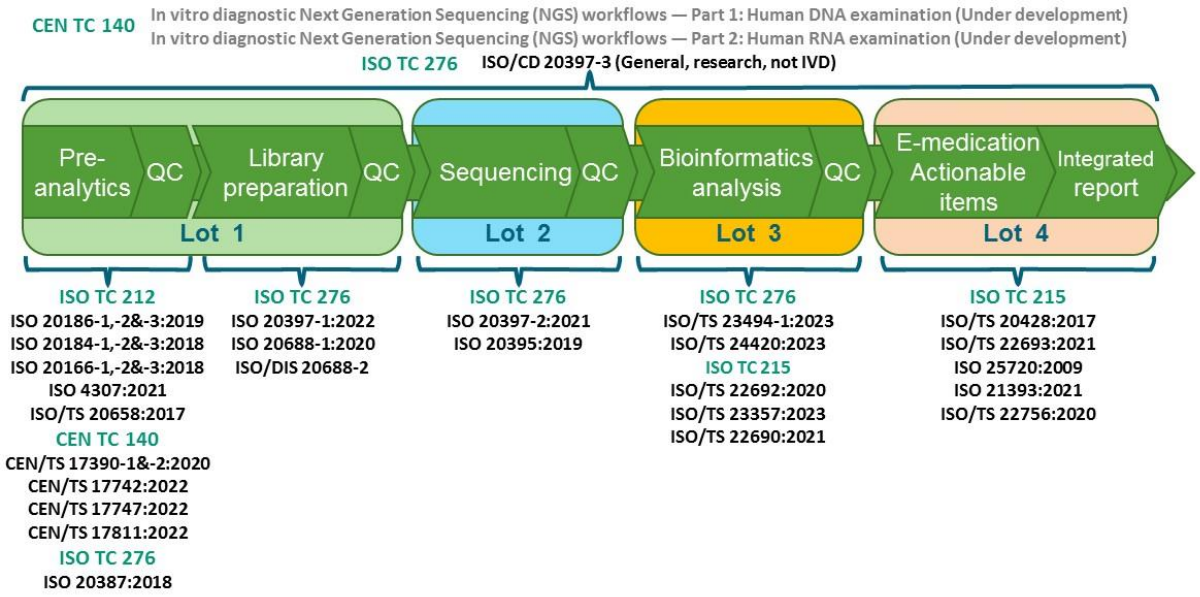
Co-funded by the European Union
Grant No. 874719

List of NGS-Relevant Standardization Documents

(status: September 2023)

Background

Instand-NGS4P has prepared a list of relevant existing “published” and ongoing “under development” NGS-relevant standardization documents and projects within the International Standardization Organization (ISO) and the European Standardization Organization (CEN). Only the published documents can be applied to the product development within Instand-NGS4P.
In addition to the existing and ongoing projects, the Instand-NGS4P consortium is partnering with CEN/TC 140/WG 3 to develop a standardization document for the entire NGS workflow. Participation in the development of this standard is encouraged, and interested parties should contact their national standardisation body to enquire about nomination to the CEN/TC 140 Working Group 3.



The relevant standards (published or under development) are listed below under the following topics:

1. Standards for specimen/sample pre-analytics (Lot 1a)
2. Standards for library preparation and NGS-analysis (Lot 1b and Lot 2)
3. Standards for NGS-data (Lots 3 and 4)

The scope of each published document can be found in the Annex.

1. Standards for specimen/sample pre-analytics (Lot 1a)

The following projects cover the necessary pre-analytical steps which need to be performed before starting the analysis. Most of these standardization documents include detailed processes for specific specimen/sample types depending on the analytes of interest. Following these processes is key to preserving the target properties and analytes of the specimen/sample, and thus to obtain good quality

samples for NGS analysis. If specimens/samples are obtained from a biobank, ISO 20387 covers additional general requirements (e.g., for traceability, documentation, handling, storage, information management and a quality management system) contributing to their quality attributes as well as the quality of their associated data. The relevant preanalytics requirements for NGS analysis are sufficiently covered in the following documents and can be referenced.

