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English Version

**Molecular in vitro diagnostic examinations - Specifications for
pre-examination processes for FFPE tissue - Part 3: Isolated
DNA**

Tests de diagnostic moléculaire in vitro - Spécifications
relatives aux processus préanalytiques pour les tissus
FFPE - Partie 3: ADN isolé

Molekularanalytische in-vitro-diagnostische Verfahren -
Spezifikationen für präanalytische Prozesse für FFPE-
Gewebeproben - Teil 3: Isolierte DNS

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European foreword

This document (CEN/TS 16827-3:2015) 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 signatures of nucleic acids, proteins, and metabolites in human tissues and body fluids. However, the profiles and/or integrity 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 molecular pattern generated during the pre-examination process. Studies have been undertaken to determine the influencing factors for DNA analysis from formalin fixed and paraffin embedded (FFPE) tissue. These studies demonstrated that a standardization of the entire process from primary sample collection to DNA analysis is needed. This Technical Specification draws upon such work to codify and standardize the steps for FFPE tissue with regard to DNA analysis in what is referred to as the preanalytical phase.

1 Scope

This Technical Specification gives recommendations for the handling, documentation and processing of FFPE tissue specimens intended for DNA analysis during the preanalytical phase before a molecular assay is performed. This Technical Specification is applicable to molecular *in vitro* diagnostic examinations (e.g., *in vitro* diagnostic laboratories, laboratory customers, developers and manufacturers of *in vitro* diagnostics, institutions and commercial organizations performing biomedical research, biobanks, and regulatory authorities).

DNA integrity in tissues can change before and during formalin fixation, processing and storage. Chemical modifications introduced into DNA during tissue fixation might lead to fragmentation and sequence alterations [1], changes in the methylation status or even structural changes which can lead to e.g., spurious copy number changes in array-CGH profiles [2]. These modifications of the DNA molecules can impact the validity and reliability of the analytical test results. Therefore, it is essential to take special measures to minimize the described modifications for subsequent DNA analysis.

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 kinds of parameter testing or chemical manipulation for quantitative or qualitative analysis

3.3

cold ischemia

condition after removal of the tissue from the body until its stabilization or fixation

3.4

DNA

deoxyribonucleic acid

polymer of deoxyribonucleotides occurring in a double-stranded (dsDNA) or single-stranded (ssDNA) form

[SOURCE: EN ISO 22174:2005, 3.1.2]

3.5

FFPE

formalin fixation and paraffin embedding