Editorial

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Biobanking – current questions and positions

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An essential prerequisite for both, basic and translational medical research is the availability of high-quality, well-characterized biological samples. In recent years, biobanks able to provide such materials have, therefore, become an indispensable part of national as well as international research infrastructures. Biobanks support the entire workflow from the planning and set-up of sample collections, via actual sampling, sample transfer, sample processing and storage, to the selection and delivery of samples for defined research projects. In addition to the standardization, quality control and quality assurance of directly sample-related processes, biobanks are also significantly involved in the implementation of governance structures and procedural rules to ensure adherence to applicable ethical and legal regulations. Based on the extensive experience gained over the last decades in the pre-analytics, automated operation of laboratory infrastructures, and quality-assured routine handling and analysis of thousands of samples, laboratory medicine is virtually predestined for the establishment and operation of biobanks, particularly disease-oriented liquid biobanks. In this issue of the *Journal of Laboratory Medicine*, a number of current questions and positions on biobanking will hence be presented and discussed to further support the development of biobanking and the set-up of healthcare-integrated biobank infrastructures in the context of laboratory medicine.

One indispensable precondition for biobanking human biosamples and using them for research is the existence of a written informed consent that specifies i.a. the purpose of the collection, storage time and intended use of the biosamples. However, if the informed consent is restricted to a specific research question only, e.g. the investigation of a defined disease entity or the inclusion in a specific clinical study, valuable biosamples that have been collected in a costly and time-consuming manner, of course, cannot be used for other research questions, particularly those arising in the future and outside the scope of the original consent. One possible solution to overcome these limitations is the use of the broad consent template recently developed by the Working Party of the German Medical Ethics Committees (WP-GMEC). This consent,

when applied in combination with the safeguarding measures as described by Jahns et al. in the first article of this issue [1], can facilitate future use and exchange of biological samples for upcoming research questions. To protect the donors' interests, each individual research project that requests biosamples collected under the broad consent has to be approved by an independent ethics committee and the donor should also be able to exclude the use of his/her samples for specific research fields. Provided that policies and objectives for use of broad consent biosamples are publically available, have been standardized and agreed between biobanks, it is to be expected that the exchange of biosamples across biobanks will help to answer many future research questions, particularly if a critical number of samples is required.

Another important issue of biobanking is compliance with regulatory frameworks to ensure data protection. This aspect is discussed in an article by Drepper, in particular with special emphasis on the European General Data Protection Regulation (GDPR) which has been in force since 2016 [2]. Despite the complexity of the regulatory framework, Drepper manages to provide a comprehensive overview from a practical point of view on what has to be taken into account during set-up and operation of biobanks. Starting with a general overview of the legal framework, the author discusses the legal basis for the collection, storage and processing of samples and associated health data based on consent as well as on special regulations, e.g. research clauses in the German Federal Data Protection Act and some German state hospital laws, and data processing by a processor according to GDPR regulations. Regarding patients' rights, extensive information obligations are described, with reference to problems in their practical implementation, particularly in the context of a broad consent where it cannot be excluded, for example, that information with regard to future recipients of data and samples might be incomplete at the time point of sample collection, or the problem that a donor cannot decide to be notified about potential test results without knowing which tests will be carried out in future research studies. Furthermore, Drepper focusses on the implementation of a data protection concept for biobanks according to the guidelines for medical research projects and the generic data protection concept of the TMF e.v.

(Technology, Methods, and Infrastructure for Networked Medical Research [TMF]).

In the third article of this special issue, Goebel asks the question whether a special biobanking law might be helpful to support the set-up and operation of biobanks [3]. From a lawyer's point of view, and by discussing two recent proposals for a biobank act, he concludes that numerous existing laws, regulations and procedural rules as well as model solutions that have been successfully developed during the recent years by the biobank community leave no regulatory gap justifying the development of a biobank legislation. However, within the biobank community, there is controversial discussion about the potential benefits of a biobank law. In principle, a biobank law should rather reduce the complexity of regulatory frameworks because, in day-to-day practice of biobanks, negotiation of contractual arrangements with sample owners, cooperation partners and sample users already takes more time than the actual searching, compiling and delivery of samples for research projects, even when using predefined generic templates provided by the biobank community.

Another important component besides the aforementioned ethical, legal and data protection issues, particularly with regard to the interoperability of biobanks, is the set-up of quality-controlled biobank processes according to predefined and agreed international standards. So far, biobanks act on the basis of best practice guidelines, developed by certain organizations (International Society for Biological and Environmental Repositories [ISBER], European, Middle Eastern and African Society for Biobanking [ESBB], National Institutes of Health [NIH], European Union [EU]), or are certified according to DIN EN ISO 9001. Moreover, some biobanks make use of partial processes, accredited according to DIN EN ISO norms, e.g. DIN EN ISO 17020, 17025 and 17034, applicable for inspection bodies, testing laboratories or manufacturers of reference materials, respectively. However, the establishment of the new biobank-specific norm DIN EN ISO 20387 [ISO 20387:2018-08; Biotechnology – Biobanking – General requirements for biobanking Beuth Verlag (2018)] has paved the way for international standardization and thus accreditation of comprehensive biobank activities. The article by Meinung et al. describes the background, development and involvement of biobank experts in the establishment of ISO 20387 [4]. It can be assumed that biobanks showing conformity with this new standard will have several advantages over competitors, not only, for example, in providing standardized high-quality samples for research, but also in the context of the new In Vitro

Diagnostica Regulation (IVDR), the Medical Device Regulation (MDR), and in cooperation with diagnostic and pharmaceutical partners from the industry.

