Biobanking

Edited by: M. Kiehntopf

Daniela Popp, Romanus Diekmann, Lutz Binder, Abdul R. Asif and Sara Y. Nussbeck*

Liquid materials for biomedical research: a highly IT-integrated and automated biobanking solution

<https://doi.org/10.1515/labmed-2017-0118>

Received October 1, 2017; accepted March 24, 2019; previously published online June 22, 2019

Abstract: Various information technology (IT) infrastructures for biobanking, networks of biobanks and biomaterial management are described in the literature. As pre-analytical variables play a major role in the downstream interpretation of clinical as well as research results, their documentation is essential. A description for mainly automated documentation of the complete life-cycle of each biospecimen is lacking so far. Here, the example taken is from the University Medical Center Göttingen (UMG), where the workflow of liquid biomaterials is standardized between the central laboratory and the central biobank. The workflow of liquid biomaterials from sample withdrawal to long-term storage in a biobank was analyzed. Essential data such as time and temperature for processing and freezing can be automatically collected. The proposed solution involves only one major interface between the main IT systems of the laboratory and the biobank. It is key to talk to all the involved stakeholders to ensure a functional and accepted solution. Although IT components differ widely between clinics, the proposed way of documenting the complete life-cycle of each biospecimen can be transferred to other university medical centers. The complete documentation of the life-cycle of each biospecimen ensures a good interpretability of downstream routine as well as research results.

Keywords: biobanking; interfaces; IT-integration.

*Correspondence: Sara Y. Nussbeck, UMG Biobank, University Medical Center Göttingen, Robert-Koch-Str. 40, 37075 Göttingen, Germany; and Department of Medical Informatics, University Medical Center Göttingen, Robert-Koch-Str. 40, 37075 Göttingen, Germany, E-Mail: sara.nussbeck@med.uni-goettingen.de

Daniela Popp: UMG Biobank, University Medical Center Göttingen, Göttingen, Germany

Romanus Diekmann: UMG Biobank, University Medical Center Göttingen, Göttingen, Germany; and Department of Medical Informatics, University Medical Center Göttingen, Göttingen, Germany

Lutz Binder and Abdul R. Asif: UMG Laboratory, University Medical Center Göttingen, Göttingen, Germany

Introduction

In our global digital world, where medical research tends to spread over borders, the requirement to interconnect biobanks is not new. Thus, concepts for interconnecting biobanks with already existing software components were published earlier [1–3]. The main challenges for such an endeavor are heterogeneous information technology (IT) systems, common language for documentation, keeping the sovereignty of the data of each single biobank [4] as well as privacy protection [5, 6]. Additionally, stakeholder requirements for connecting biobanks should be collected [7] before implementation. However, there are voices challenging the benefit of such interconnections of biobanks due to the low frequency of the citing of biobank networks in publications [8].

Zooming into individual university medical centers, biobanks have to be seen as part of the research data pipeline [9]. Here, biomaterials are seen as a separate finite type of data, and they only become valuable for research, if standardized associated data are available additionally. These biospecimen-associated data are distributed in different databases and have to be linked in a non-coding pseudonymized fashion for research [10] as described earlier [11, 12].

Speaking a common language between biobanks has been addressed in different publications. Just to mention a few: the Clinical Data Interchange Standards Consortium (CDISC) could be used for biobanking data [13]. Within the EU, the Minimum Information about Biobank Data Sharing (MIABIS) Core 2.0 is widely implemented as the biobank information standard [14]. With OBIB, even an ontology for biobanking [15] was described.

Looking into the practical aspects of biobanking and interfaces to biobanking/laboratory equipment, the integration of a blood fractionation system into laboratory information management systems (LIMS) for biobanking was described [16]. The inclusion of a liquid handling array robot was only based on an Excel spread sheet solution [17].

However, to the best of our knowledge, the complete documentation of the life-cycle of a biospecimen using

IT interfaces, minimizing the manual data entry as far as possible, has not yet been described. In this article, the complete documentation of the life-cycle of a biospecimen is illustrated taking the example of liquid biomaterials such as blood.

