MAKING NEW TREAT MENTS POSSIBLE

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The EU Framework Programme for Research and Innovation

SPIDIA4P

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CEN/TS & ISO PRE-ANALYTICS STANDARDS

AT A GLANCE

CORNELIA STUMPTNER

MEDICAL UNIVERSITY OF GRAZ (BBMRI.AT, SPIDIA4P)

H2020 Project SPIDIA4P, GA No. 733112

Funded by:
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(2018-2023)

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HORIZON 2020
The EU Framework Programme for Research and Innovation

CEN Technical Specifications (CEN/TS) & ISO Standards for **“Molecular in vitro diagnostic examinations – Specifications for pre-examination processes …”**

- ✓ Why?
- Which?
- Where to get?
- For whom?
- What are they about?
- Do YOU meet the requirments?

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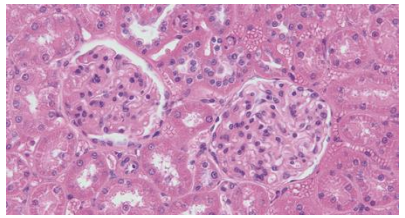
WHICH?

ISO STANDARDS & CEN TECHNICAL SPECIFICATIONS (CEN/TS)

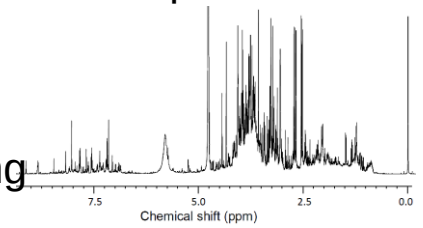
MOLELCULAR IN VITRO DIAGNOSTIC-EXAMINATIONS – SPECIFICATIONS FOR PREEXAMINATION PROCESSES FOR:



- ISO 20184-1: 2018 (former CEN/TS 16826-1), frozen tissue – Part 1: Isolated RNA
- ISO 20184-2: 2018 (former CEN/TS 16826-2), frozen tissue – Part 2: Isolated proteins
- CEN/TS16826-3: 2018, frozen tissue – Part 3: Isolated DNA

- EN ISO 20166-1: 2018 (former CEN/TS 16827-1), FFPE tissue – Part 1: Isolated RNA
- EN ISO 20166-2: 2018 (former CEN/TS 16827-2), FFPE tissue – Part 2: Isolated proteins
- EN ISO 20166-3: 2018 (former CEN/TS 16827-3), FFPE tissue – Part 3: Isolated DNA

- EN ISO 20186-1: 2019, (former CEN/TS 16835-1), venous whole blood – Part 1: Isol.cellular RNA
- EN ISO 20186-2: 2019, (former CEN/TS 16835-2), venous whole blood – Part 2: Isol. genomic DNA
- EN ISO 20186-3: 2019, (former CEN/TS 16835-3), venous whole blood – Part 3: Isol. Circ. cell free DNA from plasma



- CEN/TS 17390-1:2020, circulating tumor cells (CTCS) – Part 1: Isolated RNA
- CEN/TS 17390-2:2020, circulating tumor cells (CTCS) – Part 2: Isolated DNA
- CEN/TS 17390-3:2020, circulating tumor cells (CTCS) – Part 3: Preparation for analytical CTC staining

- CEN/TS 16945:2016, metabolomics in urine, serum and plasma

- CEN/TS 17305:2019, saliva – Isolated human DNA

www.iso.org/standard; https://standards.cen.eu

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WHICH?

NEW CEN/TS AND ISO STANDARDS

IN THE PIPELINE UNTIL 2020/2021

- 1 CEN/TS for exosomes & extracell. vesicles in venous whole blood – isol. DNA / RNA / proteins
- 1 CEN/TS for urine and other body fluids – isolated cell free DNA
- 3 CEN/TS for fine needle aspirates - isolated cellular RNA, genomic DNA, proteins
- 1 CEN/TS for venous whole blood - isolated circulating cell free RNA from plasma
- 1 CEN/TS for human specimens – microbiome DNA] Coordinated by K. Zatloukal/C. Stumptner
- ISO 20166-4 for FFPE tissues - in-situ staining procedures] Coordinated by K. Zatloukal/B. Sheppard/ C. Stumptner
- 1 ISO for metabolomics - urine, blood plasma, blood serum
- 1 ISO for frozen tissue – Part 2: Isolated DNA (to replace CEN/TS16826-3: 2018)

