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Midterm Report

German Biobank Node & German Biobank Alliance
05/2017-12/2018

Imprint

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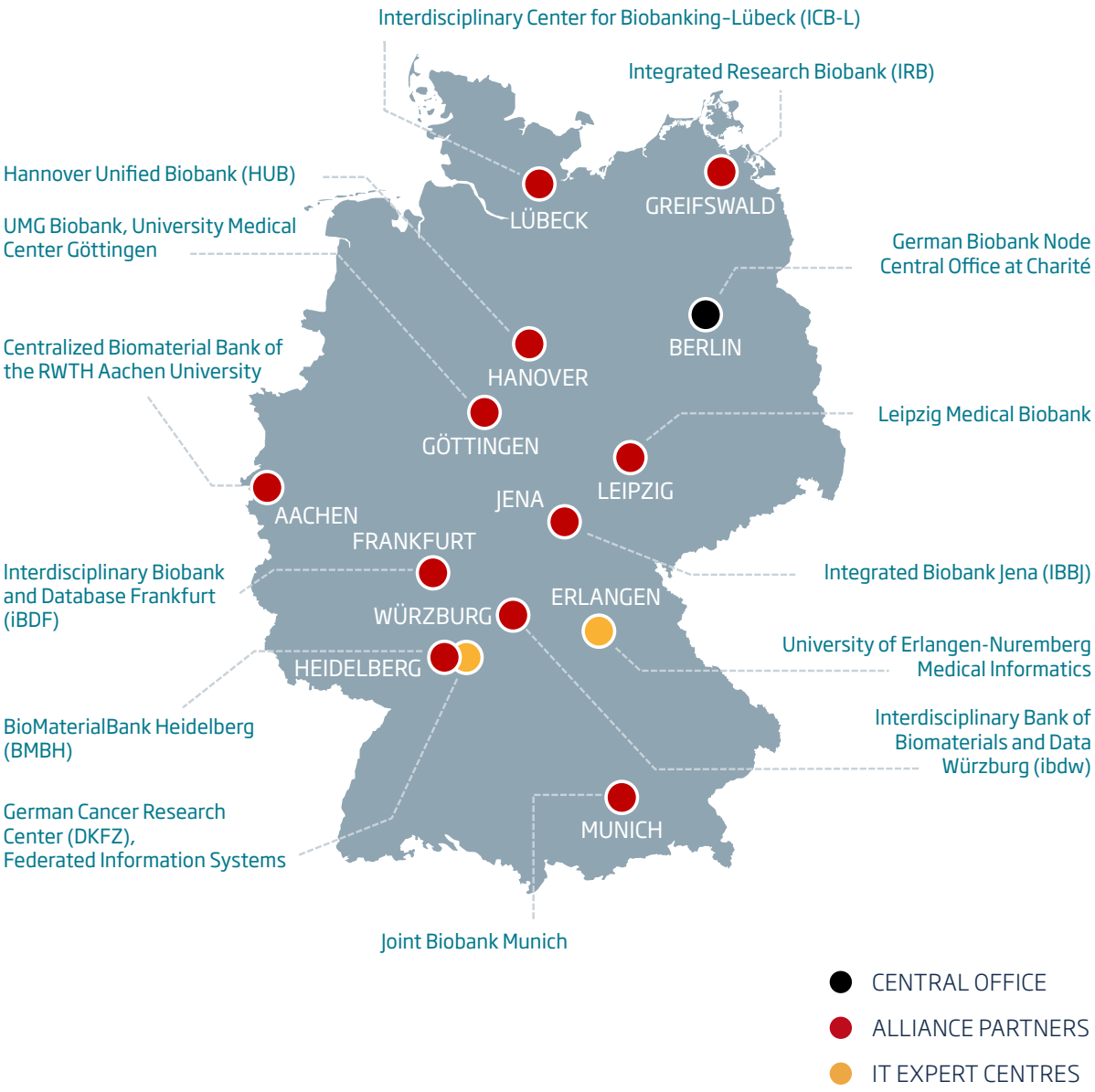