There is growing evidence that the pre-analytical phase of liquid samples for biomedical research as well as patient care accounts for up to 75% of errors [18, 19]. Pre-analytical errors influence downstream analyses. From a biobanking perspective, samples have to be fit-for-purpose. This means that the quality of a sample depends on the type of analyte to be investigated and the analysis to be conducted. For example, an RNA integrity number (RIN) of 8 is sufficient for RNA microarrays but might not be good enough for RNA sequencing. From our perspective, there are three ways to control and/or indicate the sample quality as follows: 1. standardization and harmonization of the pre-analytical phase; 2. complete documentation of the life-cycle of every single sample; and/or 3. spiking each sample with an internal quality indicator, such as a synthetic reporter peptide and measuring its decay [20], and thereby making the sample independent of the specific characteristics of a certain disease.

Towards the first aspect, a European initiative was established in 2012 for the standardization and harmonization of the routine pre-analytical phase in Europe [21, 22], the European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for the Preanalytical Phase (WG-PRE). This initiative focuses on patient safety. Addressing the second aspect coming from the research site, it was postulated to document pre-analytical variables [23]. From a biobanking perspective, the Standard PRE-analytical Code (SPREC) was developed and published to be used for documentation [24–27]. The third aspect is the most difficult one. To the best of our knowledge, the existence of a generic internal quality indicator has not yet been published, although urgently needed.

This paper focuses on the second aspect: the complete documentation of the life-cycle of every single sample for research, taking the example of liquid biomaterials, starting from the wards throughout the clinics, towards the central laboratory and from there into the biobank. It was published earlier that a LIMS should be used as an IT system for the documentation of pre-analytical variables [28]. This would require the full IT integration of the central LIMS of a hospital with the IT system of the hospital-integrated biobank.

The example taken here is from the University Medical Center Göttingen (UMG), Germany, with its central laboratory, the UMG Laboratory, and its centralized core facility, the UMG Biobank.

Methods

A literature search in PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>) was conducted to identify relevant references. The “advanced search” was chosen using the filter “title/abstract”. Keywords included were as follows: “biobank IT”, “biobank data management”, “clinical biobank data”, “IT components biobanking”, “IT integration biobank”, “biobank laboratory data”, “biobank interface” and “automated biobank”. The identified references were screened for relevance by reading their titles. If the title was promising, the abstract was read. If the abstract seemed to be relevant to this paper, the whole paper was retrieved, read and eventually cited. The literature search was conducted between June 25 and June 28, 2018.

The existing workflows for liquid samples and their associated data at the University Medical Center were analyzed. Taking the required documentation of the SPREC [24] into consideration, a target state workflow of liquid samples as well as accompanying data management within the UMG was described. From the perspectives of clinical chemistry, biobank quality management and medical informatics, the pre-analytical variables and other information relevant for later interpretation of analysis results were noted. Table 1 gives an overview of the involved IT systems.

Results

The target state workflow of liquid samples is illustrated in Figure 1. It starts with the consent of the patient, the ordering of the biomaterial for biobanking, the withdrawal of the samples in the wards, their transport to the central laboratory for processing, aliquotation and intermediate storage. From there, samples are transferred to the biobank for long-term storage and later on distribution for analyses.

Informed consent

From the legal and ethical point of view, the informed consent from a patient is the most important document for downstream research. In Germany, it is the physician’s duty to conduct the informed consent discussion and document it. However, the attending physician is often not identical with the person withdrawing the liquid samples. Thus, the information, whether the patient has consented to donate biomaterials and data for research, has to be communicated or has to be available to the person potentially

Table 1: Overview of the different involved IT systems.

IT system	Description	Local product
HIS	An IT system for the documentation of clinical information and analysis of the results of patients during medical treatment	Ixserv by ixmid, Cologne, Germany
LIMS	An IT system within central laboratories that collects all information from connected software and hardware systems (e.g. centrifuge) and therefore contains all relevant pre-analytical information of a biospecimen	OPUS::L by OSM, Vertrieb GmbH, Essen, Germany
BIMS	An IT system where all biomaterial information (e.g. quality and location) of a sample is documented. In this system, no clinical information or identifying data will be stored	Starlims by Abbott Informatics, Hollywood, FL, USA
Software of the LHR	This software controls and documents the liquid handling process. The collected data is sent to the LIMS	Inpeco, SA, Novazzano, Switzerland

BIMS, biomaterial information management system; HIS, hospital information system; LHR, liquid handling robot; LIMS, laboratory information management system; IT, information technology.

Figure 1: Target workflow of the data integration process for liquid samples.