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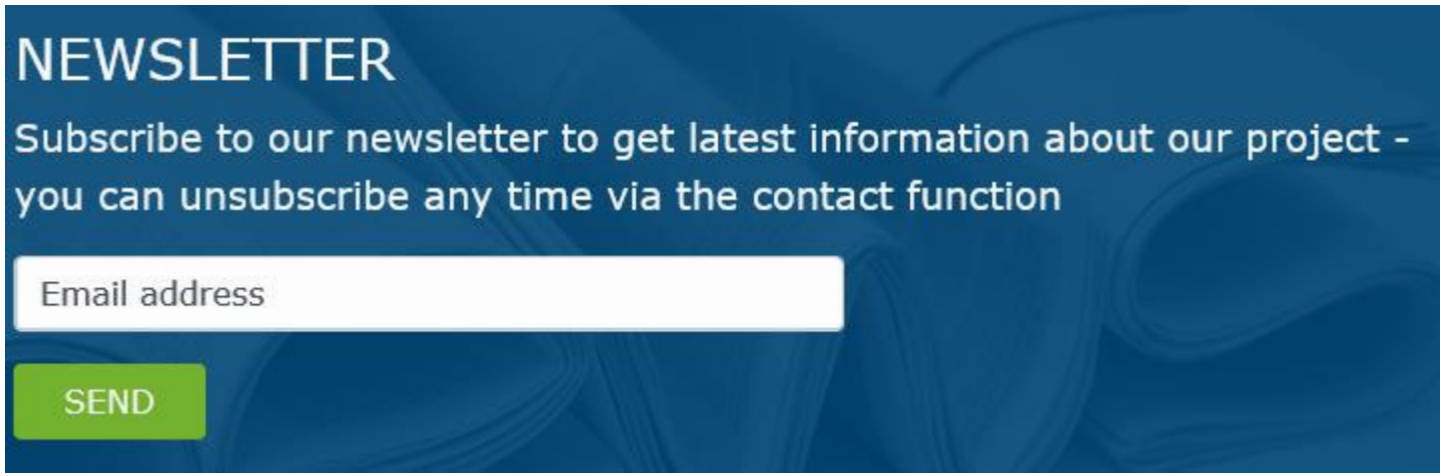
WHICH?

NEW CEN/TS AND ISO STANDARDS

IN THE PIPELINE UNTIL 2020/2021

- 1 CEN/TS … NA / RNA / proteins
- 1 CEN/TS …
- 3 CEN/TS … oteins
- 1 CEN/TS … sma
- 1 CEN/TS … Zatloukal/C. Stumptner
- ISO 2016 … Zatloukal/B. Sheppard/C.
- 1 ISO for …
- 1 ISO for … 018)

Overview & latest pre-analytics standards:
www.spidia.eu/projects/standard-documents



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WHERE TO GET?
TO BE PURCHASED AT

€ 65,- to 75,- / standard as pdf
(single user licence)

International Organization for Standardization
www.iso.org

European Committee for Standardization
www.iso.org

National Standardization Bodies* e.g.
ASI – Austrian Standards Institute

* https://standards.cen.eu/dyn/www/f?p=CENWEB:5


ICS 11.100.10

AUSTRIAN STANDARDS ONR

ONR CEN/TS 16826-3

Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for snap frozen tissue — Part 3: Isolated DNA (CEN/TS 16826-3:2018)

Molekularanalytische in-vitro-diagnostische Verfahren — Spezifikationen für präanalytische Prozesse für schockgefrorene Gewebeproben — Teil 3: Isolierte DNA (CEN/TS 16826-3:2018)

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FOR WHOM?

PREANALYTICAL CEN/TS & ISO STANDARDS

SCOPE

"This document gives guidelines on the handling, documentation, storage and processing of […] specimens intended for […] examination 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."

Source: ISO 20166-3:2018 FFPE - DNA (ASI preview)

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FOR WHOM?

