PD CEN/TS 16835-3:2015

BSI Standards Publication

Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood

Part 3: Isolated circulating cell free DNA from plasma

This Published Document is the UK implementation of CEN/TS 16835-3:2015.

The UK participation in its preparation was entrusted to Technical Committee CH/212, IVDs.

A list of organizations represented on this committee can be obtained on request to its secretary.

Published by BSI Standards Limited 2015

ISBN 978 0 580 85027 1
ICS 11.100.30

Compliance with a British Standard cannot confer immunity from legal obligations.

This Published Document was published under the authority of the Standards Policy and Strategy Committee on 31 October 2015.

Amendments/corrigenda issued since publication

Date	Text affected

TECHNICAL SPECIFICATION CEN/TS 16835-3

SPÉCIFICATION TECHNIQUE

TECHNISCHE SPEZIFIKATION October 2015

ICS 11.100.30

English Version

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 3: Isolated circulating cell free DNA from plasma

Tests de diagnostic moléculaire in vitro - Spécifications relatives aux processus pré-analytiques pour le sang total veineux - Partie 3: ADN libre circulant extrait du plasma

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für venöse Vollblutproben - Teil 3: Aus Plasma isolierte zirkulierende zellfreie DNS

This Technical Specification (CEN/TS) was approved by CEN on 31 August 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

Ref. No. CEN/TS 16835-3:2015 E

Contents

Page

European foreword

This document (CEN/TS 16835-3:2015) 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.

Introduction

Molecular *in vitro* diagnostics has enabled a significant progress in medicine. Further progress is expected by new technologies analysing 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 primary sample collection to circulating cell free DNA (ccfDNA) 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 circulating cell free DNA analysis from plasma prepared from human venous whole blood 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 circulating cell free DNA (ccfDNA) 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 ccfDNA profiles can change significantly after blood collection from the donor (e.g. release of genomic DNA from white blood cells, ccfDNA fragmentation and ccfDNA quantity change). Special measures need to be taken to secure good quality blood samples for ccfDNA analysis and storage.

Different dedicated measures need to be taken for preserving blood genomic DNA. These are not described in this Technical Specification. Blood genomic DNA is covered in CEN/TS 16835-2, *Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 2: Isolated genomic DNA*

NOTE CcfDNA obtained from blood by the procedures suggested in this document can contain DNA present in exosomes [3] [4].

DNA from 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
ccfDNA
circulating cell free DNA
extracellular human DNA present in blood, serum and plasma

Note 1 to entry: ccfDNA can include DNA present in vesicles such as exosomes [3] [4].