Workflow of a liquid sample (blue, top line), the corresponding IT system collecting and storing data (green), and additionally generated data within this step (orange, bottom line).

withdrawing the samples. The consent should contain information on what the patient allows and forbids to do with his/her samples and data. After the implementation of the EU General Data Protection Regulation (GDPR) [29] on May 25, 2018 in the European Economic Area, it is important to be aware of the changes and to review (and possibly adapt) existing informed consents. The biobank needs detailed information about the consent status of each patient/sample to address them accordingly, when samples are being requested for research. The consent should be digitalized and detailed information about the status of consent should be saved in a searchable format. As the biobank works with patient pseudonyms only, a process for withdrawal needs to be in place. This comprises a procedure to get from the name of the donor and their contact details to the coded samples to address the withdrawal.

Order entry

The order entry system, as part of the hospital information system (HIS) of the UMG, is used to order sample analyses on the fully automated lab track in the central laboratory. After the samples arrive at the lab track, they are recognized and processed according to their barcode that is linked to the order.

The order entry system was upgraded by the vendor with a customized module to additionally allow the order of processing biobank samples. As a result, a nurse can select an appropriate biobank sample set for processing on the automated lab track similar to the order of analyses for routine samples. The content of a biobanking sample set is defined by the UMG collection strategy or study-specific requirements.

Challenges and pitfalls: The collection strategy can be adapted on an annual basis according to new research requirements. Therefore, the IT system where sample processing is ordered for the biobank (here: HIS) needs to be flexibly adaptable to define new collection goals. The IT system needs to be scalable for new material types and lab ware or even new hardware. If the existing software is not open source, additional implementations by the vendor could be necessary.

Biomaterial withdrawal

Biomaterial withdrawal from the donor has to follow standard operating procedures (SOPs) as withdrawing and processing samples has a huge impact on the sample quality. Depending on the type of analysis, a sample might be or might not be of sufficient quality. Thus, it is crucial to document all pre-analytic steps in detail [24]. To maintain a homogeneous quality of documentation and ensure data integrity, as much relevant data as possible should be collected automatically by IT systems. As an example, this includes the timestamp of biomaterial withdrawal, patient (ID), sample container and material type. The latter two have been already defined in the order entry step. Therefore, it has to be ensured to document the time of withdrawal and patient (ID) correctly with minimal effort. A mobile barcode scanner can be used to scan the barcode of the sample container and the patient ID of the wristband just before drawing a sample. This information is automatically stored in the HIS.

Sample transport to the central laboratory

Samples need to be transported immediately after collection from the ward to the centralized laboratory for processing. In this step, the most important data to document is the way of transport, the transport temperature and the duration of the transport. This information can be utilized to calculate the SPREC [24–27] automatically. In case of using timestamps and temperature loggers, it is necessary to think about the location of data storage. In the end, the data has to be available to the biobank staff and at best stored in the biomaterial information management system (BIMS) directly linked to the affected samples.

Sample processing

The UMG Central Laboratory has a fully automated lab track to process samples from clinical routine. All

necessary timestamps (e.g. transfer time and centrifugation time) are documented automatically in the firmware of the lab track and passed on to the LIMS. As the processing of samples in routine is well proved (the laboratory is accredited according to DIN ISO 15189 and 17025), it was planned to process all liquid biobanking samples the same way, if possible. Based on this idea, the main goal was to minimize the number of interfaces between IT systems and therefore collect all information within the context of the laboratory in the LIMS and transfer the aggregated data to the BIMS of the UMG Biobank. The workflow of processing biobanking samples is the following: the biobanking samples arrive at the laboratory and will be manually transferred to the input module of the lab track. The lab track system uses the tube barcodes to identify the samples as biobank samples and processes them (e.g. centrifugation) according to the order entered in this HIS earlier. All processing steps are documented (e.g. for centrifugation duration, temperature and speed) with their timestamps. At the end of processing on the lab track, samples are transferred to the connected liquid handling robot (LHR).

Sample aliquoting

To standardize sample processing, the splitting of samples into several aliquots is done by a fully automated and integrated LHR of the vendor Inpeco. Based on the biobank processing order in the HIS, the LHR can identify the barcode of the parent sample and starts to aliquot samples into standardized two-dimensional (2D)-coded sample containers according to a predefined scheme. The LHR can handle different kinds of biobank sample containers and fully processes (decapping of sample container, pipetting and recapping of sample containers) the aliquotation. All necessary data, such as timestamps of aliquotation, volume of each aliquot, genealogy of parent sample as well as the rack position and rack ID, will be collected by the LHR. All data are stored in the LIMS and are transferred to the BIMS where this sample information is stored.