PRE-ANALYTICAL CEN/TS & ISO STANDARDS

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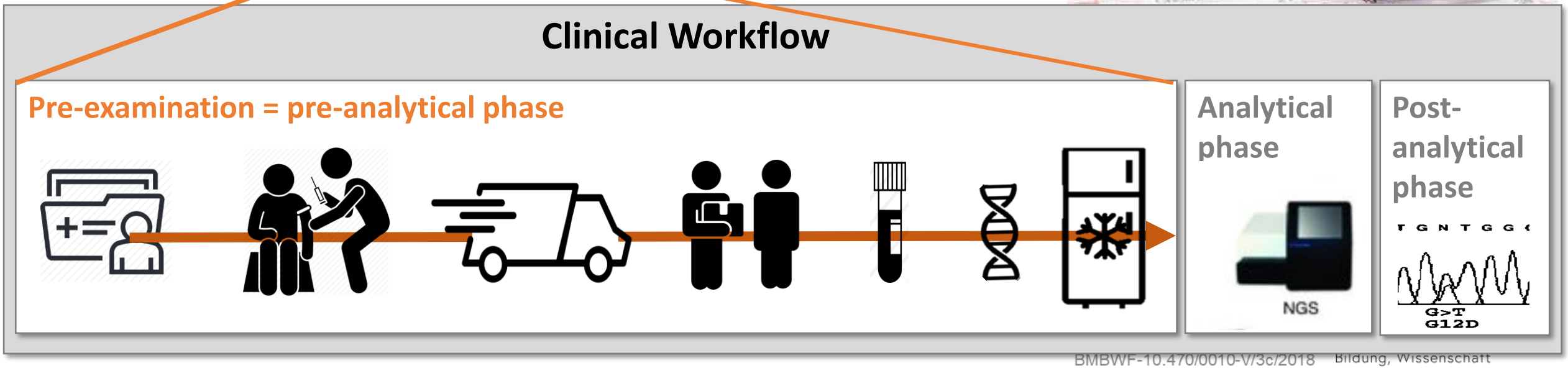
"This document gives guidelines on the handling, documentation, storage and processing of […] specimens intended for […] examination during the pre-examination phase before a molecular assay is performed."



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CONTENT

PREANALYTICAL CEN/TS & ISO STANDARDS

SCOPE

"This document gives guidelines on the handling, documentation, storage and processing of […] specimens intended for […] examination during the pre-examination phase before a molecular assay

This

exam d by

medi is also intended to be used by laboratory customers, in vitro diagnostics developers and manufacturers, biobanks, ….."

"shall" - **requirement**
"should" - **recommendation**
"may" - permission
"can" – possibility/capability

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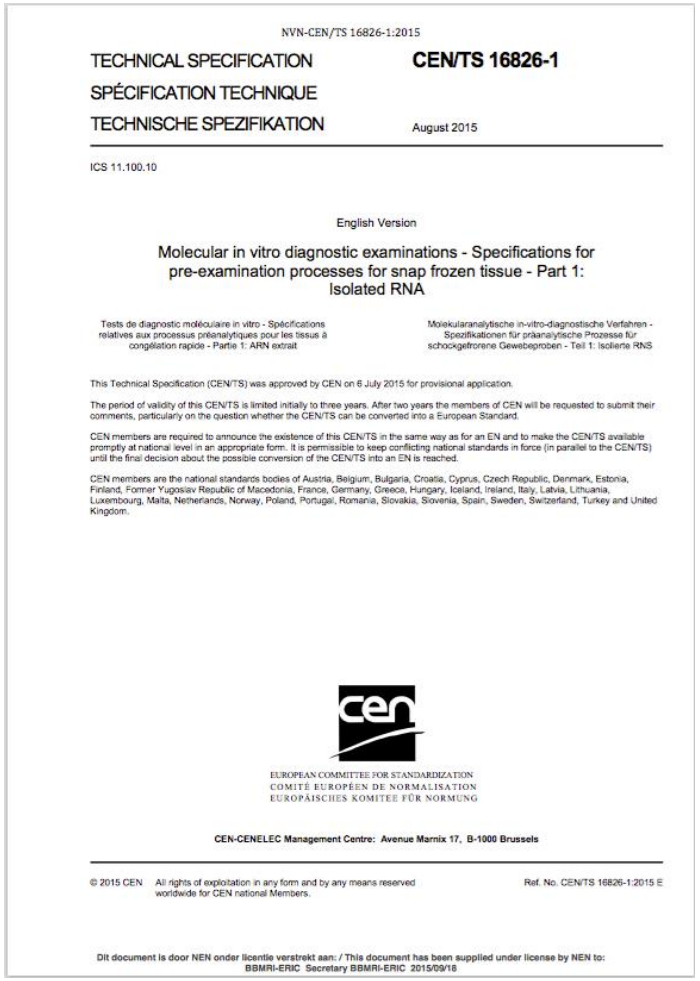
CONTENT