Published:

EN ISO 20166-1:2018, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue — Part 1: Isolated RNA

EN ISO 20166-2:2018, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue — Part 2: Isolated Proteins

EN ISO 20166-3:2019, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue — Part 3: Isolated DNA

EN ISO 20184-1:2018, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for frozen tissue — Part 1: Isolated RNA

EN ISO 20184-2:2018, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for frozen tissue — Part 2: Isolated proteins

EN ISO 20184-3:2021, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for frozen tissue — Part 3: Isolated DNA

EN ISO 20186-1:2019, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 1: Isolated cellular RNA

EN ISO 20186-2:2019, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 2: Isolated genomic DNA

EN ISO 20186-3:2019, Molecular in-vitro diagnostic examinations — Specifications for pre-examination processes for venous whole blood — Part 3: Isolated circulating cell free DNA from plasma

ISO 4307:2021, Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for saliva – Isolated human DNA

CEN/TS 17390-1:2020, Molecular in vitro diagnostic examinations — for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood — Part 1: Isolated RNA

CEN/TS 17390-2:2020, Molecular in vitro diagnostic examinations — for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood — Part 2: Isolated DNA

ISO/TS 20658:2017 Medical laboratories — Requirements for collection, transport, receipt, and handling of samples

CEN/TS 17742:2022, Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Isolated circulating cell free RNA from plasma

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

CEN/TS 17811:2022, Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for urine and other body fluids - Isolated cell free DNA

EN ISO 20387_2018, Biotechnology — Biobanking — General requirements for biobanking

2. Standards for library preparation and NGS-analysis (Lot 1b and 2)

Projects listed within this chapter are either directly relevant to the library preparation, NGS-analysis or to closely related components used in or needed for the NGS-analysis, such as nucleic acids.

Published:

ISO/DIS 20397-1:2022, Biotechnology — General Requirements for Massive Parallel Sequencing — Part 1: Nucleic acid and library preparation

ISO 20688-1:2020, Biotechnology — Nucleic acid synthesis — Part 1: Requirements for the production and quality control of synthesized oligonucleotides

ISO 20397-2:2021, Biotechnology — Massively parallel sequencing — Part 2: Quality evaluation of sequencing data

ISO 20395:2019, Biotechnology — Requirements for evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR

Under development:

ISO/DIS 20688-2, Biotechnology — Nucleic acid synthesis — Part 2: General definitions and requirements for the production and quality control of synthesized gene fragments, genes, and genomes

ISO/AWI 20397-3, Biotechnology — Massively parallel sequencing — Part 3: General requirements and guidance for metagenomics

3. Standards for NGS-data (Lots 3 and 4)

ISO projects listed within this chapter are related to data obtained either by NGS directly or within a specimen's/sample's life cycle including NGS. They give requirements for data collection, analysis, processing, storage, sharing, define data types, relationships, optionality, cardinalities and the bindings of particular terminology of the data, and thus contribute to the imteroperability of data. Interoperability of data is important for the exchange, traceability and comparability of data and their bigger picture (e.g., for the use in or comparison of studies or publications).

Published:

ISO/TS 22692:2020, Genomics Informatics — Quality control metrics for DNA sequencing

ISO/TS 22690:2021, Genomics informatics — Reliability assessment criteria for high-throughput gene-expression data

ISO/TS 20428:2017, Health informatics — Data elements and their metadata for describing structured clinical genomic sequence information in electronic health records

ISO/TS 22693:2021, Genomics informatics — Structured clinical gene fusion report in electronic health records

ISO 25720:2009, Health informatics — Genomic Sequence Variation Markup Language (GSVML)

ISO 21393:2021, Genomics informatics — Omics Markup Language (OML)

ISO/TS 22756:2020, Health Informatics — Requirements for a knowledge base for clinical decision support systems to be used in medication-related processes

ISO/TR 3985:2021, Development of International Standards in Biotechnology — Data Publication — Preliminary Considerations and Concepts

ISO/TS 23494-1:2023, Biotechnology — Provenance information model for biological material and data — Part 1: Design concepts and general requirements

ISO/TS 24420:2023, Biotechnology — Massively parallel DNA sequencing — General requirements for data processing of shotgun metagenomic sequences

ISO/TS 23357:2023, Genomics Informatics —Clinical genomics data sharing specification for next generation sequencing

