WG TISSUE

ACTIVITY REPORT & RECOMMENDATIONS

— OCTOBER 2017

The working group (WG) Tissue of Swiss Biobanking Platform is composed of experts and operational biobank managers from the five Swiss Pathology Institutes of University hospitals and the Cantonal Hospital of St-Gallen. The mandate of the group is to analyse the actual Tissue sampling practices and bridge the gap with existing international and European guidelines. The overall mission is to improve sample quality, to harmonise practices and to propose solutions to support interoperability among biobanks. This document summarizes the main conclusions and decisions of the group.

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1)
PRE-ANALYTICAL DATA SOURCE DOCUMENTS AND RECOMMENDATIONS

In 2018, a new ISO standard for biobanks (ISO 20387) will be published, giving the Biobanks a specific base on which to build their quality management. Linked to this effort, the European Commission for Standardization has released several pre-analytical CEN/TS specifications, which address important pre-analytical workflows applied to molecular in vitro diagnostic. The operational members of the WG Tissue have then evaluated the five already published CEN documents concerning tissue and pre-analytical tissue samples (see list below - these documents can be purchase on http://shop.snv.ch).

Specifications on snap frozen tissue

- **CEN/TS 16826-1**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for snap frozen tissue
  Part 1: Isolated RNA

- **CEN/TS 16826-2**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for snap frozen tissue
  Part 2: Isolated proteins

- **CEN/TS 16827-1**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for FFPE tissue
  Part 1: Isolated RNA

- **CEN/TS 16827-2**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for FFPE tissue
  Part 2: Isolated proteins

- **CEN/TS 16827-3**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for FFPE tissue
  Part 3: Isolated DNA

Many of the pre-analytics described in the CEN specifications are also listed in the Standard Pre-analytical Code (SPREC) as developed by the ISBER Biospecimen Science Working Group. The SPREC identifies and records the 9 main pre-analytical factors that may have impact on the integrity of sampled solid biospecimens and their simple derivatives, during collection, processing, and storage.

The actual compliance with the CEN specifications and the SPREC was analysed through a survey answered by all Institutes. Part of the results are displayed in *figure 1*.

As a conclusion, the group underlines the importance of the CEN guidelines that contain a very extensive checklist of pre-analytical variables, which are relevant for sample quality, with respect to various downstream analyses. These guidelines thus provide an excellent source for defining pre-analytical SOPs for specific downstream analyses.

- **The WG Tissue has used the specifications as the base to define the dataset that will be documented in each institute.**

The documentation of the 9 pre-analytical factors needed to generate the SPREC code is required in the CEN specifications as well. The WG Tissue has used the variables defined in the code to develop the dataset to allow the generation of the code if needed.

- **The group has decided that the 9 pre-analytical variables would be followed in order to be able to generate the SPREC code. Consequently, it will enhance the potential of interoperability among biobanks.**

Fig.1
Evaluation of documentation of the 9 pre-analytic variables needed to generate the SPREC code in the Pathology Institutes

Pre-analytics required to generate SPREC

- Clamping time
- Removal time
- Tissue type
- Tissue condition
- Organ of origin
- Fixation type (FFPE vs FF)
- Time of fixation
- Duration of fixation
- Long term storage ToC

The colors represent the percentage of documentation of the pre-analytics (mean between Institutes):
● documented in 0% of the institutes, ● documented in 25% of the institutes, ● documented in 75% of the institutes, ● documented in 100% of the institutes.