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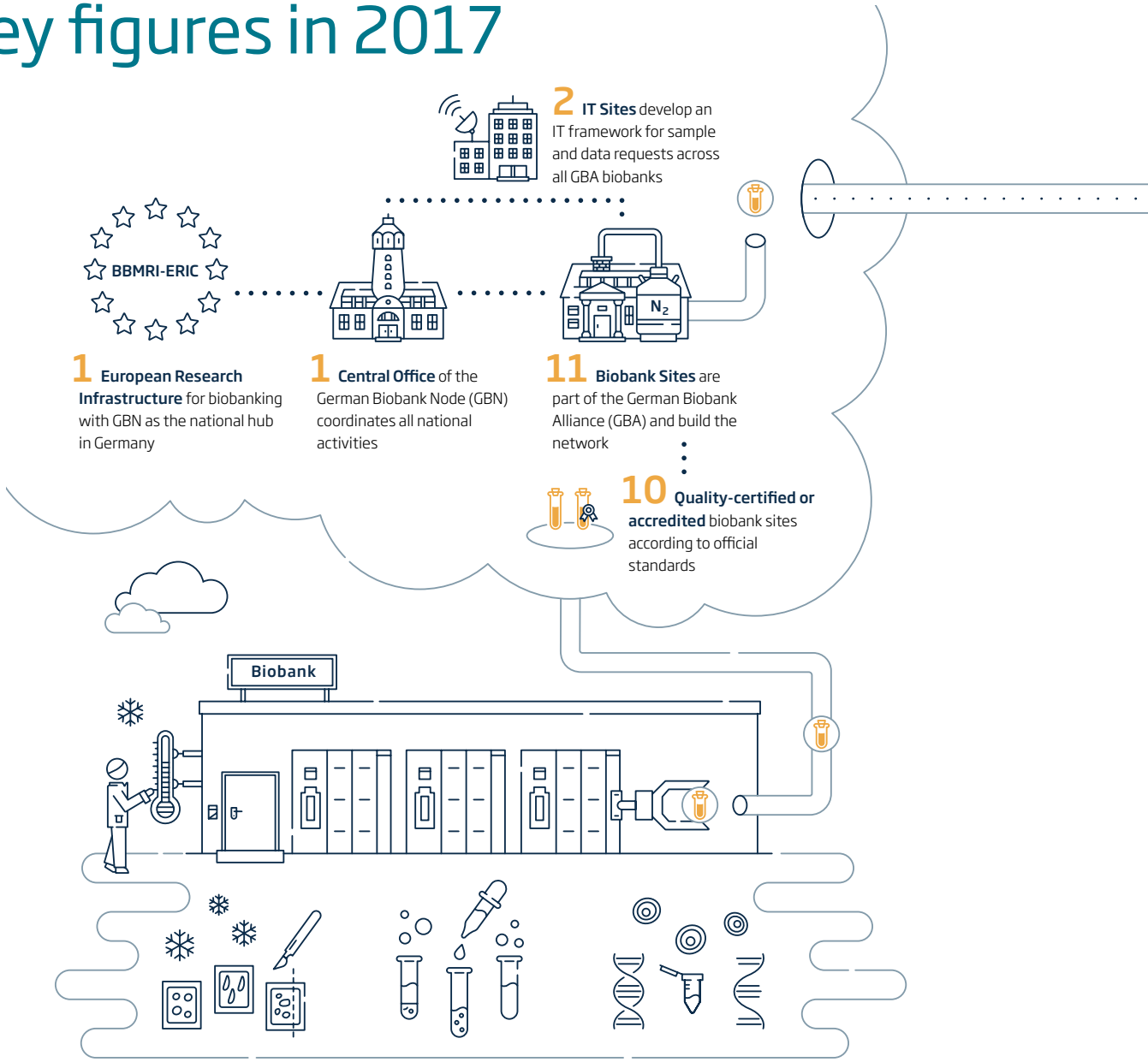
Key figures in 2017



2 **IT Sites** develop an IT framework for sample and data requests across all GBA biobanks

1 **European Research Infrastructure** for biobanking with GBN as the national hub in Germany

1 **Central Office** of the German Biobank Node (GBN) coordinates all national activities

11 **Biobank Sites** are part of the German Biobank Alliance (GBA) and build the network

10 **Quality-certified or accredited** biobank sites according to official standards