Temporary storage

After finishing the aliquotation process, the SBS racks (standardized rack footprint independent of the vendor or sample amount and size; https://www.slas.org/SLAS/assets/File/ANSI_SLAS_1-2004_FootprintDimensions.pdf) with samples are taken out by a lab technician, the one-dimensional (1D) barcode of the rack is scanned and the rack is temporarily placed in a -150°C freezer.

Whilst scanning the barcode of the rack, the timestamp of the temporary storage and the information about the samples in the freezer are stored in the LIMS. As the LHR saves the position of the samples in the SBS rack, only the rack needs to be scanned and not all samples individually. Most importantly, the connection between the parent and the secondary samples and the information about the material within a sample container is already stored in the LIMS by the LHR.

Sample transport to the biobank

Samples are regularly transported from the temporary freezer to the long-term storage in the UMG Biobank. For these transports, a cryo cart (transport cart that is cooled by LN_2 and can hold up to 174 SBS racks) is used. When putting the racks with samples from the -150°C freezer into the cryo cart, the barcode of the SBS rack is scanned and stored in the BIMS. With this, the beginning of the transport is documented and the current sample location is updated.

The cryo cart is equipped with a mobile temperature logger to document the temperature throughout the transport. Deviations from the predefined temperature range will be documented manually. Currently, the only option to digitally document temperature deviations associated with the sample is inconvenient as it needs to be done individually for each sample. An automatic integration of the temperature chart of the temperature logger into the BIMS associated to each sample is intended.

Long-term storage in the UMG Biobank

After arriving in the UMG Biobank rooms, the SBS racks are either scanned on a rack scanner for storing in liquid nitrogen tanks or are directly transferred to the fully automated storage robot that scans the samples. In both cases, the information about the storage location is forwarded to the BIMS. In case of the liquid nitrogen tanks, the BIMS knows the exact location of the samples and the rack. In case of the storage robot, the BIMS knows that the required sample is within the storage robot. When ordering such a sample within the BIMS, the order is forwarded to the storage robot and the robot takes the sample out of the store.

Discussion

One way for the complete documentation of the life-cycle of liquid biospecimen was depicted here. This solution is based on integrating the IT of the central laboratory with

the one in the hospital-integrated biobank. Within this workflow, several IT systems collect and store data. The main goal was to accomplish a solution based on existing IT systems and to minimize the number of interfaces between the systems. The LIMS was chosen as the key component of the central laboratory as it holds data of different sources such as HIS, LHR and lab track. It collects all additional data for biobanking and sends them to the BIMS of the biobank. With this concept, only one major interface was needed. On the one hand, the costs are kept low and on the other hand, only one interface needs to be updated and maintained. While planning this interface and the type of data to be collected, standards such as SPREC, biospecimen reporting for improved study quality (BRISQ) and MIABIS [14, 24, 25, 27, 30] were analyzed and implemented. As a result, it is possible to calculate the SPREC automatically by the collected data instead of entering it manually, as suggested earlier [26]. This might help to overcome the issue of irreproducibility caused by the insufficient description of biological reagents [31]. This insufficient description accounts for about one-third of the 28.2 billion US dollars spent annually in the US on preclinical research resulting in irreproducible research data [31].

Although the solution described from the UMG focused on the workflow of liquid biomaterials, the recommendations can be transferred to solid biomaterial workflows as well. The key IT component would then be the pathology systems; however, data collection and minimizing the number of required interfaces are key for other scenarios as well.

The portability of this described solution technically depends on the IT components used in the central laboratory and the pathology department, and the centralized biobank of other university medical centers. There are also solutions for biospecimen and biobank data management tools which are cloud-based instead of using a LIMS [32] or which focus on a clinical data warehouse system [33].

Looking into multicenter studies, the LIMS might not be the IT system of choice for the documentation of pre-analytical variables at each participating site. However, these variables should be documented for every sample, no matter whether this takes place in an automated or manual fashion [26].

In Göttingen, the full integration of the documentation of data accompanying the life-cycle of liquid samples for biomedical research took about 3 years. Roughly €75,000 were spent on adaptations of existing software systems. This cost excludes any additional time spent by personnel for this endeavor. In addition to the technical implementation, the huge effort of different stakeholders is required, even if they do not profit from the alterations, or worse, more work will result from this, for example, the

technical assistants in the laboratory need to be aware of the finished jobs of the LHR in order to put the samples in the temporary freezer in time.