Standardization and harmonization across biobanks of the different pre-analytical steps of the biobanking workflow is a precondition for collection and storage of biosamples with comparable (high) quality. Automation is one important tool to ensure process quality in this regard. In their article, Baber et al. provide insights into the opportunities and challenges of automation in biobanking by discussing automated solutions for sample transport, processing, freezing and storage [5]. Although high sample quality cannot be guaranteed by automation alone, the latter may still be a critical driver for the implementation of high-quality processes. However, advantages and disadvantages of automation must be carefully weighed against each other prior to the implementation of presumably rather costly automated solutions.

In addition to automation, selection of appropriate storage devices is of utmost importance to ensure storage at the highest possible quality. Besides straws for e.g. storage in the vapor phase of liquid nitrogen, several biobanks use two-dimensional (2D)-barcode cryotubes in a 96-Well Society for Biomolecular Sciences (SBS) format, which can be managed easily by automated liquid handling stations and fully automated -80°C storage systems. However, standardized criteria for evaluation and selection of appropriate storage devices are currently not available. A first attempt toward the definition and reflection of such criteria is described in the article by Petersmann et al. based on 5 years of experience with tubes that are used in the German NaKo Health Study for storage of >20 million samples [6]. It will be important for the biobank community to expand the specifications for lab ware, presented by Petersmann et al., by key performance indicators that give dedicated information about the conservation of sample integrity, even after long-term storage in different devices.

With regard to documentation and the provision of sample quality, it is essential to monitor every step of the lifecycle of some given biological samples. Automated workflows which allow continuous documentation of time stamps will help in this regard. However, this requires an appropriate information technology (IT) infrastructure that allows integration of all relevant data of the biobanking workflow, starting with the donors' consent for collection and use of biosamples and data, followed by the documentation of the collection process itself and the complete pre-analytical workflow, to the storage and delivery of samples for research projects and finally

re-transfer of results from these research projects to the biobank. Based on the workflow of the University Medical Center Göttingen (UMG) Biobank in Göttingen, Popp et al. describe a highly IT-integrated and automated solution, as an example for documentation of the lifecycle of individual samples in liquid biobanking [7]. The authors also give valuable recommendations for the implementation of an appropriate IT infrastructure. However, when reading this article, it becomes clear as well that IT integration is based upon, and benefits from, the advantages of a tight integration of workflows between routine clinical laboratories and biobanks (healthcare-integrated biobanking [HIB]).

Another example of the advantages of an integrated biobank solution is presented in an article by Winter et al., showing that the close association of biobanks with clinical laboratories facilitates not only tight control of pre-analytical conditions but also post-biobanking analysis of biosamples [8]. Using special adapters for barcoded cryotubes, biosamples from the biobank can be analyzed directly by a random-access clinical chemistry analyzer, without the need for additional sample sub-aliquotation that might impair sample quality. Moreover, linking the laboratory information and management systems (LIMS) to the biobank information and management system (BIMS) also allows immediate transfer of analytical results from the corresponding sample. Linking BIMS and LIMS, however, requires standardized and digital communication of parameters relevant for the description of e.g. the method and analytical performance of the assay used for analysis.

One internationally used standard code system for the communication of laboratory results is LOINC (Logical Observation Identifiers Names and Codes). LOINC is fit for data sharing through all common data exchange formats and protocols and will thus be of importance for the biobank community as well, particularly when it comes to the interoperability of biobanks. In his article, Semler gives a comprehensive overview of the history, basic principles, development and perspectives of LOINC, particularly with regard to medical research and biobanking [9]. Moreover, he also discusses the added value of LOINC in biobanking beyond already established standards such as MIABIS (Minimum Information About Biobank Data Sharing), for standardized annotation and the exchange of phenotypic data, e.g. laboratory results, together with corresponding biosamples. Together with the current standardization activities of the German Medical Informatics Initiative, it can be assumed that the use and importance of LOINC in biobanking will increase considerably in the near future.

Future aspects of biobanking, particularly of national and international biobank networks supporting personalized medicine, are discussed in the last contribution of this special issue by Hummel and Specht [10]. In recent years, it has become more and more apparent that subgrouping and diversification of diseases entities, a hallmark of personalized medicine, will lead to an increased demand for the collection and distribution of sufficient numbers of samples from small disease subgroups. From a biobanking point of view, interoperability of biobanks to allow the provision of samples of comparably high quality and of associated clinical data will thus be one of the key challenges for biobanks in the near future. This challenge can be met best by biobank networks committing to similar quality standards. The establishment of such a network in Germany is exemplified by Hummel et al. alluding to the German Biobank Alliance (GBA), implemented recently under the umbrella of the German Biobank Node (GBN).

In summary, the articles collated in this special issue highlight the importance of biobanking for medical research and the valuable contribution that laboratory medicine can make to current and future challenges in biobanking. At the same time, they also showcase the multi-faceted problems, ranging from standardized and quality-controlled sample handling via legal and ethical issues to the complex IT requirements. Fortunately, there appears to be a great deal of effort put into finding appropriate and viable solutions, a process to which the contributions also attest.

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