10,741,579

Tissue Samples are available on request from 11 biobank sites

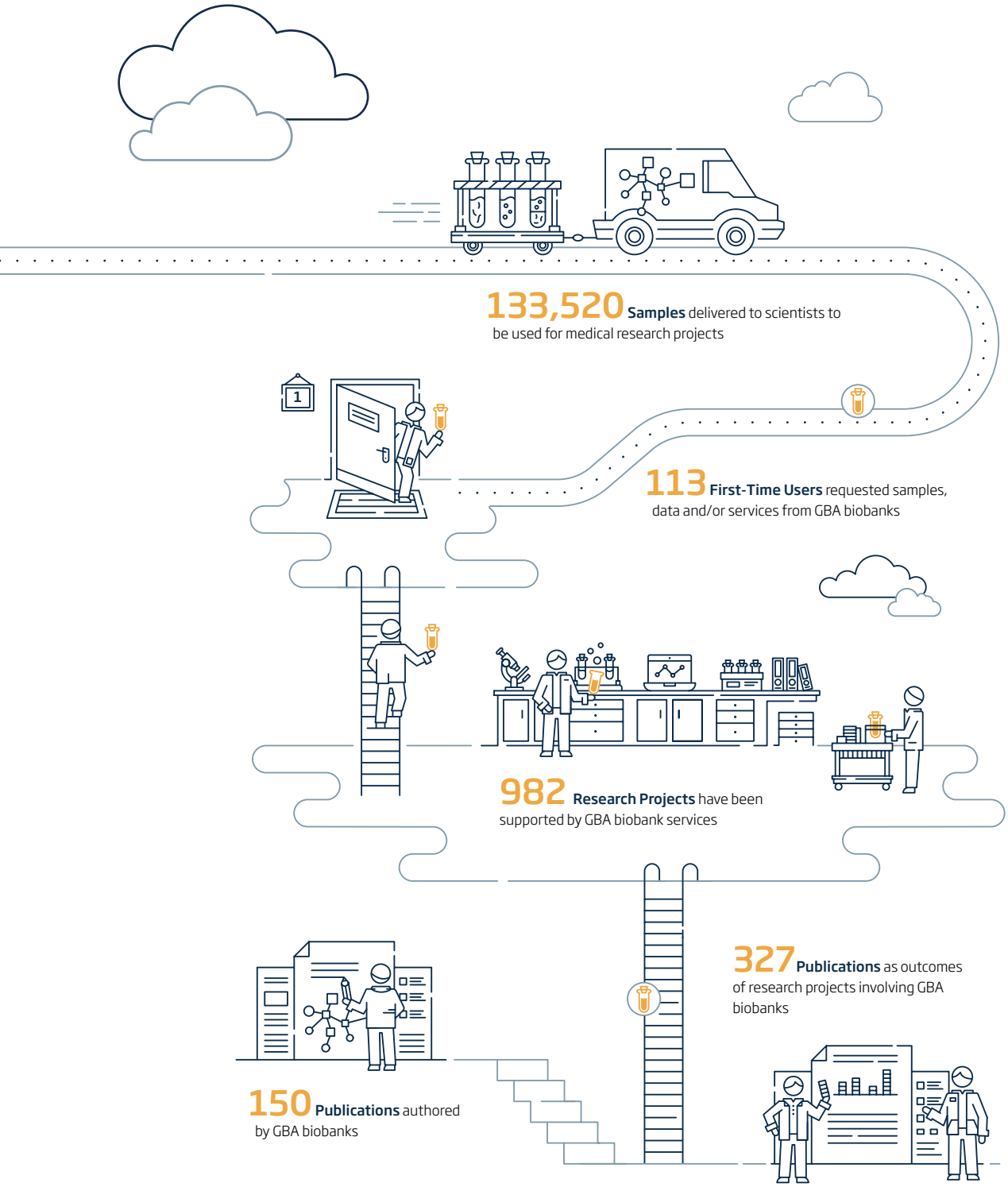
5,321,219

Liquid Samples are stored in GBA biobanks and obtainable

705,974

Derivates such as nucleic acids, cells and more are available on request

One of the most important activities has been to define key figures for the biobanks. These key figures have been collected from all GBA biobanks and will be updated annually.



133,520 **Samples** delivered to scientists to be used for medical research projects

113 **First-Time Users** requested samples, data and/or services from GBA biobanks

982 **Research Projects** have been supported by GBA biobank services

327 **Publications** as outcomes of research projects involving GBA biobanks

150 **Publications** authored by GBA biobanks

Current status of the project

This chapter describes the development of the German Biobank Node and German Biobank Alliance as well as the most important results of the individual work packages during the first half of the current funding period.

1 Development of GBN and GBA – cross-network and overarching activities

Contribution of GBN and GBA biobanks to the project

The German Biobank Alliance (GBA) represents the coherent realisation of a concept developed by the German Biobank Node (GBN) during its first funding period. To this end, eleven biobank sites and two IT development centres were selected by an international reviewer committee to form a first national biobank network. Coordinated and supported by GBN in Berlin, GBA started in May 2017 to translate the GBN concepts into tangible products. Through participation in different working groups of the six work packages (WPs), each of the GBA biobanks contributes to the success of the project. In particular, each biobank is actively involved in work packages 1 (key figures), 2 (IT) and 3 (quality management, QM), indicating that none of the different sites possess only one defined field of responsibility or activity. Primarily GBN – in its function as the organisational and coordinating platform of GBA – as well as the WP leaders provide a comprehensive overview of the progress of the project in this report. As the different biobank sites participate in several activities across locations, a joint report on the results for the different WPs was generated. Each respective WP leader contributed to the preparation of this report.