What make the endeavor even more difficult are the different “languages” spoken by the different stakeholders, for example, the term “Kit” is understood by laboratory staff as “reagent kit for analyses” (DNA kit) and in some BIMS as a set of primary (withdrawal) tubes. Additionally, this language problem was also identified within the different IT systems; for example, the material (e.g. blood) is managed in a different way in the LIMS (as a number) and the BIMS (as a structure with material type, code and name). Thus, time and resources should not be underestimated, but of course depend on the current state of IT systems available and the processes implemented in each medical center.

Moreover, a close interaction with the vendors and all different stakeholders is essential. They all have to discuss their requirements at a round table at the same time. This means staff from the central laboratory, biobank-IT, software vendors and IT-administrators of the involved routine IT-systems. The successful integration would not have been possible leaving one of these parties out.

In the following, general as well as process-specific recommendations are provided.

General recommendations:

- (a) Explicitly state all data that should be collected, no matter how basic it might seem.
- (b) If software products from the routine should be interfaced with software products for research, make sure to involve both operating sites.
- (c) Update plans and concepts to include further pre-analytical variables at a later point in time should be in place before implementation starts.
- (d) Wherever possible, use existing standardized processes as a starting point.
- (e) Most importantly, be aware of the sample quality and document the data in an automatic fashion as much as possible to avoid errors caused by manual data entry.
- (f) Train all stakeholders on the importance of biomaterial and data quality.
- (g) Especially if not all data are generated automatically, regular data reviews should take place to improve the quality of data. This includes checking for integrity, credibility and accuracy.

Process-specific recommendations:

Consent: Especially for using consents which include one or more options to choose from, a digital management of these information is recommended to be able to search for restrictions, when samples are requested for research.

An example for such an option to choose could be, whether samples and data can be transferred to foreign countries with lower levels of data protection. This will ensure to implement the will of the donor for the purpose of use. This is especially critical with regard to the GDPR [29]. The IT system to store the data is not important as long as the access is restricted and a secure processing can be granted. If the number of participants in the study is low, the runtime is short or the informed consent does not include options, a manual consent management might be the better alternative. However, having a central point of contact for patients where the withdrawal of consent can be addressed to is recommended, particularly if many different parties are involved.

Order entry: This recommendation can only be partially generalized, as it requires an order entry system for routine samples and a certain degree of automation, where routine samples are processed and analysed with regard to clinical chemistry properties. If an order entry system as well as an automated lab track are available, existing processes such as the order entry for routine samples should be adapted for biobanking purposes. This endeavor will allow, for example, automated documentation of time stamps using already existing infrastructures.

Biomaterial withdrawal: In general, to ensure data quality, it is of paramount importance to identify all required data items to be collected before starting the implementation process. Identify a way of how to document them in a standardized fashion allowing for searchability and if possible, an automatic way to minimize additional work load. Wherever possible, existing infrastructure should be used for this purpose for reasons such as maintenance costs and minimizing the number of existing IT systems.

Sample transport: Generally speaking, the transport of samples from withdrawal to processing should be speedy and temperature-controlled [24]. One way to increase the compliance with short transport times is to communicate the importance to all stakeholders involved in this process, for example, staff of the transport service. This transport information should be logged and attached as a sample quality indicator to every single sample [26]. Where available, the use of a pneumatic tube system to minimize turnaround times should be evaluated, as it can interfere with the sample quality [34].

Sample processing: These recommendations are only applicable to locations where samples are processed in an automated fashion. Automated processing can avoid human errors but might cause technology-induced errors and challenges on the other hand. For example, batch aliquotation of samples using an LHR saves personnel, yields homogeneous samples and automatically stores the linkage data between parent and child sample IDs. However, at the

UMG, the lab track system is very complex and interacts with at least four IT modules. Based on this, it is important to minimize the number of interfaces. In general, using the infrastructure of routine healthcare for research purposes, it is important not to impede the usual workflows but also to ensure that the biobank samples are processed in time. Specifically for highly automated processes, a risk management plan should be in place, for example, dealing with the down time of the lab track system in case of failure or unavailability of computer programs.

Sample transport: For the transport of frozen samples to the biobank for long-term storage, we recommended to log the temperature as well. Here, mobile temperature loggers could be of help, if the number of transports legitimate the acquisition costs and the effort to integrate these data into the BIMS for every single sample.