Annex: Scope of listed projects

1. Standards for specimen/sample pre-analytics

Project number	Title	Committee
EN ISO 20166-1:2018	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 1: Isolated RNA (ISO 20166-1:2018)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, documentation, storage and processing of formalinfixed and paraffin-embedded (FFPE) tissue specimens intended for RNA examination during the preexamination phase before a molecular assay is performed. This document is applicable to molecular in vitro diagnostic examinations including laboratory developed tests performed by medical laboratories and molecular pathology laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
EN ISO 20166-2:2018	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 2: Isolated proteins (ISO 20166-2:2018)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, documentation, storage and processing of formalin-fixed and paraffin-embedded (FFPE) tissue specimens intended for the examination of isolated proteins during the pre-examination phase before a molecular assay is performed. This document is applicable to molecular in vitro diagnostic examinations including laboratory developed tests performed by medical laboratories and molecular pathology laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. This document is not applicable for protein examination by immunohistochemistry. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
EN ISO 20166-3:2019	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 3: Isolated DNA (ISO 20166-3:2018)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, documentation, storage and processing of formalinfixed and paraffin-embedded (FFPE) tissue specimens intended for DNA examination during the preexamination phase before a molecular assay is performed. This document is applicable to molecular in vitro diagnostic examinations including laboratory developed tests performed by medical laboratories and molecular pathology laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee

EN ISO 20184-1:2018	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 1: Isolated RNA (ISO 20184-1:2018)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, documentation, storage and processing of frozen tissue specimens intended for RNA examination during the pre-examination phase before a molecular assay is performed. This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories and molecular pathology laboratories that evaluate RNA extracted from frozen tissue. 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. Tissues that have undergone chemical stabilization pre-treatment before freezing are not covered in this document. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.		

Project number	Title	Committee
EN ISO 20184-2:2018	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 2: Isolated proteins (ISO 20184-2:2018)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, documentation, storage and processing of frozen tissue specimens intended for the examination of isolated proteins during the pre-examination phase before a molecular assay is performed. This document is applicable to any molecular *in vitro* diagnostic examination performed by medical laboratories and molecular pathology laboratories that evaluate proteins isolated from frozen tissue. 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. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.		

Project number	Title	Committee
EN ISO 20184-3:2021	Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for frozen tissue — Part 3: Isolated DNA	ISO/TC 212 and CEN/TC 140
Scope	This document specifies requirements and gives recommendations for the handling, storage, processing, and documentation of frozen tissue specimens intended for DNA 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 evaluate DNA isolated from frozen tissue. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. Tissues that have undergone chemical stabilization pre-treatment before freezing are not covered in this document. NOTE International, national, or regional regulations or requirements can also apply to specific topics covered in this document.		

Project number	Title	Committee
EN ISO 20186-1:2019	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 1: Isolated cellular RNA (ISO 20186-1:2019)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, storage, processing and documentation of venous whole blood specimens intended for cellular RNA examination during the pre-examination phase before a molecular assay is performed. This document covers specimens collected in venous whole blood collection tubes. This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. Different dedicated measures are taken for stabilizing		

	blood cell free circulating RNA and RNA in exosomes circulating in blood. These are not described in this document. Different dedicated measures are taken for collecting, stabilizing, transporting and storing capillary blood as well as for collecting and storing blood by paper based technologies or other technologies generating dried blood. These are not described in this document. This document does not cover the isolation of specific blood cells and subsequent isolation of cellular RNA therefrom. RNA in pathogens present in blood is not covered by this document.

Project number	Title	Committee
EN ISO 20186-2:2019	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 2: Isolated genomic DNA (ISO 20186-2:2019)	ISO/TC 212 and CEN/TC 140
Scope	This document gives guidelines on the handling, storage, processing and documentation of venous whole blood specimens intended for genomic DNA examination during the pre-examination phase before a molecular examination is performed. This document covers specimens collected in venous whole blood collection tubes. This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. Different dedicated measures are taken for stabilizing blood cell free circulating DNA, which are not described in this document. NOTE Circulating cell free DNA in blood is covered in ISO 20186-3. Different dedicated measures are taken for collecting, stabilizing, transporting and storing capillary blood as well as for collecting and storing blood by paper based technologies or other technologies generating dried blood. These are not described in this document. This document does not cover the isolation of specific blood cells and subsequent isolation of genomic DNA therefrom. DNA in pathogens present in blood is not covered by this document.	

Project number	Title	Committee
EN ISO 20186-3:2019	Molecular in-vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 3: Isolated circulating cell free DNA from plasma (ISO 20186-3:2019)	ISO/TC 212 and CEN/TC 140
Scope	This document provides recommendations and requirements on the handling, storage, processing and documentation of venous whole blood specimens intended for circulating cell free DNA (ccfDNA) examination during the pre-examination phase before an analytical test is performed. This document covers specimens collected in venous whole blood collection tubes. This document is applicable to any molecular in vitro diagnostic examination performed by medical laboratories. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. Different dedicated measures are taken for stabilizing blood genomic DNA, which are not described in this document. Blood genomic DNA is covered in ISO 20186-2. Different dedicated measures are taken for preserving DNA in circulating exosomes, which are not described in this document. NOTE ccfDNA obtained from blood by the procedures cited in this document can contain DNA originally present in exosomes [8][9]. DNA in pathogens present in blood is not covered by this document.	