II)
SAMPLE RELATED DATASET FOR BIOBANKING OF TISSUE BIOSPECIMENS

As a main outcome, for the operation of a biobank, the WG tissue emphasizes the essential need of documenting all relevant environmental and biological factors as well as all pre-analytical variables that are expected to have an influence on the sample composition. With regard to the interoperability among different biobanks, it is indeed crucial that the documentation of sample history follows common standards. The WG Tissue expresses it by defining a Dataset (DS) of pre-analytical variables. Implementation of this dataset will require combined efforts of all Swiss biobanks on the IT and process sides. This dataset is recommended to be used in the future by tissue biobanks in order to achieve the following goals:

GOAL 1 : SAMPLE QUALITY

- Define the **essential preanalytical data** that should be linked to samples
- **Raise awareness** on biobanking **processes** the detailed documentation of pre-analytical steps will allow biobanks to identify critical steps in their workflows, to monitor and improve their processes
- **Improve quality of samples** Once each step is documented, improvement can be measured

An important aim of Swiss Biobanking Platform is to promote exchange and use of biological samples. Researchers need to be able to assess the suitability of samples for their planned application. The WG focuses on the quality of biobanking process and documentation. Relevant differences in the processing of samples need thus to be documented by the biobanks in a standardized way, so that the researchers can take relevant pre-analytical differences into account in their analyses in order to avoid biased results.
Finally, in order to follow workflow and processes to analyse and improve them, a documentation at each step is needed. Part of the DS is therefore dedicated to internal processes. Sample quality improvement is one of the goal of the DS. The listing of what needs to be documented at each step supports this task.

GOAL 2 : HARMONISATION & INTEROPERABILITY

- Define the **essential health related data** that should be linked to samples
- **Make the samples** from different biobanks **comparable** in their quality attributes
- **Promote exchange**

For promoting efficient sharing of tissue samples among biobanks, the second objective of the DS is therefore to facilitate the identification of comparable samples in different biobanks by proposing a common language to describe the pre-analytical attributes of samples.
Moreover, it is essential that samples can be searchable based on some clinical attributes on a common database. The DS includes a minimal set of health related data (e.g. main diagnosis) that are required for initial searches to select suitable samples

INTERACTIONS WITH PATHOLINK

The annotation of samples with clinic/pathological data is the aim of the SNF funded PathoLINK project (Biolink), in collaboration with SBP. This project will implement a standardized pathology report and create an integration layer where samples, together with data from the standardized pathological report, can be searchable through the five Pathology Institutes via an e-catalogue.

GOAL 3 : VISIBILITY

- Define the **essential associated data** that should be visible
- **Make samples searchable** on a common database
- **Enhance visibility**

A selection of fields within the DS, considered as essential to characterized samples, are tagged as “External”. These fields are suggested as the necessary fields to construct a future e-catalog, as planned by SBP, to enhance visibility of Swiss biobanks and of the Swiss biobanking community to the international biobank network.

The definition of such a dataset clearly needs to be aligned with the current efforts of harmonising cDWHs among university hospitals in the framework of the SPHN project. For clinical follow-up data, it will be important for the involved biobanks to raise the awareness within their institution (DWH group, data management etc...) of the essential importance of associated data for biobanked samples and to communicate which one are essential for a common database.

III)
ACTIONS

The finalized DS comprise 53 fields, each field is tagged as required (mandatory) or optional (recommended) depending on their relevance. A selection of dataset fields, considered essential for correctly characterizing a sample, is tagged as “external”. These fields will be used for sample exchange.

The group has decided to adjust their practices to be able to document all «mandatory» fields.

– Warm ischemia and cold ischemia time are the priority, despite not being documented in the majority of Institutes. A pilot with a service partner was highly recommended to start and then enlarge to the other services.

– Documentation around Fresh Frozen (FF) tissue samples was as well prioritized towards FFPE sample, since FF samples are usually only stored for research, whereas documentation around FFPE, such as fixation delay, are processes implemented in the diagnostic workflow and thus more difficult to modify.

The timeline is the following:
Implementation of all mandatory data-fields in 5 Pathology Institutes by September 2018.
– By December 2017: 70% of pilot cases should be documented
– By April 2018: actions taken in the pilot should be enlarged to all services – 50% of cases are documented
– By September 2018: 70% of all cases should be documented

The final goal of PathoLINK is to be able to share all fields tagged as “external” data in a common database by September 2018. The data not yet documented will be implemented by then.

IV)
LIST OF MEMBERS

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