Conclusions

Although IT components differ widely between medical centers, the proposed way of documenting the complete life-cycle of each biospecimen can be transferred to other university medical centers. Taking all recommendations into consideration, it will be possible to develop and implement robust processes for the full documentation of the life-cycle of each biospecimen and with this contributing to the standardized sample and data quality. The latter ensures a good interpretability of downstream routine as well as research results.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: This work was supported by the German Ministry of Education and Research with the funding no. 01EY1704.

Employment or leadership: None declared.

Honorarium: None declared.

Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

References

1. Mate S, Kadioglu D, Majeed RW, Stöhr MR, Folz M, Vormstein P, et al. Proof-of-concept integration of heterogeneous biobank IT infrastructures into a hybrid biobanking network. *Stud Health Technol Inform* 2017;243:100–4.

2. Bouzille G, Jouhet V, Turlin B, Clement B, Desille M, Riou C, et al. Integrating biobank data into a clinical data research network: the IBCB project. *Stud Health Technol Inform* 2018;247:16–20.
3. Spjuth O, Krestyaninova M, Hastings J, Shen H-Y, Heikkinen J, Waldenberger M, et al. Harmonising and linking biomedical and clinical data across disparate data archives to enable integrative cross-biobank research. *Eur J Hum Genet* 2016;24:521–8.
4. Lablans M, Kadioglu D, Muscholl M, Ückert F. Exploiting distributed, heterogeneous and sensitive data stocks while maintaining the owner's data sovereignty. *Methods Inf Med* 2015;54:346–52.
5. Almqvist C, Adami HO, Franks PW, Groop L, Ingelsson E, Kere J, et al. LifeGene – a large prospective population-based study of global relevance. *Eur J Epidemiol* 2011;26:67–77. Available from: URL: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21104112.
6. Eder J, Gottweis H, Zatloukal K. IT solutions for privacy protection in biobanking. *Public Health Genomics* 2012;15:254–62.
7. Schüttler C, Buschhüter N, Döllinger C, Ebert L, Hummel M, Linde J, et al. Anforderungen an eine standortübergreifende Biobanken-IT-Infrastruktur: Erhebung des Stakeholderinputs zum Aufbau eines Biobanknetzwerks der German Biobank Alliance (GBA). [Requirements for a cross-location biobank IT infrastructure : Survey of stakeholder input on the establishment of a biobank network of the German Biobank Alliance (GBA)]. *Pathologie* 2018;39:289–96.
8. Larsson A. The need for research infrastructures: a narrative review of large-scale research infrastructures in biobanking. *Biopreserv Biobank* 2017;15:375–83.
9. Bauer CR, Umbach N, Baum B, Buckow K, Franke T, Grütz R, et al. Architecture of a biomedical informatics research data management pipeline. *Stud Health Technol Inform* 2016;228:262–6.
10. Leusmann P, Veeck J, Jäkel J, Dahl E, Knüchel-Clarke R, Spreckelsen C. Towards sustainable data management in professional biobanking. *Stud Health Technol Inform* 2015;212:94–102.
11. Demiroglu SY, Skrowny D, Quade M, Schwanke J, Budde M, Gullatz V, et al. Managing sensitive phenotypic data and biomaterial in large-scale collaborative psychiatric genetic research projects: practical considerations. *Mol Psychiatry* 2012;17:1180–5.
12. Prokosch H-U, Mate S, Christoph J, Beck A, Köpcke F, Stephan S, et al. Designing and implementing a biobanking IT framework for multiple research scenarios. *Stud Health Technol Inform* 2012;180:559–63.
13. Sato I, Kawasaki Y, Ide K, Sakakibara I, Konomura K, Yamada H, et al. Clinical data interchange standards consortium standardization of biobank data: a feasibility study. *Biopreserv Biobank* 2016;14:45–50.
14. Merino-Martinez R, Norlin L, van Enckevort D, Anton G, Schuffenhauer S, Silander K, et al. Toward global biobank integration by implementation of the minimum information about biobank data sharing (MIABIS 2.0 Core). *Biopreserv Biobank* 2016;14:298–306.
15. Brochhausen M, Zheng J, Birtwell D, Williams H, Masci AM, Ellis HJ, et al. OBIB-a novel ontology for biobanking. *J Biomed Semantics* 2016;7:23.
16. McQuillan AC, Sales SD. Designing an automated blood fractionation system. *Int J Epidemiol* 2008;37(Suppl 1):i51–5.
17. Malm J, Lindberg H, Erlinge D, Appelqvist R, Yakovleva M, Welinder C, et al. Semi-automated biobank sample processing with a 384 high density sample tube robot used in cancer and cardiovascular studies. *Clin Transl Med* 2015;4:67.