Project number	Title	Committee
CEN/TS 17305:2019, ISO 4307:2021	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for saliva – Isolated human DNA	ISO/TC 212 and CEN/TC 140
Scope	This document gives requirements on the handling, storage, processing and documentation of saliva specimens intended for human DNA examination during the pre-examination phase before a molecular examination is performed. This document is applicable to molecular in vitro diagnostic examination including laboratory developed tests performed by medical laboratories. 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. Dedicated measures that need to be taken for saliva collected on absorbing material or by mouth washes are not described in this technical specification. Neither are measures for preserving and handling of native saliva cell-free DNA, pathogens, and other bacterial or whole microbiome DNA in saliva described. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.

Project number	Title	Committee
CEN/TS 17390-1:2020	Molecular in vitro diagnostic examinations — for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood — Part 1: Isolated RNA	CEN/TC 140
Scope	This document gives guidelines on the handling, storage, processing and documentation of venous whole blood specimens intended for the examination of human cellular RNA isolated from Circulating Tumor Cells (CTCs) 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. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. This document does not cover the isolation of cellular RNA directly from venous whole blood containing CTCs. This is covered in EN ISO 20186-1. This document does not cover the isolation of specific blood cells and subsequent isolation of cellular RNA therefrom. RNA in pathogens present in blood is not covered by this document. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
CEN/TS 17390-2:2020	Molecular in vitro diagnostic examinations — for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood — Part 2: Isolated DNA	CEN/TC 140
Scope	This document gives guidelines on the handling, storage, processing and documentation of venous blood specimens intended for the examination of human genomic DNA isolated from Circulating Tumor Cells (CTCs) 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. It is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. This document does not cover the isolation of specific blood cells and subsequent isolation of genomic DNA therefrom. DNA in pathogens present in blood is not covered by this document. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
ISO/TS 20658:2017, ISO/FDIS 20658	Medical laboratories – Requirements for collection, transport, receipt, and handling of samples	ISO/TC 212
Scope	This document specifies requirements and good practice recommendations for the collection, transport, receipt and handling of samples intended for medical laboratory examinations. This document is applicable to medical laboratories and other medical	

	services involved in laboratory pre-examination processes that include the examination request, patient preparation and identification, sample collection, transport, receipt and storage. It may also be applicable to some biobanks. This document does not apply to blood and blood products intended for transfusion.

Project number	Title	Committee
CEN/TS 17742:2022	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Isolated circulating cell free RNA from plasma	CEN/TC 140
Scope	This document specifies requirements and recommendations for the pre-examination phase of circulating cell free RNA (ccfRNA) from venous whole blood specimens, including but not limited to the collection, handling, storage, processing and documentation of venous whole blood specimens intended for ccfRNA examination. This document covers specimens collected in venous whole blood collection tubes. The pre-examination process described in this document results in circulating cell free RNA isolated from blood plasma without prior enrichment of 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 laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, institutions and commercial organizations performing biomedical research, and regulatory authorities. Different dedicated measures need to be taken during the pre-examination phase for isolated RNA from enriched exosomes and other extracellular vesicles enriched from venous whole blood and for cellular RNA isolated from venous whole blood. These are not described in this document but are covered in CEN/TS 17747, Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for exosomes and other extracellular vesicles in venous whole blood - Isolated DNA, RNA and proteins, and in EN ISO 20186 1, Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 1: Isolated cellular RNA. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
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	CEN/TC 140
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.	

Project number	Title	Committee
CEN/TS 17811:2022	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for urine and other body fluids - Isolated cell free DNA	CEN/TC 140
Scope	This document specifies requirements and gives recommendations on the handling, storage, processing and documentation of body fluids specimens intended for human cfDNA examination during the pre-examination phase before a molecular examination is performed. This document is applicable to molecular in vitro diagnostic examinations performed by medical laboratories. It is also intended to be used by health 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. Dedicated measures that need to be taken for cytohistological analysis of body fluid derived nucleated cells are not described in this technical specification. Neither are measures for preserving and handling of pathogens, and other bacterial or whole microbiome DNA in body fluids described. Different dedicated measures need to be taken for preserving ccfDNA from other body fluids such as blood, lymph and others. These are not described in this document. ccfDNA from blood is covered in EN ISO 20186-3. NOTE International, national or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
EN ISO 20387:2018	Biotechnology – Biobanking – General requirements for biobanking (ISO 20387:2018)	ISO/TC 276, CEN/CENELEC JCT 1
Scope	This document defines best practice that (1) respects the existing standardization efforts of life sciences research communities, (2) normalizes key aspects of data description particularly at the level of the biology being studied (and shared) across the life sciences communities, (3) ensures that data is "findable" and useable by other researchers and (4) provides concrete guidance and metrics for judging the applicability of a particular data sharing plan. This document is applicable to domains in life sciences including biotechnology, genomics (including massively parallel nucleotide sequencing, metagenomics, epigenomics and functional genomics), transcriptomics, translatomics, proteomics, metabolomics, lipidomics, glycomics, enzymology, immunochemistry, life science imaging, synthetic biology, systems biology, systems medicine and related fields.	