Involvement of the national biobank community

While drafting the different GBN products, the national biobanks are actively involved in the development process in order to create project results and products that are tailored to the needs of its users. The most important direct interaction platform between GBN and the national biobank community is the TMF's (umbrella organisation for networked medical research in Germany) biobanking working group (AG BMB; four meetings per year) as well as the annual National Biobank Symposium with more than 250 participants. Since the project started, GBN has presented and promoted the various developments, and considered the participants' feedback accordingly.

The resulting products are subsequently offered to national biobanks. On the GBN website (www.bbmri.de/service/produkte/), biobankers can browse the range of products already available including a user satisfaction survey, a data protection template, and a large image database (www.bbmri.de/service/bilddatenbank/) from which users can select pictures in 13 different categories for their own use. Upon request, GBN also provides and adapts the patient campaign to biobanks' specific needs.

Furthermore, the GBN QM manual has now been published open access and can be downloaded via the zenodo.org online publication platform. The QM manual itself consists of the generic biobank-specific standard operating procedures. GBN is implementing the QM manual in QM software which will be available to national biobanks in April 2019.

Cooperation with BBMRI-ERIC

This section outlines the common activities of GBN in BBMRI-ERIC. In general, the GBN headquarters and members of the GBA community already cooperate with BBMRI-ERIC and are willing to intensify this cooperation in the future (Figure 1).

WP1 – Central Office: The collaboration with the European partner BBMRI-ERIC is predominantly organised by the GBN office in Berlin. Michael Hummel and/or Cornelia Specht participated in all meetings of the BBMRI-ERIC Management Committee. In addition, together with Petr Holub (BBMRI-ERIC), Michael Hummel coordinates the BBMRI-ERIC Common Service IT and is PI for work package 3 of the European collaborative project ADOPT. There is also intensive interaction between Erik Steinfelder (Director General, BBMRI-ERIC) and Michael Hummel regarding strategic developments and decisions of the European and German biobanking activities. This alignment of ideas and concepts is of utmost importance to achieve the future goals.

WP2 – IT: The collaborative design and development of IT components is key for the success of GBN, GBA and BBMRI-ERIC. Thus, there is intensive cooperation between GBN, the GBA IT teams including members at each of the GBA biobanks to achieve a smooth and productive development, closely aligned with the European efforts. Especially for the development of the SearchBroker (Sample Locator) and Negotiator (Ebert et al., 2018) this is of utter importance. Within the close cooperation with BBMRI-ERIC, the current version of those software components has been shared with the IT teams of the Austrian and Finnish BBMRI nodes. Furthermore, GBN/GBA and BBMRI-ERIC collaborate closely on harmonised data sets for basic sample information and extended versions for various diseases. This also includes the latest version of the MIABIS description. For the colon cancer data set, which is part of the H2020 project ADOPT, GBN plays a decisive role in the definition of the respective data set and establishment of the required database. The total number of validated cases is currently around 5,000 data sets of which the German biobanks contributed ~ 2,500 cases. Therefore, the col-