PREANALYTICAL CEN/TS & ISO STANDARDS

GENERAL CONTENTS



NVN-CEN/TS 16826-1:2015

TECHNICAL SPECIFICATION **CEN/TS 16826-1**

SPÉCIFICATION TECHNIQUE

TECHNISCHE SPEZIFIKATION August 2015

ICS 11.100.10

English Version

Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for snap frozen tissue - Part 1: Isolated RNA

Tests de diagnostic moléculaire in vitro - Spécifications relatives aux processus préanalytiques pour les tissus à congélation rapide - Partie 1: ARN extrait

Molekularanalytische in-vitro-diagnostische Verfahren - Spezifikationen für präanalytische Prozesse für schockgefrorene Gewebeproben - Teil 1: Isolierte RNS

This Technical Specification (CEN/TS) was approved by CEN on 6 July 2015 for provisional application.

The period of validity of this CEN/TS is limited initially to three years. After two years the members of CEN will be requested to submit their comments, particularly on the question whether the CEN/TS can be converted into a European Standard.

CEN members are required to announce the existence of this CEN/TS in the same way as for an EN and to make the CEN/TS available promptly at national level in an appropriate form. It is permissible to keep conflicting national standards in force (in parallel to the CEN/TS) until the final decision about the possible conversion of the CEN/TS into an EN is reached.

CEN members are the national standards bodies of Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.

CEN

EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

CEN-CENELEC Management Centre: Avenue Marnix 17, B-1000 Brussels

Ref. No. CEN/TS 16826-1:2015 E

- Foreword
- Introduction
- 1. Scope
- 2. Normative references
- 3. Terms & definitions
- 4. General considerations
- 5. Outside the laboratory
  - Specimen collection, processing, stabilization, storage, transport
- 6. Inside the laboratory
  - Specimen reception, evaluation of the pathology, processing (e.g. fixation, freezing, tissue processing, embedding, aliquoting, centriguation), storage,
  - Isolation of RNA/DNA/proteins, quantity & quality assessment, storage
- Annex
- Bibliography

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CONTENT

BLOOD - RNA	FFPE Tissue - DNA	FROZEN Tissue - DNA
5 Outside the laboratory	**5 Outside the laboratory**	**5 Outside the laboratory**
- Specimen collection (incl. info about donor, & specimen, selection of collection device, stabilization specimen processing and storage)	- Specimen collection (incl. info about donor & specimen, specimen processing and storage)	- Specimen collection (incl. info about donor & specimen, specimen processing and storage)
- Transport	- Transport	- Transport
6 Inside the laboratory	**6 Inside the laboratory**	**6 Inside the laboratory**
- Reception	- Reception	- Reception
	- Fixation of the specimen	- Evaluation of the pathology
- Plasma preparation	- Evaluation of the pathology	- Freezing
	- Decalcification	
	- Processing and paraffin embedding	
- Storage (plasma)	- Storage (paraffin blocks & sections)	- Storage (frozen tissue)
6.5 Isolation of RNA	6.8 Isolation of DNA	6.5 Isolation of DNA
- General information (plasma)	- General information (FFPE tissue)	- General information (frozen tissue)
- Quantity & quality assessment of RNA	- Quantity & quality assessment of DNA	- Quantity & quality assessment of DNA
- Storage of isolated RNA	- Storage of isolated DNA	- Storage of isolated DNA

Pre-analytical variables along the clinical workflow

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5 Outside the laboratory

Chapters	Workflow steps	Preanalytical variables (examples)
- **Specimen collection**	Patient	Health/disease condition, identity, demographics (age, gender, ethnicity, etc), BMI, nutrition, stress, physical activity, medication & treatment, informed consent, etc.
	Collection	Surgerical procedure, biopsy device, warm and cold ischemia time, blood collection device, labelling, etc.
	Stabilization	Stabilization method and solution: freezing, fixation (type of stabilizer, volume/specimen size, duration, temperature) etc.
	Storage	Specimen container, duration, temperature
- Transport	Transport	Transport container, duration, temperature