2. Standards for library preparation and NGS-analysis

Project number	Title	Committee
ISO/DIS 20397-1:2022	Biotechnology — Massively parallel sequencing — Part 1: Nucleic acid and library preparation	ISO/TC 276
Scope	This document provides general requirements and guidance for quality assessments of nucleic acid samples, and general guidelines for library preparations and library quality assessments prior to sequencing and data generation.	

Project number	Title	Committee
ISO 20688-1:2020	Biotechnology — Nucleic acid synthesis — Part 1: Requirements for the production and quality control of synthesized oligonucleotides	ISO/TC 276
Scope	This document specifies minimum requirements for the production and quality control of synthesized oligonucleotides (nominally up to 250 bases). This document also describes general quality attributes for synthesized oligonucleotides as well as common methods for evaluating quality attributes.	

3. Standards for NGS-data

ISO projects listed within this chapter are related to data obtained either by NGS directly or within a specimen's/sample's life cycle including NGS. They give requirements for data collection, analysis, processing, storage, sharing, define data types, relationships, optionality, cardinalities and the bindings of particular terminology of the data, and thus contribute to the imteroperability of data. Interoperability of data is important for the exchange, traceability and comparability of data and their bigger picture (e.g., for the use in or comparison of studies or publications). ISO 20397-2 covers most of the needed requirements for NGS data analysis in cancer diagnostics and will be a good reference for a diagnostic NGS-workflow.

Project number	Title	Committee
ISO 20397-2:2021	ISO 20397-2:2021, Biotechnology — Massively parallel sequencing — Part 2: Quality evaluation of sequencing data	ISO/TC 276
Scope	This document specifies the general requirements and recommendations for quality assessments and control of MPS data. It covers post raw data generation procedures, sequencing alignments, and variant calling. This document also gives general guidelines for validation and documentation of MPS data. This document does not apply to any processes related to de novo assembly.	

Project number	Title	Committee
ISO 20395:2019	ISO 20395:2019, Biotechnology — Requirements for evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR	ISO/TC 276
Scope	This document provides generic requirements for evaluating the performance and ensuring the quality of methods used for the quantification of specific nucleic acid sequences (targets). This document is applicable to the quantification of DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) target sequences using either digital (dPCR) or quantitative real-time PCR (qPCR) amplification technologies. It applies to target sequences present in nucleic acid molecules including double-stranded DNA (dsDNA) such as genomic DNA (gDNA) and plasmid DNA, single stranded DNA (ssDNA), complementary DNA (cDNA), and single stranded RNA (ssRNA) including ribosomal RNA (rRNA), messenger RNA (mRNA), and long and short non-coding RNA [microRNAs (miRNAs) and short interfering RNAs (siRNAs)], as well as double-stranded RNA (dsRNA). This document applies to nucleic acids derived from biological sources such as viruses, prokaryotic and eukaryotic cells, cell-free biological fluids (e.g. plasma or cell media) or in vitro sources [e.g. oligonucleotides, synthetic gene constructs and in vitro transcribed (IVT) RNA]. This document is not applicable to quantification of very short DNA oligonucleotides (<50 bases). This document covers: — analytical design including quantification strategies (nucleic acid copy number quantification using a calibration curve as in qPCR or through molecular counting as in dPCR, quantification relative to an independent sample and ratio measurements) and use of controls; — quantification of total nucleic acid mass concentration and quality control of a nucleic acid sample including assessment of nucleic acid quality (purity and integrity); — PCR assay design, optimization, in silico and in vitro specificity testing; — data quality control and analysis including acceptance criteria, threshold setting and normalization; — method validation (precision, linearity, limit of quantification, limit of detection, trueness and robustness) with specific requirements for qPCR and dPCR; — approaches to establishing metrological traceability and estimating measurement uncertainty.	