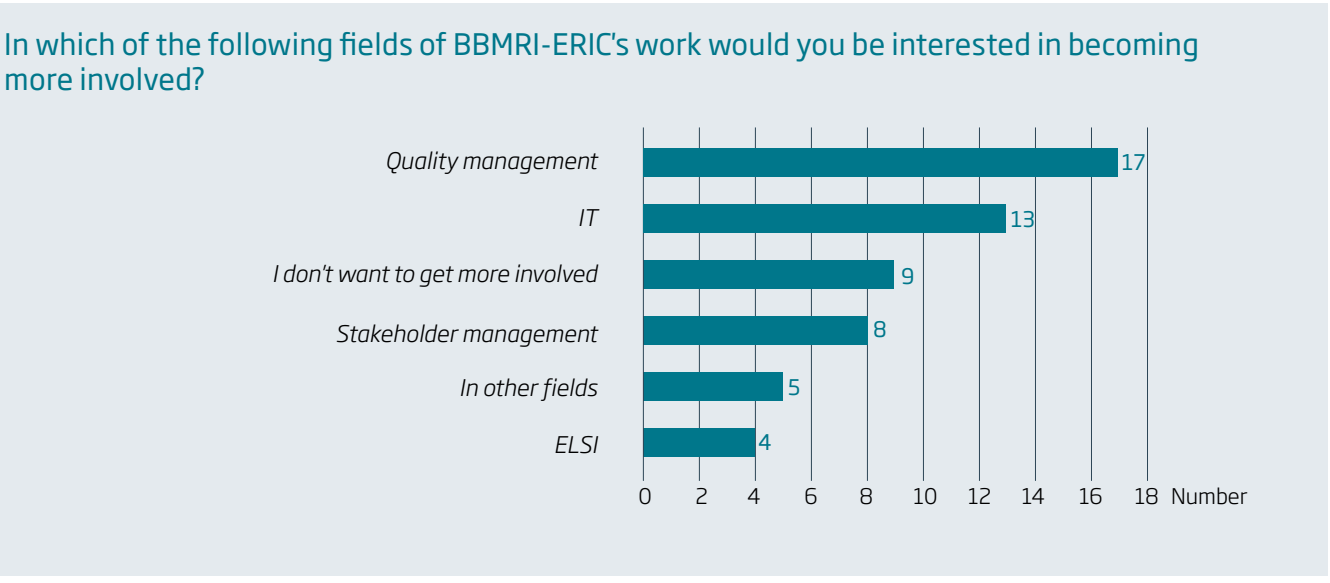


Figure 1: Attitudes to a collaboration with BBMR-ERIC. This figure illustrates the willingness of GBA collaborators to intensify their cooperation with BBMRI-ERIC with respect to specific work areas. (n=43, multiple choice)

lection of colon cancer data sets is ongoing with further contribution from German biobanks. Finally, yet importantly, in cooperation with BBMRI.nl GBN developed a German directory instance within the Dutch Molgenis database structure together with Dutch colleagues as part of WP2. This German instance is synchronised with the BBMRI-ERIC directory on a daily basis. We are currently working together to improve the directory data quality and usability.

One next big step in the activities is to go open source in order to enable national biobanks which are not funded by the Federal Ministry of Education and Research (BMBF) as well as other international biobanks to install bridgeheads (local data warehouse implementations) in their own institutions.

WP3 – QM: Since the start of this project, the QM core team has supported Andrea Wutte (BBMRI-ERIC) in the development of a European audit concept. In several web conferences, the cornerstones of the audit concept were discussed and defined. Our audit concept was developed in line with BBMRI-ERIC's concept ideas in order to maximise the efficiency of this cooperation. Furthermore, various informative topics regarding current quality-specific issues were discussed in web conferences together with all national nodes coordinated by Andrea Wutte. This is especially true of the working groups for RNA and DNA extraction from different types of biomaterials where German experts were intensively involved.

WP4 – Public Relations: GBN regularly contributes to the BBMRI-ERIC newsletters and blog, and provides articles of interest to the European biobank community. Additionally, GBN supports BBMRI-ERIC's Twitter activities e. g. shares BBMRI-ERIC's news.

WP5 – ELSI: Regarding ELSI topics, GBN/GBA actively participate in BBMRI-ERIC's working group Common Service ELSI. Irene Schlünder and Roland Jahns, who are both German representatives within the Common Service ELSI, together with Michael Hummel commented on the AG 29 draft guidelines concerning patient consent in the context of the new data protection regulations (GDPR) 2016/679. The resulting document was published by BBMRI-ERIC together with statements from other European biobank nodes.

WP6 – Education: Interaction with the European biobank community – focussing on students and biobank technicians – has been initiated in the education session of the Europe Biobank Week in Antwerp on 8 September 2018. Sara Nussbeck presented the current state of the project, raising awareness about the German developments within the international community. Due to her role as a member of ISBER's Education and Training Committee, Sara Nussbeck receives valuable input on where the international biobanking society's roadmap is heading and can give feedback to the German working group.

2 Most important results and other occurrences relevant to the project

WP1: Central Executive Management Office

The German Biobank Node (GBN) represents the central coordination and communication platform of the national biobank community and is the interface for BBMRI-ERIC.

Day-to-day management – operation of the Central Office: Since the start of the GBA project in May 2017, GBN has been responsible for coordinating GBA's work packages and tracking of the milestones. It took nine months for GBN to recruit all of the co-workers required for quality management, IT development, public relations and stakeholder management. Each of the coordinators continuously reports to Michael Hummel and ensures efficient project development across the eleven biobank sites.

GBN additionally established a communication platform (Confluence) right at the beginning of the project in which all activities, workshops, protocols, shared working spaces to prepare documents, etc. are filed. All working groups use this transparent information platform extensively.

The GBN office ...

