TECHNICAL SPECIFICATION

SPÉCIFICATION TECHNIQUE

TECHNISCHE SPEZIFIKATION

CEN/TS 17688-3

December 2021

ICS 11.100.10

English Version

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for Fine Needle Aspirates (FNAs) - Part 3: Isolated genomic DNA

Analyses moléculaires de diagnostic in vitro - Spécifications pour les processus préanalytiques pour les ponctions à l'aiguille fine - Partie 3: ADN génomique isolé

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für Feinnadelaspirate - Teil 3: Isolierte genomische DNA

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EUROPEAN COMMITTEE FOR STANDARDIZATION
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European foreword

This document (CEN/TS 17688-3:2021) 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 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.

Examination of genomic DNA (gDNA) is commonly used in clinical practice. This includes e.g. prognostic and predictive biomarker examinations. This is a fast growing field in molecular diagnostics.

Fine needle aspiration is a non-surgical procedure that uses a thin, hollow-bore needle and syringe to collect a specimen from patients for cytopathological and molecular investigation. As a minimally-invasive technique, fine needle aspirates (FNAs) are commonly used to diagnose and monitor for example a range of cancer types e.g. breast, lung and thyroid cancer, and other diseases, such as inflammatory diseases. FNAs also provide the opportunity to sample metastatic sites (e.g. lymph nodes) and otherwise non-resectable tissues.

Besides cytological assessment, molecular biological analysis of FNAs is expected to become increasingly used for cancer and other disease diagnostics, including companion diagnostics.

One of the challenges facing molecular analysis of FNA samples is their small size and diversity in composition (cells, blood, body fluid). The low cellular content of FNAs means that the yield of isolated gDNA is typically towards the lower end of detection for molecular examination. Therefore, the gDNA isolation procedure should provide a sufficient amount of gDNA as required by the specific examination.

After specimen collection, gDNA can fragment and degrade by e.g. fixation, processing and storage. Additionally, chemical modifications introduced into gDNA during FNA fixation might lead to sequence alterations or changes in the methylation status. The described changes of the gDNA molecules can impact the validity, reliability and sensitivity of the examination results.

Therefore, standardization of the entire process from specimen collection to gDNA examination is needed to minimize gDNA changes introduced by e.g. degradation, fragmentation and modification after FNA collection. This document describes special measures which need to be taken to obtain good quality FNA specimens/samples and isolated gDNA therefrom for molecular examination.

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, documentation, storage and processing of fine needle aspirates (FNAs) intended for gDNA examination during the pre-examination phase before a molecular examination is performed.

This document is applicable to molecular *in vitro* diagnostic examinations including laboratory developed tests performed by medical laboratories and molecular pathology laboratories that examine gDNA isolated from FNAs. It is also intended to be used by laboratory customers, *in vitro* diagnostics developers and manufacturers, biobanks, institutions and commercial organisations performing biomedical research, and regulatory authorities.

Different dedicated measures are taken for collecting, stabilizing, transporting and storing of core needle biopsies (FNA Biopsy or FNA B) and are not covered in this document, but EN ISO 20184-3, *Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for frozen tissue — Part 3: Isolated DNA* and EN ISO 20166-3, *Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue — Part 3: Isolated DNA.*

This document is not applicable for pathogen DNA examination and gDNA examination by *in situ* detection.

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)*

3 Terms and definitions

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

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
aliquot
portion of a larger amount of homogenous material, assumed to be taken with negligible sampling error

Note 1 to entry: The term is usually applied to fluids. Tissues are heterogeneous and therefore cannot be aliquoted.

Note 2 to entry: The definition is derived from the Compendium of Chemical Terminology Gold Book. International Union of Pure and Applied Chemistry. Version 2.3.3., 2014; the PAC, 1990,62,1193 (Nomenclature for sampling in analytical chemistry (Recommendations 1990)) p. 1206; and the PAC 1990, 62, 2167 (Glossary of atmospheric chemistry terms (Recommendations 1990)) p. 2173.