



BSI Standards Publication

Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for circulating tumour cells (CTCs) in venous whole blood

Part 3: Preparations for analytical CTC staining

National foreword

This Published Document is the UK implementation of CEN ISO/TS 7552-3:2024. It is identical to ISO/TS 7552-3:2024. It supersedes PD CEN/TS 17390-3:2020, which is withdrawn.

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 committee manager.

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English Version

**Molecular in vitro diagnostic examinations - Specifications
for pre-examination processes for circulating tumour cells
(CTCs) in venous whole blood - Part 3: Preparations for
analytical CTC staining (ISO/TS 7552-3:2024)**

Analyses de diagnostic moléculaire in vitro -
Spécifications relatives aux processus préanalytiques
pour les cellules tumorales circulantes (CTC) dans le
sang total veineux - Partie 3: Préparations pour
l'analyse par coloration des CTC (ISO/TS 7552-3:2024)

Spezifikationen für präanalytische Prozesse für
zirkulierende Tumorzellen (CTC) in venösen
Vollblutproben - Teil 3: Vorbereitungen für die
analytische CTC-Färbung (ISO/TS 7552-3:2024)

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European foreword

This document (CEN ISO/TS 7552-3:2024) has been prepared by Technical Committee ISO/TC 212 "Medical laboratories and in vitro diagnostic systems" in collaboration with 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 shall not be held responsible for identifying any or all such patent rights.

This document supersedes CEN/TS 17390-3:2020.

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Endorsement notice

The text of ISO/TS 7552-3:2024 has been approved by CEN as CEN ISO/TS 7552-3:2024 without any modification.

Contents

Page

Foreword	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 General considerations	5
5 Activities outside the laboratory	6
5.1 Specimen collection	6
5.1.1 General	6
5.1.2 Information about the specimen donor/patient	6
5.1.3 Selection of the venous whole blood collection tube by the laboratory	6
5.1.4 Venous whole blood specimen collection from the patient/donor	7
5.2 Specimen storage and transport	7
5.2.1 General	7
5.2.2 Storage and transport using blood collection tubes with stabilizers	8
5.2.3 Storage and transport using blood collection tubes without stabilizers	8
6 Activities inside the laboratory	8
6.1 Specimen reception	8
6.2 Specimen storage after transport and reception	9
6.3 Enrichment of CTCs	9
6.3.1 General	9
6.3.2 Using a commercial CTC enrichment system intended for diagnostic use	9
6.3.3 Using the laboratory developed CTC enrichment procedure	10
6.4 Quality of enriched CTCs	10
6.5 Storage of enriched CTCs	10
6.6 Preparation for CTC staining	10
6.6.1 General	10
6.6.2 Pretreatment for different staining techniques (antibody, colour staining, in situ techniques)	11
Annex A (informative) Decision guideline for critical steps of the CTC pre-analytical workflow	12
Bibliography	14

Foreword

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Introduction

Solid tumours release cells and bioanalytes into blood and other body fluids. This has opened the option of utilizing such body fluids (liquid biopsies) for a minimally-invasive procedure for tumour detection, diagnosis and characterization. Liquid biopsies can enable earlier detection and diagnosis of cancers and advance personalized patient treatment.^[19,20]

These applications have become one of the fastest growing segments of the entire diagnostic market.

Circulating tumour cells (CTCs) in venous whole blood can reflect the disease complexity that evolves during tumour progression, with distinct genetic, epigenetic and expression features.^[21]

Besides the prognostic role of CTC identification and enumeration in cancer progression, CTC identification and analysis can improve disease outcome prediction, therapeutic guidance and post-treatment monitoring of the patient.^[19]

CTCs are now considered as a surrogate of tumour tissue in cancer early development, progression and metastatic phase.^[22]

Molecular characterization of CTCs can provide a strategy for monitoring cancer during systemic therapies,^[23] identifying mechanisms of disease progression, identifying novel targets for treatment^[24] and selecting targeted therapies^[19].

CTCs are fragile and tend to degrade within a few hours when collected in conventional blood collection tubes, e.g. EDTA containing tubes, without dedicated CTC stabilizers. CTCs are extremely rare, especially in early disease, e.g. less than 10 cells per 10 ml of blood, representing a ratio of approximately 1:10⁷ CTCs to white blood cells (WBCs). This low ratio represents a significant challenge to CTC enrichment required for identification and examination as tumour-derived cells.

Furthermore, CTC morphology and biomolecules can change during the pre-examination process. This can lead to changes in protein quantity, integrity, modification, conformation, and localization within the cell. This can impact the validity and reliability of the examination result.

CTC examination usually requires a CTC enrichment step (e.g. based on biological properties of the CTCs, such as expression of surface molecules, or physical properties, such as size and density, or their combination) prior to cytomorphological examination or immunofluorescent staining.

CTC enrichment technologies can provide CTCs attached on a solid surface, ready for cytological examination, or CTCs in suspension, requiring extra processing steps prior to the examination. This can lead to potential cell loss.^[25]

CTC enrichment is usually followed by their identification by conventional cytochemical or protein-targeted staining procedures that allow detection of the cell traits.

Standardization includes all steps of the pre-examination process, including blood collection and stabilization, transport, storage, CTC enrichment, and CTC isolation (if included). This pre-examination standardization is crucial to ensure reliable examination results in current clinical use and is also critical to develop new CTC based diagnostic examinations and to establish these in clinical healthcare.^[26]

An illustration of critical steps of the pre-analytical workflow for CTC staining is provided in [Annex A](#).

This document describes measures to standardize the pre-examination process to obtain appropriate CTC staining.