Stumptner et al; Crucial Role of High Quality Biosamples in Biomarker Development; Handbook of Biomarkers and Precision Medicine (2019)
Zatloukal, Stumptner et al; Biobanks in personalized medicine; Exp Rev Prec Med (2018)

Pre-analytical variables along the clinical workflow

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6 Inside the laboratory

Chapter	Workflow steps	Preanalytical variables - examples
- Reception	Reception	Reception (person, date/time, condition, …)
- Pathol. evaluation, fixation, decalcification, processing, embedding / Freezing / Plasma prep	Specimen processing	Macroscopy/grossing of tissues, sample selection, fixation (duration, condition), decalcification, tissue processing, paraffin embedding; freezing method; centrifugation, aliquoting, etc.
- Storage	Storage	Specimen container, duration, temperature, etc.
- Isolation of DNA/RNA/prot	Pre-processing for analysis & storage until analysis	Sample region for isolation, (RNA, DNA, protein) isolation kit/method; quantity & quality assessment, storage;
- Other pre-processing		sectioning of tissues, deparaffinization, storage, etc.

Stumptner et al; Crucial Role of High Quality Biosamples in Biomarker Development; Handbook of Biomarkers and Precision Medicine (2019)
Zatloukal, Stumptner et al; Biobanks in personalized medicine; Exp Rev Prec Med (2018)

MEET THE REQUIREMENTS?

BBMRI SELF-ASSESSMENT SURVEY

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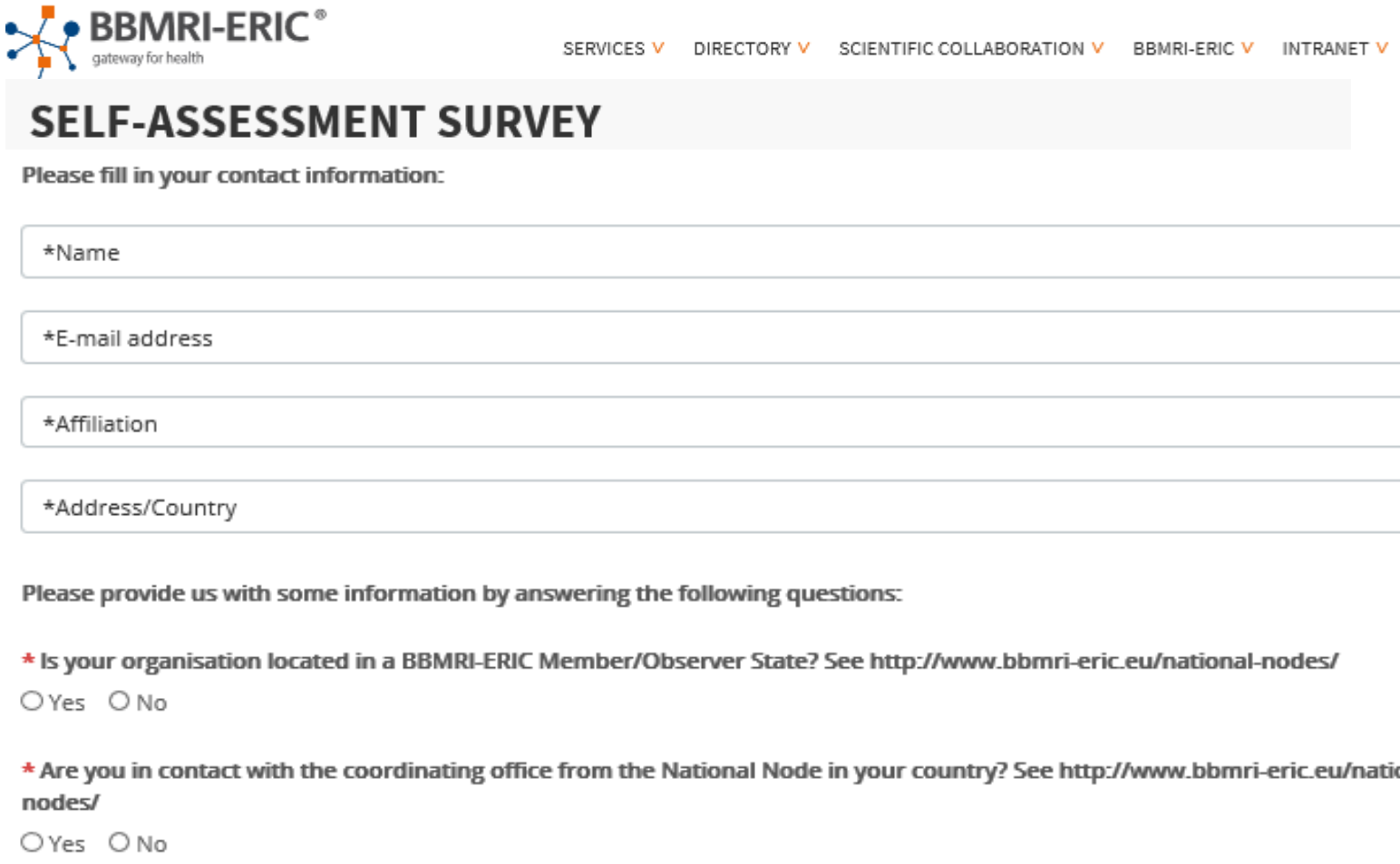
BBMRI-ERIC gateway for health

