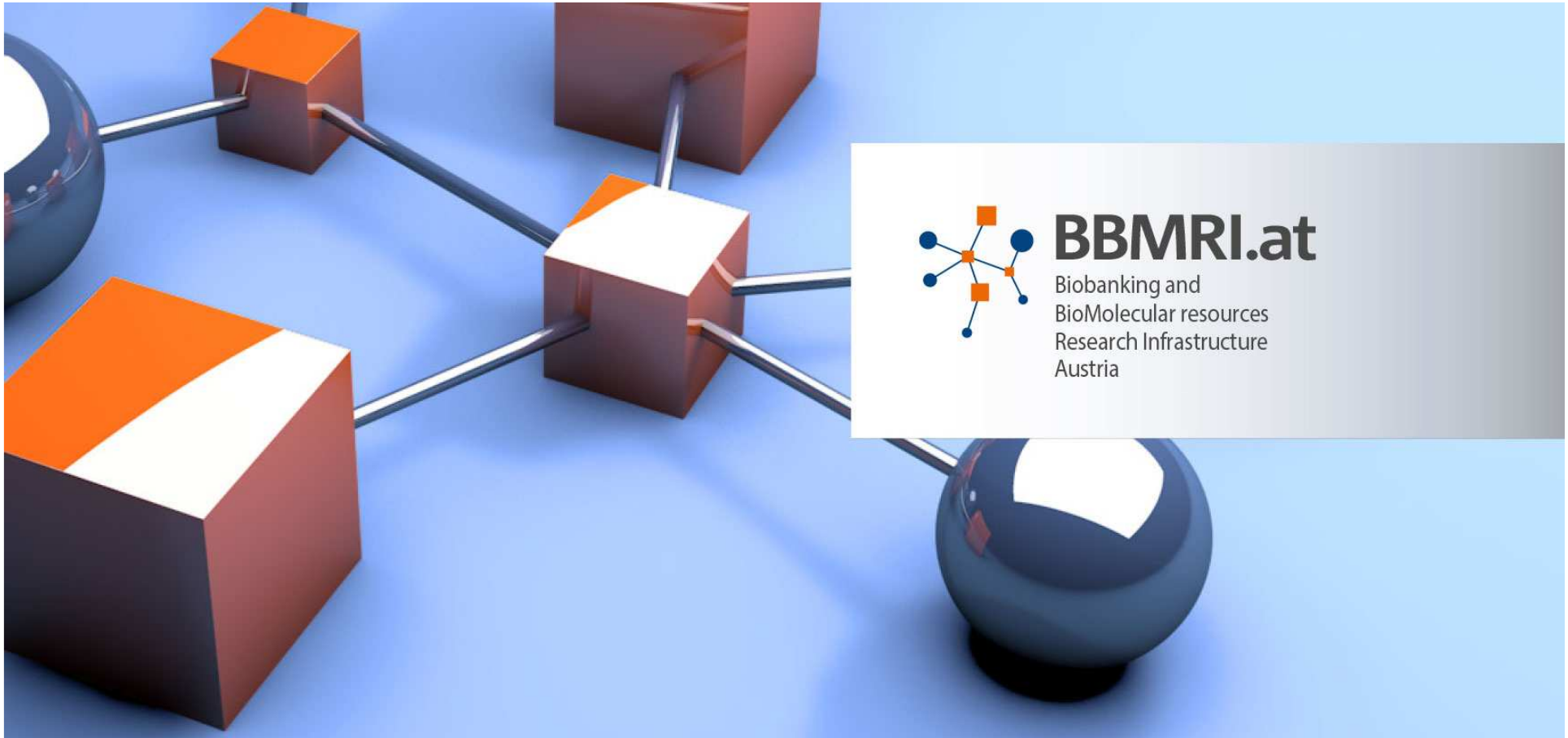

BBMRI.at
Biobanking and
BioMolecular resources
Research Infrastructure
Austria

Conformity with CEN/TS and ISO Standards

Cornelia Stumptner

Pre-Analytics Course | Graz| Feb 8-10, 2017

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Funded by
GZ 10.470/0016-II/3/2013

CEN Technical Specifications for Pre-examination Processes

CEN/TS: CEN/TC 140 Technical Specifications for molecular in vitro diagnostic examinations – Specifications for pre-examination processes

- CEN/TS 16827-1:2015 FFPE tissue — RNA
- CEN/TS 16827-2:2015 FFPE tissue — Proteins
- CEN/TS 16827-3:2015 FFPE tissue — DNA
- CEN/TS 16826-1:2015 Frozen tissue — RNA
- CEN/TS 16826-2:2015 Frozen tissue — Proteins
- CEN/TS 16835-1:2015 Blood — Cellular RNA
- CEN/TS 16835-2:2015 Blood — Genomic DNA
- CEN/TS 16835-3:2015 Blood — Circul. cell free DNA
- CEN/TS 16945:2016 Metabolomics in urine, serum & plasma

~€ 55-60

CEN Technical Specifications for Pre-examination Processes

CEN/TS: CEN/TC 140 Technical Specifications for molecular in vitro diagnostic examinations – Specifications for pre-examination processes

Target groups

- ✓ *In-vitro* diagnostic laboratories
- ✓ *In-vitro* diagnostics developers and manufacturers
- ✓ Institutions and commercial organizations performing biomedical research
- ✓ Biobanks
- ✓ Regulation authorities

CEN Technical Specifications for Pre-examination Processes

CEN/TS: CEN/TC 140 Technical Specifications for molecular in vitro diagnostic examinations – Specifications for pre-examination processes

Why necessary?

