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Irish Standard Recommendation
S.R. CEN/TS 17747:2022

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for exosomes and other extracellular vesicles in venous whole blood - DNA, RNA and proteins

S.R. CEN/TS 17747:2022

Incorporating amendments/corrigenda/National Annexes issued since publication:

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NSAI	T +353 1 807 3800	Sales:
1 Swift Square,	F +353 1 807 3838	T +353 1 857 6730
Northwood, Santry	E standards@nsai.ie	F +353 1 857 6729
Dublin 9	W NSAI.ie	W standards.ie

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National Foreword

S.R. CEN/TS 17747:2022 is the adopted Irish version of the European Document CEN/TS 17747:2022, Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for exosomes and other extracellular vesicles in venous whole blood - DNA, RNA and proteins

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TECHNICAL SPECIFICATION

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English Version

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for exosomes and other extracellular vesicles in venous whole blood - DNA, RNA and proteins

Analyses de diagnostic moléculaire in vitro - Spécifications relatives aux processuses préanalytiques pour exosomes et autres vésicules extracellulaires dans le sang total veineux - ADN, ARN et protéines

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für Exosomen und andere extrazelluläre Vesikel im venösen Vollblut - DNA, RNA und Proteine

This Technical Specification (CEN/TS) was approved by CEN on 13 March 2022 for provisional application.

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CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

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European foreword

This document (CEN/TS 17747:2022) has been prepared by Technical Committee CEN/TC 140 “In vitro diagnostic medical devices”, the secretariat of which is held by DIN.

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Introduction

Molecular *in vitro* diagnostics has enabled a significant progress in medicine. Further progress is expected by new technologies analysing profiles of nucleic acids, proteins, and metabolites in human tissues and body fluids. However, the profiles of these molecules can change drastically during the pre-examination process, including the specimen collection, transport, storage and processing.

Consequently, this makes the outcome from diagnostics or research unreliable or even impossible because the subsequent examination might not determine the real situation in the patient but an artificial profile generated during the pre-examination process.

Besides cell free circulating nucleic acids, circulating tumour cells (CTCs) and other rare cells, exosomes and other extracellular vesicles represent another key component of liquid biopsies. Therefore, there is a strongly increasing interest in research and emerging diagnostics in exosomes and other extracellular vesicles.

The pre-examination process described in this document results in enriched extracellular vesicles (EV) (e.g. exosomes) or DNA, RNA and proteins isolated therefrom.

New additional extracellular vesicles can be released and existing extracellular vesicles can be lost after blood collection, thus changing the overall EV DNA/RNA/protein profiles. Also, different anticoagulants in different types of blood collection tubes can influence the release of EVs from different cells present in blood, including those from platelets. Further factors can influence the post collection changes of the entire blood EV composition, such as storage and transport temperature and duration, centrifugation parameters, etc.

Standardization of the entire workflow from the specimen collection to the EV surface protein and isolated DNA, RNA and protein examination from EVs is therefore needed. Studies have been undertaken to determine the important influencing factors. This document draws upon such work to codify and standardize the steps of EV surface protein examination and of DNA, RNA and protein examination from EVs in what is referred to as the pre-examination phase.

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.

1 Scope

This document gives guidelines on the handling, storage, processing and documentation of venous whole blood specimens intended for DNA, RNA and protein examination from exosomes and other extracellular vesicles during the pre-examination phase before a molecular examination is performed. This document covers specimens collected in venous whole blood collection tubes.

The pre-examination process described in this document results in isolated DNA, RNA and proteins from enriched exosomes and other extracellular vesicles.

This document is applicable to molecular *in vitro* diagnostic examinations performed by medical laboratories. It is also intended to be used by health care institutions including facilities collecting and handling specimen, laboratory customers, *in vitro* diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities.

Different dedicated measures are taken during the pre-examination phase for venous whole blood circulating cell-free RNA (ccfRNA) examination and for venous whole blood circulating cell-free DNA (ccfDNA) examination, both without prior enrichment of exosomes and other extracellular vesicles. These are not described in this document but are covered in EN ISO 20186-3, *Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 3: Isolated circulating cell free DNA from plasma* and CEN/TS 17742, *Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Isolated circulating cell free RNA from plasma*.

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.

EN ISO 15189, *Medical laboratories - Requirements for quality and competence (ISO 15189)*

ISO 15190, *Medical laboratories — Requirements for safety*

ISO/TS 20658, *Medical laboratories — Requirements for collection, transport, receipt, and handling of samples*