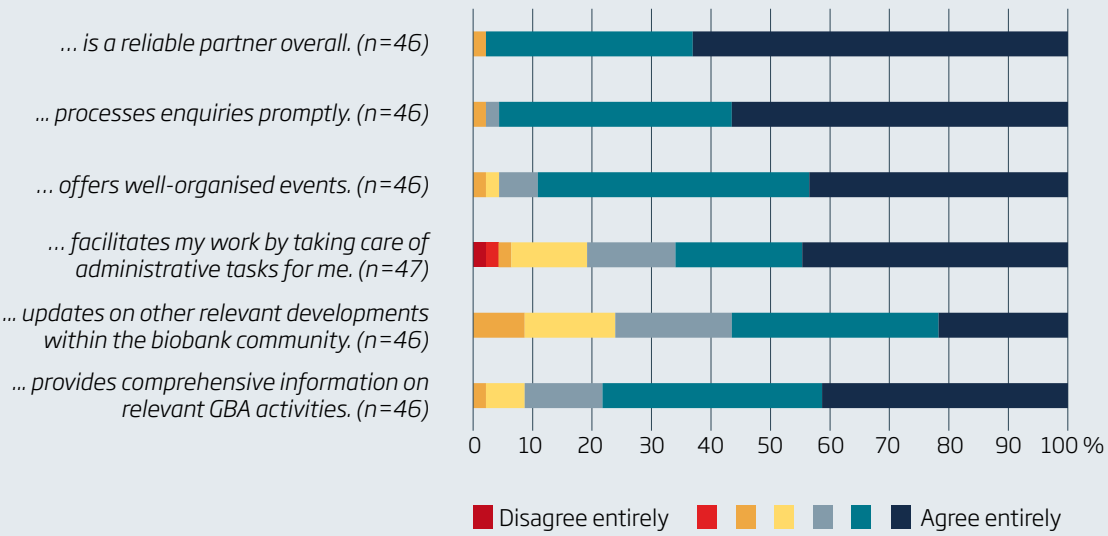


Figure 2: Results of the online survey among GBA collaborators: Feedback from GBA members regarding the work of the GBN central office.

Establishment of a governance structure and GBA consortium: At the start of the project, the main task of GBN was to establish a governance structure and allocate responsibilities within the alliance. Thomas Illig was elected as vice coordinator and Michael Hummel's deputy. The core decision-making body of this structure is the Steering Committee, which comprises one responsible representative (usually the head of the biobank) from each biobank site. During monthly face-to-face meetings or web conferences, the Steering Committee discusses the project progress as well as upcoming issues. The proper follow-up and implementation of decisions reached by the Steering Committee are monitored by GBN. Fifteen meetings of the committee were successfully conducted by 31 December 2018. One of the key milestones achieved five months after the project start was the signing of the consortium agreement by all project partners.

Stakeholder involvement: The stakeholder involvement has a very prominent role in the work programme of GBN/GBA. The different stakeholder activities are coordinated by GBN together with an interdisciplinary working group consisting of quality managers, biobank directors and managers, communication officers and project managers. During regular meetings and web conferences, the working group generates, revises and implements measures to enable the appropriate stakeholder involvement in our activities and respective work packages. The group is coordinated by the GBN office.

The most relevant stakeholder groups addressed by the different measures are biobank users such as academic and industrial researchers, potential users of samples and data (see: User involvement, chapter 4), GBA biobanks, technical personnel and other staff at biobanks, the general public, biomaterial donors and patients.

The success of the different measures is continuously evaluated based on specific stakeholder KPIs, which were defined at the beginning of the project. As a part of the stakeholder analysis and for the evaluation of GBN/GBA products and services, a series of online surveys has been developed and distributed within the community. The results are described respectively.

Stakeholder 'GBA biobanks': To evaluate the work of GBN as well as the services and products being developed, an online survey was distributed among all GBA collaborators in May 2018, one year after the start of the project.

The survey aimed to obtain information from the first line of GBN stakeholders – the GBA biobanks – in order to adapt and improve services and products in line with their users' needs. We received very positive feedback about the work of GBN's central office, the cooperation within GBA and the existing products (Figures 2 and 3).

The results from this survey are due to be published. Towards the end of the project, the questionnaire will be redistributed to all GBA partners as well as all national biobanks in order to evaluate the overall value of the different GBN products.