18. Lippi G, Becan-McBride K, Behúlová D, Bowen RA, Church S, Delanghe J, et al. Preanalytical quality improvement: in quality we trust. *Clin Chem Lab Med* 2013;51:229–41.
19. Green SF. The cost of poor blood specimen quality and errors in preanalytical processes. *Clin Biochem* 2013;46:1175–9.
20. Findeisen P, Thumfart JO, Costina V, Hofheinz R, Neumaier M. MS-based monitoring of proteolytic decay of synthetic reporter peptides for quality control of plasma and serum specimens. *Am J Clin Pathol* 2013;140:314–23.
21. Lippi G, Simundic A-M. The EFLM strategy for harmonization of the preanalytical phase. *Clin Chem Lab Med* 2017;56:1660–6.
22. Cornes MP, Church S, van Dongen-Lases E, Grankvist K, Guimarães JT, Ibarz M, et al. The Role of European Federation of Clinical Chemistry and Laboratory Medicine Working Group for Preanalytical Phase in standardization and harmonization of the preanalytical phase in Europe. *Ann Clin Biochem* 2016;53(Pt 5):539–47.
23. Ellervik C, Vaught J. Preanalytical variables affecting the integrity of human biospecimens in biobanking. *Clin Chem* 2015;61:914–34.
24. Betsou F, Lehmann S, Ashton G, Barnes M, Benson EE, Coppola D, et al. Standard preanalytical coding for biospecimens: defining the sample PREanalytical code. *Cancer Epidemiol Biomarkers Prev* 2010;19:1004–11.
25. Lehmann S, Guadagni F, Moore H, Ashton G, Barnes M, Benson E, et al. Standard preanalytical coding for biospecimens: review and implementation of the Sample PREanalytical Code (SPREC). *Biopreserv Biobank* 2012;10:366–74.
26. Nussbeck SY, Benson EE, Betsou F, Guadagni F, Lehmann S, Umbach N. Is there a protocol for using the SPREC? *Biopreserv Biobank* 2013;11:260–6.
27. Betsou F, Bilbao R, Case J, Chuaqui R, Clements JA, de Souza Y, et al. Standard PREanalytical Code version 3.0. *Biopreserv Biobank* 2018. doi: 10.1089/bio.2017.0109. [Epub ahead of print].
28. West J, Atherton J, Costelloe SJ, Pourmahram G, Stretton A, Cornes M, et al. Preanalytical errors in medical laboratories: a review of the available methodologies of data collection and analysis. *Ann Clin Biochem* 2017;54:14–9.
29. Pollirer H-J, Weiss EM, Knyrim R, Haidinger V, eds. DSGVO: Datenschutz-Grundverordnung. Wien: MANZ'sche Verlags- und Universitätsbuchhandlung, 2017. (Manz'sche Gesetzausgaben/SonderausgabeNr. 128). Available at: <https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1528874672298&uri=CELEX%3A32016R0679>. Accessed: 1 May 2019.
30. Moore HM, Kelly AB, Jewell SD, McShane LM, Clark DP, Greenspan R, et al. Biospecimen reporting for improved study quality (BRISQ). *Cancer Cytopathol* 2011;119:92–101.
31. Freedman LP, Cockburn IM, Simcoe TS. The economics of reproducibility in preclinical research. *PLoS Biol* 2015;13:e1002165.
32. Paul S, Gade A, Mallipeddi S. The state of cloud-based biospecimen and biobank data management tools. *Biopreserv Biobank* 2017;15:169–72.
33. Prokosch HU, Beck A, Ganslandt T, Hummel M, Kiehntopf M, Sax U, et al. IT infrastructure components for biobanking. *Appl Clin Inform* 2010;1:419–29.
34. Lee A-J, Suk Suh H, Jeon C-H, Kim S-G. Effects of one directional pneumatic tube system on routine hematology and chemistry parameters: a validation study at a tertiary care hospital. *Pract Lab Med* 2017;9:12–7.