	This document does not provide requirements or acceptance criteria for the sampling of biological materials or processing of biological samples (i.e. collection, preservation, transportation, storage, treatment and nucleic acid extraction). Nor does it provide requirements and acceptance criteria for specific applications (e.g. food or clinical applications where specific matrix issues can arise).

Project number	Title	Committee
ISO/TS 22692:2020	Genomics Informatics — Quality control metrics for DNA sequencing	ISO/TC 215/SC 1
Scope	This Technical Specification identifies quality metrics for the detection of DNA variants using next generation sequencing (NGS) technology. For the safety of NGS based applications, it is necessary to review the metrics of the whole data production process. This includes the quality-related data for the entire process of the NGS of DNA of all human-originated specimens, including DNA extraction, library preparation, sequencing, and data processing. It also defines the data types, relationships, optionality, cardinalities and the bindings of particular terminology of the data. In summary, this TS is intended to serve as a catalogue of sequencing data elements necessary to address quality metrics for various clinical applications. This document is not intended for • Sequencing methods other than NGS, such as the Sanger sequencing; • Targets other than genome, such as transcriptome or proteome; and • Specimens of species other than human.	

Project number	Title	Committee
ISO/TS 22690:2021	Genomics informatics — Reliability assessment criteria for high-throughput gene-expression data	ISO/TC 215/SC 1
Scope	This document specifies reliability assessment criteria for high-throughput gene-expression data. It is applicable to assessing the accuracy, reproducibility, and comparability of gene-expression data that are generated from microarray, next-generation sequencing, and other forms of high-throughput technologies. This document identifies the quality-related data for the process of the next-generation sequencing of RNA (RNA-seq). The sequencing platform covered by this document is limited to short-read sequencers. The use of RNA-seq for mutation detection and virus identification is outside of the scope of this document. This document is applicable to human health associated species such as human, cell lines, and preclinical animals. Other biological species are outside the scope of this document. From a biological point of view, expression profiles of all genetic sequences including genes, transcripts, isoforms, exons, and junctions are within the scope of this document	

Project number	Title	Committee
ISO/TS 20428:2017	Health informatics — Data elements and their metadata for describing structured clinical genomic sequence information in electronic health records	ISO/TC 215
Scope	ISO/TS 20428 defines the data elements and their necessary metadata to implement a structured clinical genomic sequencing report and their metadata in electronic health records particularly focusing on the genomic data generated by next generation sequencing technology. This document - defines the composition of a structured clinical sequencing report (see Clause 5), - defines the required data fields and their metadata for a structured clinical sequencing report (see Clause 6), - defines the optional data (see Clause 7), - covers the DNA-level variation from human samples using whole genome sequencing, whole exome sequencing, and targeted sequencing (disease-targeted gene panels) by next generation sequencing technologies. Though whole transcriptome sequencing and other technologies are important to provide better patient care and enable precision medicine, this document only deals with DNA-level changes, - covers mainly clinical applications and clinical research such as clinical trials and translational research which uses clinical data. However, the necessary steps such as de-identification or consent from patient should be applied. The basic research and other scientific areas are outside the scope of this	

	document, - does not cover the other biological species, i.e. genomes of viruses and microbes, and - does not cover the Sanger sequencing methods.

Project number	Title	Committee
ISO/TS 22693:2021	Genomics informatics — Structured clinical gene fusion report in electronic health records	ISO/TC 215/SC 1
Scope	The document defines the data elements and their necessary metadata to implement a structured clinical gene fusion report whose data are generated by next generation sequencing technologies. This document — describes the reporting guideline for RNA sequencing approaches focusing on detecting novel and known fusion partners, — defines the required data fields and their metadata for a structured clinical gene fusion report, — defines the optional data fields and their metadata, — covers the fusion gene from human specimen using whole transcriptome sequencing by next generation sequencing technologies for clinical practice and translational research, — does not cover the fusion gene detection using DNA sequencing methods, — does not cover the basic research and other scientific areas, — does not cover the other biological species, — does not cover the Sanger sequencing methods, and — does not cover the other structural variations. This document only defines the data elements and their metadata for the structured clinical sequencing report in electronic health records. Therefore, its layout can be designed based on the institutional decision if all elements are included as in this document.	