ADOPT BBMRI-ERIC gateway for health

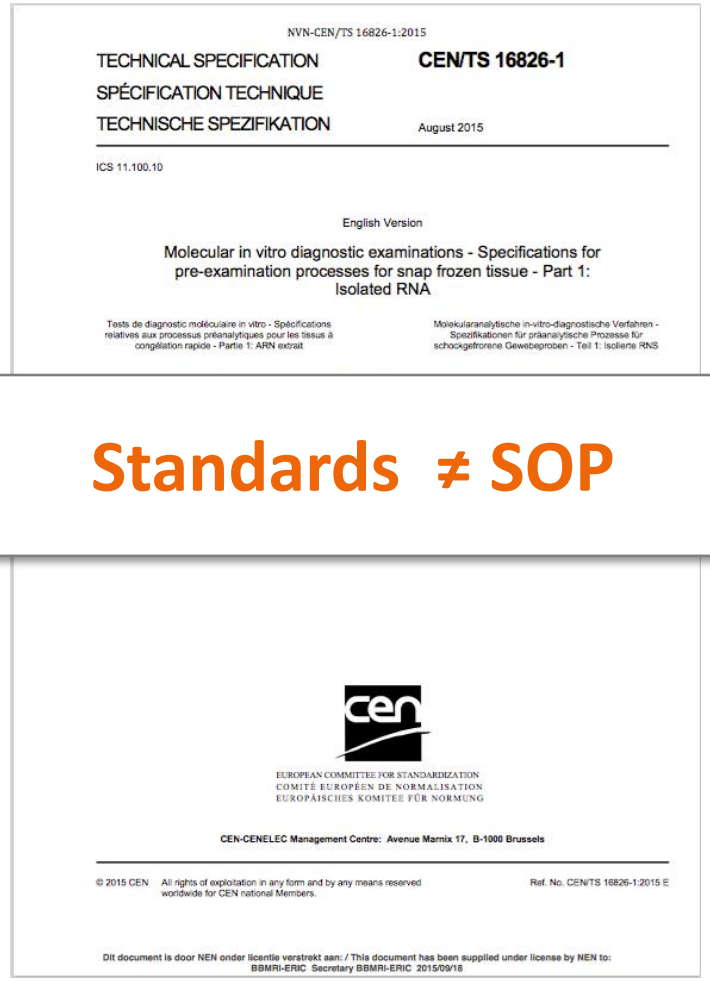


Access under:

www.bbmri-eric.eu/services/self-assessment-survey/

CONTENT

PREANALYTICAL CEN/TS & ISO STANDARDS



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cen

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Ref. No. CEN/TS 16826-1:2015 E

Contain only some details, e.g.

- **FFPE:** Standard buffered formalin
  = 37 % formaldehyde by mass (corresponding to 40 % by volume)
- **Blood:** Immediately after blood collection mix tube with stabilizer

Standards ≠ SOP

=> Documentation

- **Basis for QM processes and SOPs**
- **Identification of source of variation**
- **Sample exclusion in a cohort selection**

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Thank you

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