CEN Standards: From Paper to Action

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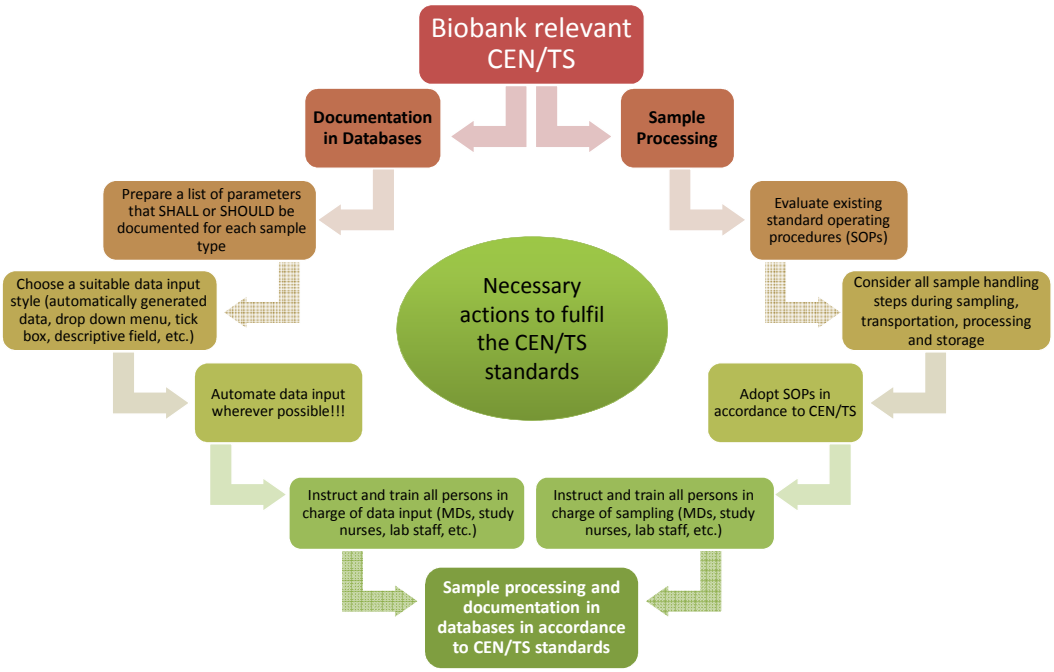
Background

Recently, the European Committee for Standardization published several European Technical Specifications (CEN/TS) with high relevance for biobanks. In detail, technical specifications for the pre-examination processes of urine, venous whole blood, serum, plasma, snap frozen tissue and FFPE tissue are waiting for their realization in biobanking (see overview on the left). Here we present a guideline for the successful application of these CEN/TS in biobanks.

CEN/TS ready for implementation in biobanking

Reference	Titel	Affected Sample Type	Status
CEN/TS 16945:2016	Molecular in vitro diagnostic examinations — Specifications for pre-examination processes for metabolomics in urine, venous blood serum and plasma	urine, venous whole blood, serum, plasma	published standard
CEN/TS 16835-1:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 1: Isolated cellular RNA	whole blood	published standard
CEN/TS 16835-2:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 2: Isolated genomic DNA	whole blood	published standard
CEN/TS 16835-3:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for venous whole blood – Part 3: Isolated circulating cell free DNA from plasma	venous whole blood, plasma	published standard
CEN/TS 16827-1:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for FFPE – Part 1: Isolated RNA	any tissue preserved in FFPE	published standard
CEN/TS 16827-1:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for FFPE – Part 2: Isolated proteins	any tissue preserved in FFPE	published standard
CEN/TS 16827-1:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for FFPE – Part 3: Isolated DNA	any tissue preserved in FFPE	published standard
CEN/TS 16826-1:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for snap frozen tissue – Part 1: Isolated RNA	any snap frozen tissue	published standard
CEN/TS 16827-2:2015	Molecular in vitro diagnostic examinations – Specifications for pre-examination processes for snap frozen tissue – Part 2: Isolated proteins	any snap frozen tissue	published standard
prEN ISO 20166-1	Molecular in-vitro diagnostic examinations - Specifications for preexamination processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 1: Isolated RNA	any tissue preserved in FFPE	under approval
prEN ISO 20166-2	Molecular in vitro diagnostic examinations - Specifications for pre-examinations processes for formalin-fixed and paraffin-embedded (FFPE) tissue - Part 2: Isolated proteins	any tissue preserved in FFPE	under approval
prEN 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	any tissue preserved in FFPE	under approval
prEN ISO 20184-1	Molecular in-vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 1: Isolated RNA	any frozen tissue	under approval
prEN ISO 20184-2	Molecular in-vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 2: Isolated proteins	any frozen tissue	under approval
prEN ISO 20186-1	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 1: Isolated cellular RNA	whole blood	under approval
prEN ISO 20186-2	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for venous whole blood - Part 2: Isolated genomic DNA	whole blood	under approval
prEN ISO 20186-3	Molecular in-vitro diagnostic examinations - Specifications for pre-examination processes for blood - Cellular RNA - Part 3: Isolated circulating cell free DNA from plasma	whole blood, plasma	under approval
ISO/DIS 20387	Biotechnology — Biobanking — General requirements for biobanking	all sample types stored in biobanks	under developement
prCEN/TS 16823-3	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for frozen tissue - Part 3: Isolated DNA	any frozen tissue	under drafting
not available	Molecular in vitro diagnostic examinations - Specifications for preexamination processes for saliva - Isolated DNA	saliva	under drafting
not available	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 1: Isolated RNA	venous whole blood, circulation tumor cells	under drafting
not available	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 2: Isolated DNA	venous whole blood, circulation tumor cells	under drafting
not available	Molecular in vitro diagnostic examinations - Specifications for pre-examination processes for circulating tumor cells (CTCs) in venous whole blood - Part 3: Preparations for analytical CTC staining	venous whole blood, circulation tumor cells	under drafting



Methods

To identify the relevant parameters and responsible stakeholders, the workflows for all relevant CEN/TS were divided into two major parts: documentation and sample processing.

Standard operating procedures (SOPs) affected by CEN/TS were defined and adapted accordingly. Moreover, all critical steps with relevance for documentation were collected. Databases need to be modified to comply with CEN/TS requirements and data input devices must be adapted. Finally, responsible staff needs to be instructed concerning the new procedures.

Results

Existing cohorts were evaluated regarding their CEN/TS status quo – and a few identified to already follow CEN/TS (see directory of BBMRI-ERIC). Thereafter, adaptation of SOPs and existing databases according to CEN/TS was the major focus. Fast and sound data assessment, data collection and future data query is of great importance. Plain text fields need to be avoided wherever possible and tick boxes, drop down lists or automatically generated data (time points, temperatures, volumes, barcode numbers etc.) should be used instead.

It turned out that for clinical biobanks receiving the majority of samples from clinical routine; sampling, intermediate storage and transportation can be a bottleneck since the biobank might not have (enough) influence on the sample handling and documentation steps during this early phase of pre-analytics.

Conclusion

CEN/TS were not predominantly elaborated for biobanking, which challenges biobanks. Likewise, we need to evaluate the applicability of CEN/TS in daily routine. Nevertheless, strategic approaches can enable biobanks to accomplish CEN/TS, to assure highest quality and provide biological material with reliable value in the long run.

Funded by
Bundesministerium für Wissenschaft, Forschung und Wirtschaft
BBMRI.at Biobanking and BioMolecular resources Research Infrastructure Austria
GZ 10.470/0016-II/3/2013
ZUKUNFTSFONDS STEIERMARK