Project number	Title	Committee
ISO/TS 25720:2009	Health informatics — Genomic Sequence Variation Markup Language (GSVML)	ISO/TC 215/SC 1
Scope	ISO 25720:2009 is applicable to the data exchange format that is designed to facilitate the exchange of the genomic sequence variation data around the world, without forcing change of any database schema. From an informatics perspective, GSVML defines the data exchange format based on XML. The scope of ISO 25720:2009 is the data exchange format, but the database schema itself is outside the scope of this International Standard. From a biological point of view, all genetic sequence variations are taken into consideration and are within the scope of this International Standard, while polymorphisms, especially SNP, are the main focus of this International Standard. In other words, the annotations of variation as clinical concerns and -omics concerns are within the scope of ISO 25720:2009. Though SNPs exist in various biological species, the scope of this International Standard covers the human health associated species as human, cell line, and preclinical animals. The other biological species are outside the scope of ISO 25720:2009. The clinical field is within the scope of this International Standard, but the basic research fields and other scientific fields are outside the scope of ISO 25720:2009. Here, clinical research including drug discovery is within the scope of this International Standard. As for supposed application fields, our main focus is in human health including clinical practice, preventive medicine, translational research and clinical researches.	

Project number	Title	Committee
ISO/TR 21393:2021	Genomics informatics — Omics Markup Language (OML)	ISO/TC 215
Scope	This document is applicable to the data exchange format that is designed to facilitate exchanging omics data around the world without forcing changes of any database schema. This document specifies the characteristics of OML from the following perspectives. From an informatics perspective, OML defines the data exchange format based on XML. This document gives guidelines for the specifications of the data exchange format, but this document excludes the database schema itself. From a molecular side of view, this document is applicable to all kinds of omics data, while this document excludes the details of the molecules (e.g., details of genomic sequence	

	variations or whole genomic sequence). This document is also applicable to the molecular annotations including clinical concerns and relations with other omics concerns. From an application side of view, this document is applicable to the clinical field including clinical practice, preventive medicine, translational research, and clinical research including drug discovery. This document does not apply to basic research and other scientific fields. From a biological species side of view, this document is applicable to the human health-associated species as human, preclinical animals, and cell lines. This document does not apply to the other biological species.

Project number	Title	Committee
ISO/TS 22756:2020	Health Informatics — Requirements for a knowledge base for clinical decision support systems to be used in medication-related processes	ISO/TC 215
Scope	This document specifies the requirements for developing a knowledge base for drug-related problems that cohere with the intended drug use, to be used in rule-based clinical decision support systems (CDSS), such as the criteria for selecting a raw data source and the quality criteria for the development and maintenance for the rules or clinical rules for drug safety. It also describes the process of how to develop a knowledge base, the topics to be considered by the developers of a knowledge base, and it gives guidance on how to do this. This document gives guidelines for the development of a knowledge base: — with rules to enhance decisions and actions in drug-related problems that cohere with the intended drug use; — which can be used by all kinds of healthcare professionals, such as those who prescribe, dispense, administer or monitor medicines; — which can be used in every care setting, including chronic and acute care, primary and specialized care; — which is a repository of evidence/practice bases rules, assessed by experts; — which is meant to be used in conjunction with a medicinal product dictionary; — whose knowledge is structured in rules and therefore to be used in the type of rule-based CDSS. This document does not: — describe the exact content of a knowledge base i.e. the outcome of the process of developing rules. — provide the requirements for a clinical decision support system, the software that uses the knowledge base combined with the patient's data, and presents the outcome of the rules to the healthcare professional. These requirements are described in ISO/DTS 22703[1]. — give the requirements for non-medication knowledge bases. Some aspects of the requirements in this document are general in nature and applicable to other kinds of knowledge bases, but this document does not address all of the requirements of non-medication knowledge bases. [1] Under preparation. Stage at the time of publication: ISO/DTS 22703.	

Project number	Title	Committee
ISO/TR 3985:2021	Development of International Standards in Biotechnology — Data Publication — Preliminary Considerations and Concepts	ISO/TC 276
Scope	This document defines best practice that (1) respects the existing standardization efforts of life sciences research communities, (2) normalizes key aspects of data description particularly at the level of the biology being studied (and shared) across the life sciences communities, (3) ensures that data is "findable" and useable by other researchers and (4) provides concrete guidance and metrics for judging the applicability of a particular data sharing plan. This document is applicable to domains in life sciences including biotechnology, genomics (including massively parallel nucleotide sequencing, metagenomics, epigenomics and functional genomics), transcriptomics, translatomics, proteomics, metabolomics, lipidomics, glycomics, enzymology, immunochemistry, life science imaging, synthetic biology, systems biology, systems medicine and related fields.	

