.1 General information on operated experiments in Annex A and Annex B..... | 12 |
| A.2 Influence of blood collection tube type (with or without blood cellular RNA profile stabilizer) on the analysis of specific blood cellular RNA profiles..... | 12 |
| A.2.1 Unstable blood cellular RNA profiles | 12 |
| A.2.2 Stable blood cellular RNA profiles..... | 14 |
| Annex B (informative) Influence of blood storage temperature on blood cellular RNA profiles | 16 |
| Bibliography..... | 19 |

Foreword

This document (CEN/TS 16835-1:2015) has been prepared by Technical Committee CEN/TC 140 "In vitro diagnostic medical devices", the secretariat of which is held by DIN.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to announce this Technical Specification: 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, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

This document is a preview generated by EVS

Introduction

Molecular *in vitro* diagnostics has enabled a significant progress in medicine. Further progress is expected by new technologies analyzing signatures of nucleic acids, proteins, and metabolites in human tissues and body fluids. However, the profiles of these molecules can change drastically during primary sample 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. Therefore, a standardization of the entire process from sample collection to RNA analysis is needed. Studies have been undertaken to determine the important influencing factors. This Technical Specification draws upon such work to codify and standardize the steps for venous whole blood cellular RNA analysis in what is referred to as the preanalytical phase.

1 Scope

This Technical Specification recommends the handling, documentation and processing of venous whole blood specimens intended for cellular RNA analysis during the preanalytical phase before a molecular assay is performed. This Technical Specification covers specimens collected by venous whole blood collection tubes. This Technical Specification is applicable to molecular *in vitro* diagnostic examinations (e.g. *in vitro* diagnostic laboratories, laboratory customers, *in vitro* diagnostics developers and manufacturers, institutions and commercial organizations performing biomedical research, biobanks, and regulatory authorities).

Blood cellular RNA profiles can change significantly after collection. Therefore, special measures need to be taken to secure good quality blood samples for cellular RNA analysis and storage.

Different dedicated measures need to be taken for stabilizing blood cell free circulating RNA and RNA in exosomes circulating in blood, which are not described in this Technical Specification.

Different dedicated measures need to be taken for collecting, stabilizing, transporting and storing capillary blood as well as for collecting and storing blood by paper based technologies. These are not described in this Technical Specification.

RNA in pathogens present in blood is not covered by this Technical Specification.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

EN ISO 15189:2012, *Medical laboratories - Requirements for quality and competence (ISO 15189:2012, Corrected version 2014-08-15)*

ISO 15190, *Medical laboratories — Requirements for safety*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in EN ISO 15189:2012 and the following apply.

3.1

ambient temperature

unregulated temperature of the surrounding air

3.2

analytical phase

processes that start with the isolated analyte and include all kind of parameter testing or chemical manipulation for quantitative or qualitative analysis

3.3

blood cellular RNA

cellular RNA

RNA molecules present in blood cells

3.4

blood cellular RNA profiles

amounts of different RNA molecules, that are present in blood cells and that can be measured in the absence of any losses, inhibition and interference