Stakeholder 'Technical personnel': The quality of biosamples depends on proper handling by the responsible technical personnel. Since national education and training programmes do not cater sufficiently to this group of employees, GBN is currently developing an educational programme for technical personnel at biobanks. To tailor the content to the needs of this group, a questionnaire addressing their educational requirements had been designed. The online questionnaire was

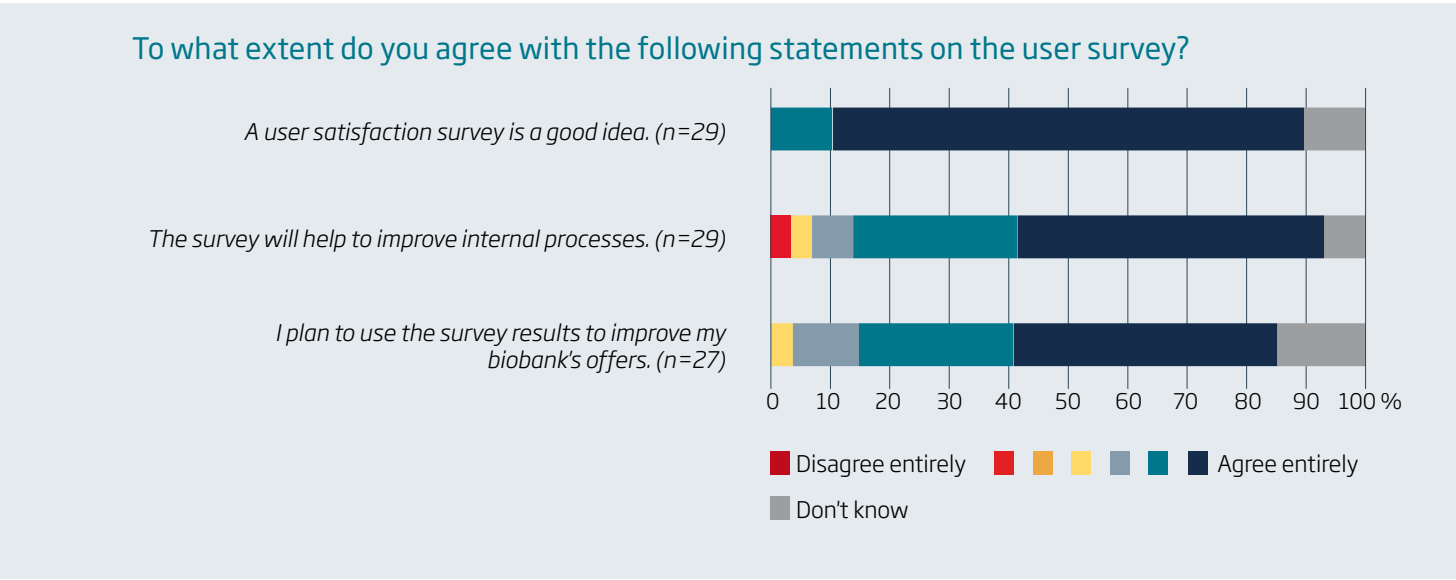


Figure 3: Evaluation of the user survey as a tool for GBA biobanks: GBA members positively agreed that the survey represents a helpful tool to improve internal processes as well as the products and services of their biobank.

sent to GBA biobanks and to other national biobanks participating in the biobanking working group of the TMF. In total, 79 persons completed the questionnaire, 43 of whom were technicians. The results were analysed by GBN and the WP6 team, and brought necessary information to generate learning objectives for the practical on-site training as well as for the development of the online education modules. In addition, further specifics of the educational requirements were discussed in a face-to-face meeting with 16 technicians.

Once a prototype of the education module is available (development is currently ongoing), it will be tested by voluntary technicians in order to obtain their direct feedback. Furthermore, an educational expert will revise all content generated for the online education modules.

A detailed description of the education programme is provided in WP6.

Stakeholder 'General public and biomaterial donors': Involvement of the general public and biomaterial donors is addressed by the Stakeholder Dialogue Forum. Here, critical issues in biobanking that concern biomaterial donors and patients are discussed with experts in the field. The topics and results of the first workshop entitled "My genes belong to me!" will be described in WP5.

The Stakeholder Dialogue Forum is complemented by an information campaign developed within WP4. The concept of this campaign is based on a survey among 200 patients conducted during GBN's first funding period. Core elements of the campaign include a website, four different poster motifs and an accompanying flyer. The posters and flyers have been tailored to the individual biobanks, which cooperated with the clinics in their university for display. The website is the overarching information platform that aims to explain the importance of biobanks for biomedical research to prospective biomaterial donors. Several biobanks contributed to the content with a success story from their site. More details about the information campaign can be found in WP4.

