SLOVENSKI STANDARD
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Molekularne diagnostične preiskave in vitro - Specifikacije za predpreiskovalne procese pri aspiraciji s tanko iglo (FNA) - 3. del: Iz genoma izolirana DNK

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

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

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

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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

This draft Technical Specification is submitted to CEN members for Vote. It has been drawn up by the Technical Committee CEN/TC 140.

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Recipients of this draft are invited to submit, with their comments, notification of any relevant patent rights of which they are aware and to provide supporting documentation.

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European foreword

This document (FprCEN/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.

This document is currently submitted to the Vote on TS.

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.

3.2
ambient temperature
unregulated temperature of the surrounding air

[SOURCE: EN ISO 20166-1:2018, 3.2]

3.3
analyte
component represented in the name of a measurable quantity

[SOURCE: ISO 17511:2020, 3.2, modified — deleted example.]

3.4
analytical test performance
analytical performance
accuracy, precision, and sensitivity of a test to measure the analyte of interest

Note 1 to entry: Other test performance characteristics such as robustness, repeatability can apply as well.

[SOURCE: EN ISO 20184-1:2018, 3.4]

3.5
biomolecule
organic molecule produced by living organisms that is involved in the maintenance and metabolic processes of organisms

Note 1 to entry: Examples of organic molecules are protein, carbohydrate, lipid, or nucleic acid.

3.6
cell block
paraffin-embedded cell clot

3.7
cell clot
cell-rich liquid specimen/sample concentrated into a compact cell aggregate for subsequent processing

3.8
closed system
non-modifiable system provided by the vendor including all necessary components for the analysis (i.e., hardware, software, procedures and reagents)

3.9
cytocentrifugation
cytology method that is specifically designed to concentrate cells on a slide by centrifugation

3.10
deoxyribonucleic acid
DNA
polymer of deoxyribonucleotides occurring in a double-stranded (dsDNA) or single-stranded (ssDNA) form

[SOURCE: EN ISO 22174:2005, 3.1.2]

3.11
deoxyribonuclease
DNase
enzyme that catalyses the degradation of DNA into smaller components

3.12
diagnosis
identification of a disease from its signs and symptoms, where the diagnostic process can involve examinations and tests for classification of an individual's condition into separate and distinct categories or subclasses that allow medical decisions about treatment and prognosis to be made

[SOURCE: EN ISO 20166-1:2018, 3.7]

3.13
examination
analytical test
set of operations with the objective of determining the value or characteristics of a property

Note 1 to entry: Processes that include all kinds of parameter testing or chemical manipulation for quantitative or qualitative examination.

[SOURCE: ISO 15189:2012, 3.7, modified — Notes to entry 1 to 3 have been removed. Note 1 to entry has been added and “analytical test” has been added as a preferred term.]

3.14
examination manufacturer
analytical test manufacturer
entity that manufactures and/or produces a specific analytical test

3.15
examination performance
analytical test performance
analytical performance
accuracy, precision, and sensitivity of a test to measure the analyte of interest

Note 1 to entry: Other test performance characteristics such as robustness, repeatability can apply as well.

[SOURCE: EN ISO 20184-1:2018, 3.4]

3.16
fixative
solution used to preserve or harden FNA specimens for microscopic and molecular examination

3.17
formalin
saturated aqueous formaldehyde solution which at 100 % contains 37 % formaldehyde by mass (corresponding to 40 % by volume)

[SOURCE: EN ISO 20166-1:2018, 3.11]

3.18
fine needle aspirate
FNA
specimen withdrawn by a non-operative procedure that uses a thin, hollow-bore needle

3.19
FNA primary collection device
thin, hollow-bore needle or syringe used for collecting the FNA specimen from the donor/patient

3.20
FNA secondary collection device
suitable container into which the specimen is transferred from the FNA primary collection device

3.21
genomic DNA
gDNA
chromosomal DNA, in contrast to extra-chromosomal DNAs such as mitochondrial DNA

3.22
homogeneous
uniform in structure and composition

[SOURCE: EN ISO 20166-1:2018, 3.31]

3.23
interfering substances
endogenous substances of a specimen/sample or exogenous substances that can alter an examination result

Note 1 to entry: Examples of endogenous substances include blood components in the FNA specimen.

Note 2 to entry: Examples of exogenous substances include compounds of stabilization solutions.

3.24
laboratory developed procedure
modified commercially available *in vitro* diagnostic device or fully in house developed procedure

3.25
paraffin embedding
process in which a sample is placed in paraffin to generate a hard surrounding matrix so that thin microscopic sections can be cut

3.26
pre-examination process
pre-analytical workflow
pre-analytical phase
pre-examination phase
process that starts, in chronological order, from the clinician's request and includes the examination request, preparation and identification of the patient, collection of the primary sample(s), transportation to and within the analytical laboratory, isolation of analytes, and ends when the analytical examination begins

Note 1 to entry: The pre-examination phase includes preparative processes that influence the outcome of the intended examination.

[SOURCE: ISO 15189:2012, 3.15, modified — An additional term was added and more detail was included.]

3.27
primary sample
specimen
discrete portion of a body fluid, breath, hair or tissue taken for examination, study or analysis of one or more quantities or properties assumed to apply for the whole

[SOURCE: ISO 15189:2012, 3.16, modified — The term and definition is used here without the original notes.]

3.28
proficiency test
evaluation of participant performance against pre-established criteria by means of inter-laboratory comparisons

[SOURCE: EN ISO/IEC 17043:2010, 3.7, modified — Term and definition are used here without the original notes.]

3.29
ribonucleic acid
RNA
polymer of ribonucleotides occurring in a double-stranded or single-stranded form

[SOURCE: EN ISO 22174:2005, 3.1.3]

3.30
ribonuclease
RNase
enzyme that catalyses the degradation of RNA into smaller components

3.31
room temperature
temperature in the range of 18 °C to 25 °C

Note 1 to entry: Local or national regulations can have different definitions.

[SOURCE: EN ISO 20166-1:2018, 3.22]