WG LIQUID

ACTIVITY REPORT & RECOMMENDATIONS

— OCTOBER 2017

The working group (WG) Liquid of Swiss Biobanking Platform is composed of experts and operational biobanks managers from University hospitals. This group was mandated to review existing guidelines and propose a pre-analytical dataset to support the interoperability between biobanks and their internal quality management related to the biobanking of liquid biomaterials. This report summarizes the main conclusions of the current pre-analytical guidelines review. Finally, this document discusses the implications of the main conclusions on the definition of a data set for documenting pre-analytical process of liquid biospecimens.

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1)
DOCUMENT REVIEW

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, pan-European pre-analytical CEN/TS documents have been developed to address important pre-analytical workflows applied to molecular in vitro analytics in the context of the discovery, development, and validation of biomarkers. Thus, these documents are highly relevant for biobanks providing specimens and human-derived materials for research (cf. SPIDI4P funded by the European Union's Horizon 2020 research and innovation program).

Between February and April 2017, the operational members of the WG Liquid has conducted a review of the four already published CEN/TS documents released by the European Commission for Standardization and related to the pre-analytics liquid samples (see list below – these documents can be purchase on http://shop.snv.ch).

- **CEN/TS 16831-1**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for venous whole blood
  Part 1: Isolated cellular RNA

- **CEN/TS 16835-2**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for venous whole blood
  Part 2: Isolated genomic DNA

- **CEN/TS 16835-3**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for venous whole blood
  Part 3: Isolated circulating cell free DNA from plasma

- **CEN/TS 16945**
  Molecular in vitro diagnostic examinations
  Specifications for pre-examination processes for metabolomics in urine, venous blood serum and plasma

The Standard Pre-analytical Code (SPREC) developed by ISBER Biospecimen Science Working Group, identifies and records the main pre-analytical factors that may have impact on the integrity of clinical fluids, solid biospecimens, and their simple derivatives, during collection, processing, and storage. The SPREC for liquid has been reviewed by the group as well.

CONCLUSIONS AND RECOMMENDATIONS

The main conclusions and recommendations of this review drawn by the WG members were:

1)

The pre-analytics of liquid biological samples developed for one type of research application (e.g., proteomics or metabolomics) do not always apply for other types of research. Thus, there is no single pre-analytical SOP's that would provide high-quality samples for every type of research purpose. The CEN guidelines take this aspect into account and comprehensively integrate all currently relevant literature on the pre-analytics of the covered downstream analysis methods (e.g., metabolomics and liquid biopsy). They represent a very extensive checklist of pre-analytical variables, whichare relevant for sample quality with respect to various downstream analyses.

- **CEN specifications provide an excellent source for defining pre-analytical SOPs for specific downstream analyses. The WG liquid recommends using these guidelines as references or checklists.**

It is the responsibility of the investigators to anticipate what type of analyses they plan to perform on biobanked samples before initiating collection, and to identify optimal pre-analytical conditions.

2)

Many of the pre-analytical variables addressed in the CEN specifications are also listed in the SPREC code.

- **The group recommends that biobanks document the pre-analytical variables in such a way that information can be translated into the SPREC code in order to enhance the potential of interoperability between biobanks.**

- **The group recommends that SPREC code is not used for the primary documentation of sample attributes, since the code in many instances is not sufficiently accurate with regard to particular downstream applications. For example, actual times for sample processing should be recorded, instead directly in the coded form (e.g. "A" SPREC code for measured value <2h).**

3)

The definition of appropriate pre-analytical SOPs represents a moving target for liquid biospecimens as new downstream analysis methods are being developed (e.g., liquid biopsies). At best, the SOPs are evidence-based. Thus, pilot feasibility studies are of great value to obtain an unbiased view on the suitability of the collected samples for downstream analyses.

- **Since it is not realistic to define/adjust SOPs for all possible downstream applications to the biobank community, SBP proposes to create a network of experts (2-3 experts per field, including liquid biopsy, proteomics, pharmacology, metabolomics, etc…). This experts' panel could support researchers by answering their questions through a web portal hosted by SBP.**

4)

All reviewed guidelines highlight the importance of documenting relevant pre-analytical variables that may have impact on the sample quality and that may introduce analytical biases in downstream analyses. This also includes the documentation of the individual biological and environmental variables that are known or suspected to affect quantity and characteristics of an analyte in a given sample (e.g., age, diet, medication, seasonal changes, etc.). Depending on the planned analyses, such factors need to be documented and/or standardized so that they can be taken into account when interpreting results.

- **Documentation at all steps of the pre-analytical process is recommended in order to avoid hidden biases in future studies. SOPs should be defined according to their potential effects on intended downstream analyses.**

- **The WG Liquid proposes to define a list of pre-analytical variables that need to be recorded (= sample related data set (DS), see below) in order to ensure the interoperability between biobanks and to support the quality management within biobanks.**

II)

SAMPLE RELATED DATASET FOR BIOBANKING OF LIQUID BIOSPECIMENS

As a main outcome, for the operation of a biobank, the WG liquid emphasizes the essential need of documenting all relevant environmental and biological factors as well as all pre-analytical variables expected to have an influence on the sample composition. With regard to the interoperability between different biobanks, it is crucial that the documentation of sample history follows common standards. The WG liquid expresses it by defining a Data Set (DS) of pre-analytical variables for liquid biobank samples. This DS is recommended to be used in the future by liquid biobanks in order to achieve the following goal:

GOAL I: SAMPLE QUALITY

- Define the **essential pre-analytical 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 downstream application. Quality is to be comprehended from a quality assurance point of view and not from an analytical-use-case point of view. The WG wants to focus on the quality of biobanking process and documentation. Relevant differences in the processing of the 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.

This first version of the DS covers documentation of generic use cases and does not explicitly document matrix- or application specific use cases. The DS is sample specific and excludes information on biobank or on biobank-infrastructure. The latter information will be specified and recorded at a SBP central level since it is common to all specimen types.

GOAL 2 : HARMONIZATION & INTEROPERABILITY

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

For promoting efficient sharing of liquid 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 of different biobanks can be selected by researchers based on some clinical attributes. The DS includes a minimal set of health related data (e.g. main diagnosis) that are required for initial searches to select suitable samples.

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 set clearly needs to be aligned with the current efforts of harmonizing cDWHs among university hospitals in the framework of the SPHN project. It will be thus important that this part of the DS is jointly evaluated by all involved WGs of the SBP and SPHN, respectively. The WG liquid proposes that the coordination of this joint evaluation is carried out by the central office of SBP. Such a set also needs to be curated and updated as our knowledge on pre-analytical variables will evolve and new downstream analyses with specific sample quality requirements are emerging.

It is also worth noting that depending on the IT-infrastructure in place, associated data will not be collected by the biobanks themselves, as data needs to be extracted from the patient electronic medical record. Thus, 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 health related data for biobanked samples and to communicate, which records are essential and available for a common database.

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