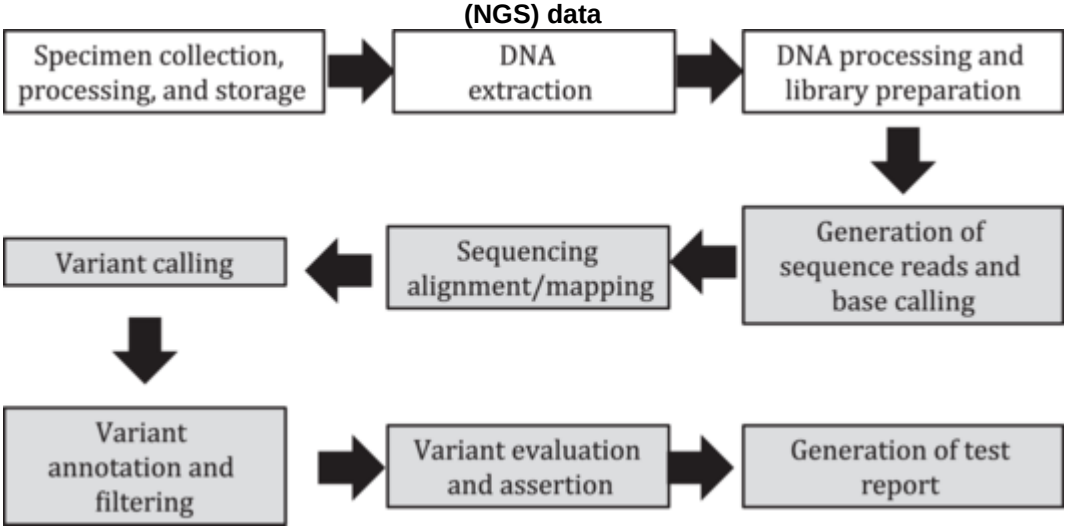
Project number	Title	Committee
ISO/TS 23494-1:2023	Biotechnology — Provenance information model for biological material and data — Part 1: Design concepts and general requirements	ISO/TC 276
Scope	This document specifies a general concept for a provenance information model for biological material and data and requirements for provenance data interoperability and serialization. The provenance information model covers any information relevant to the quality and fitness for purpose of the biological material generated throughout the preanalytical phase of the materials life cycle from collection to analysis, data originating from analytical procedures applied to the biological material and results from further mathematical processing of the data. This document is applicable to organizations, authorities and industries that are: • a) collecting, processing or distributing biological material for research; • b) generating, collecting, analysing or storing data on biological material. This document does not apply to biological material and data used for other than research or in fields that are regulated by national, regional or international laws, such as medical diagnosis and therapy or food production. NOTE International, national, or regional regulations or requirements can also apply to specific topics covered in this document.	

Project number	Title	Committee
ISO/TS 24420:2023	Biotechnology — Massively parallel DNA sequencing — General requirements for data processing of shotgun metagenomic sequences	ISO/TC 276
Scope	This document illustrates the workflow of shotgun metagenomic sequence data processing of host-derived microbiome and environmental metagenomes. This document specifies the requirements for quality control of shotgun metagenomic sequence data processing for massively parallel DNA sequencing. This document provides guidelines for data directory, data archive and metadata for shotgun metagenomic sequence data. This document applies to data storage, sharing and interoperability of shotgun metagenomic sequence data. This document applies to shotgun metagenomic sequence data processing and analyses, but excludes functional analysis.	

Project number	Title	Committee
ISO/TS 23357:2023	Genomics Informatics —Clinical genomics data sharing specification for next generation sequencing	ISO/TC 215
Scope	This document specifies clinical sequencing information generated by massive parallel sequencing technology for sharing health information via massively parallel sequencing. This document covers the data fields and their metadata from the generation of sequence reads and base calling to variant evaluation and assertion for archiving reproducibility during health information exchange of clinical sequence information. However, the specimen collection, processing and storage, DNA extraction and DNA processing and library preparation, and the generation of test report are not in the scope of this document. This document hence defines the data types, relationship, optionality, cardinalities and bindings of terminology of the data. In essence, this document specifies: • — the required data fields and their metadata from generation of sequence reads and base calling to variant evaluation and assertion for sharing clinical genomic sequencing data files generated by massively parallel sequencing technology, as shown in Figure 1;	

- — the sequencing information from human samples using DNA sequencing by massively parallel sequencing technologies for clinical practice.

Figure 1 — Clinical application processes based on next-generation sequencing (NGS) data



NOTE The grey shaded text indicates the scope of this document.