- ↳ 70% decisions in hospital based on diagnostics or lab test results
- ↳ 10% of patients die due to diagnostic errors
- ↳ Pre-analytical phase accounts for 46% to 68% of diagnostic errors
- ↳ This caused ~1.2 Mill US-D in an US mid-sized hospital
- ↳ 28 bill US-D in pharma due to irreproducible pre-clinical results
- ↳ 40-70% of published research findings are not reproducible

N Kaushik et al, 2014; LP Freedman et al, 2015; Economist 2013

CEN Technical Specifications for Pre-examination Processes

CEN/TS: CEN/TC 140 Technical Specifications for molecular in vitro diagnostic examinations – Specifications for pre-examination processes

Scientific evidence-based

e.g. SPIDIA

Public & private researchers, standardization & improvement of pre-analytical procedures

ISO/TC212 WG4

ISO/DIS 20184-1 Frozen - RNA
ISO/DIS 20184-2 Frozen – Prot.
ISO/DIS 20166-1 FFPE – RNA
ISO/DIS 20166-2 FFPE – Prot.
ISO/DIS 20166-3 FFPE – DNA, …

ISO/TC 276 Biotechnology

CEN Technical Specifications for Pre-examination Processes

BBMRI.at

SPIDIA4P

Development of 11 new CEN/TS and 2 ISO standards &
Raising awareness for and implementation of standards

3 Venous whole blood circul. tumor/organ cells — RNA, DNA, protein & staining 1 Venous whole blood exosomes — cfc RNA 1 Saliva — DNA 1 Frozen tissue — DNA 1 Urine/other body fluids - cfcDNA 3 fine needle aspirates – RNA, DNA, protein 1 Saliva & stool – DNA 1 Saliva — DNA	**CEN/TS**
1 FFPE tissue – in-situ st aining 1 Metabolomics – urine, plasma, serum	**ISO**

1 Scope

This Technical Specification gives recommendations for the handling, documentation and processing of FFPE tissue specimens intended for RNA 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).

The formalin fixation and the paraffin embedding process lead to modifications of the RNA molecules, which can impact the validity and reliability of the analytical test results.

Therefore, it is essential to take special measures to minimize the described profile changes and modifications within the tissue for subsequent RNA 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

Structure

FFPE Tissue - RNA

Outside the laboratory

Collection of primary tissue
Transport requirements

Inside the laboratory

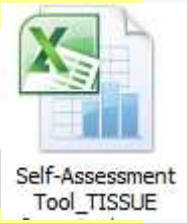
Primary tissue sample receipt
Fixation of the specimen
Evaluation of the pathology
Processing and paraffin embedding
Storage requirements (paraffin blocks & sections)

Isolation of total RNA

General information (FFPE, PFPE)
Quantity and quality assessment of RNA
Storage of isolated RNA

Content

FFPE Tissue - RNA	FROZEN-RNA
Outside the laboratory	**Outside the laboratory**
Collection of primary tissue	Collection of tissue
Transport requirements	Transport requirements
Inside the laboratory	**Inside the laboratory**
Primary tissue sample receipt	Primary tissue sample receipt
Fixation of the specimen	Evaluation of the pathology
Evaluation of the pathology	Cryo storage (stabilization)
Processing and paraffin embedding	Storage requirements (cryo)
Storage requirements (paraffin blocks & sections)	
Isolation of total RNA	**Isolation of total RNA**
General information (FFPE, PFPE)	General information (cryo)
Quantity and quality assessment of RNA	Quantity and quality assessment of RNA
Storage of isolated RNA	Storage of isolated RNA



BBMRI Self-Assessment Tool

	BBMR.at CEN/TS Self Assessment Tool			**FFPE**	
	Based on: FFPE-RNA (ONR CEN/TS 16827-1_2015-11-01) Frozen-RNA (ONR CEN/TS 16826-1_2015-09-15)			**ADVANCED with Specific Sample Data**	
	Outside the laboratory			**Sample data**	
	Collection of tissue			FFPE	Source of data
1	**Information about sample donor**			FFPE	Source of data
should	1.1. **Donor/Patient ID** documented	*e.g. code*			
should	1.2. **Health status of donor/patient** documented	*e.g. healthy, disease type, concomitant disease*			
should	1.3. **Medical treatment** documented	*e.g. anaesthetics, medications, surgical or diagnostic procedures (e.g. biopsy device used for the collection);*			
should	1.4. **Start of warm ischemia** documented	Surgery: Date of vessel ligation/arterial clamping time			
should		Surgery: Time of vessel ligation/arterial clamping time			
2	**Information on the primary tissue sample**			FFPE	
shall	2.2. **Cold ischemia (start)** documented	Date of tissue removal from body			
		Time of tissue removal from body			
shall	2.3. **Tissue type and condition** documented	General tissue type and condition			
		Organ of origin + location within			
shall	2.4. **Type and start of fixation (if started outside the biobank)** documented	Date of start			
		Time of start			
		Fixative type			
		Fixation condition			

Self-Assessment_Tool_TISSUE

Primary tissue collection

-

Information about the sample donor

Donor/patient ID documented? should — ○ Yes ○ No (e.g. code)

Health status of donor/patient documented? should — ○ Yes ○ No (e.g. healthy, disease type

Medical treatment prior to tissue collection documented? should — ○ Yes ○ No (e.g. anaesthetics, medica diagnostic procedures)

Start of ischemia within the body (warm ischemia) documented? should — ○ Yes ○ No

Date of vessel ligation/arterial clamping time (warm ischemia)? should — ○ Yes ○ No

Time of vessel ligation/arterial clamping time (warm ischemia)? should — ○ Yes ○ No

[Online SAT „FFPE – RNA“ >>]

[Online SAT „Frozen – RNA“ >>]

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THANK YOU!

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