OUTLOOK FOR WP1

- Integration of further national biobanks into GBA
- ISBER symposium on biospecimen research (02/2019)
- Hosting of the National Biobank Symposium in 2019 in cooperation with TMF
- Second Stakeholder Dialogue Forum on patients' perspectives on using biosamples in collaborations with industry

WP2: The biobanking IT network for Germany and BBMRI-ERIC

Biobanking IT framework: At the beginning of the project, all relevant IT positions could be successively filled and a GBA-wide agile development process successfully established. A description of the IT development structure across the different biobanks sites can be found in the publication by Sahr et al. (2018).

In the initial project phase, collection of the stakeholder needs for the overarching IT framework and its components was a top priority. Thus, the first stakeholder workshop was organised with biobank managers and biobank IT staff on 28 September 2017. The results of this workshop were consolidated and discussed with members of the Steering Committee. This discussion led to a refined version of the biobanking IT framework as well as to a peer-reviewed journal publication in "Der Pathologe" (Schüttler et al., 2018). A second stakeholder workshop involving patient representatives was organised in October 2018. The framework concept was also published (Ebert et al., 2018). Latest steps have taken the central IT components towards open source development to enable further dissemination of the product.

At the end of September 2018 we gave the first live demonstrations of the federated search function via a preliminary graphical user interface (GUI) at the Scientific and Ethical Advisory Board meeting (28/09) in Berlin, at BBMRI-ERIC's Management Committee meeting (09/10) in London, and three in October at the GBA sites in Göttingen, Lübeck and Munich (HMGU) as well as at the consortium SMITH (02/11) of the German Medical Informatics Initiative (MII) – a large, BMBF-funded initiative for interoperability in the German health care system. Eight of the eleven GBA biobank sites are currently providing real data via their bridgeheads, connected to the pilot search function. Further bridgeheads are continuously being added.

German and EU data protection: A data protection concept has been created and received a positive vote from the TMF working group for data protection. This vote is accepted by all data protection officers of the German federal states and thus greatly facilitates the review by the data protection officers at the participating biobank sites. Currently, eight out of eleven biobank sites have received approval to fill their bridgeheads with clinical data.

Pseudonymisation and ID management for sample and data tracking: We conducted a status survey concerning local pseudonymisation and ID management tools across all sites that resulted in a change in the work plan (see chapter 3).

Semantics and metadata repository (MDR): The MDR is a central IT component within the GBA architecture and serves to support the data harmonisation process. Use of a common MDR is required to transform the heterogeneous vocabularies among the participating

sites into a globally usable terminology. A semantic concept has been developed for the data harmonisation that describes the modules and processes for extraction, transformation and loading (ETL). This will provide IT support for the semi-automatic loading and mapping of biobank data into the local data warehouse. Common data sets were created including existing terminologies, which were previously accepted by all GBA biobanks. The data sets were subsequently integrated into a central MDR that was set up for this purpose. Local MDR instances are consequently no longer necessary, since locally applied data items can be described with their metadata in respective namespaces of the central MDR.

Designing and implementing an enhanced graphical user interface (GUI) for such federated queries across the GBA biobanks as well as comprising further data sets on different pathologies (i. e. cardiology, oncology) are main focus areas of our work in the next term. This module will then be fully integrated into all local and network GBA IT components. Wherever possible, collaborations with other networks (i. e. BBMRI-ERIC, MII) are chosen in order to avoid parallel developments. Here, the cooperation with MII has been strengthened with a joint GBA/MII workshop in December 2018.

IT support for sample and data request management: The stakeholder and requirements analyses for sample and data requests as well as the definition of the sample and data requesting processes have been pursued (Schüttler et al., 2018; Neumann et al., 2017). The SearchBroker (cf. Sample Locator) has been set up. Additionally, the data integration servers – so called bridgeheads – (cf. Connector) have been set up at all biobanks and are currently being populated with data. Concerning the project proposal and follow-up management, we are discussing possible alignments with MII which is planning a similar central "data projects management and portal".

Donor empowerment and contact as well as consent management: As part of the above-mentioned stakeholder workshop, a requirements analysis was conducted on consent and contact management. In addition, aspects and requirements for the implementation of a donor portal were discussed. The results were assessed and summarised in "Der Pathologe" (Schüttler et al., 2018).

Furthermore, a low-fidelity mock-up for a patient/donor portal has been developed and was applied as a basis for semi-structured interviews with patient representatives in the second stakeholder workshop in October 2018. Thus, a user centred design process considering viewpoints and requirements of patients and patient representatives has been initiated. The results have been concluded and will be presented to the Steering Committee to decide on further action.

OUTLOOK FOR WP2

- Feedback regarding availability of research data for biobanks
- Full accomplishment of an IT network for comprehensive sample-level federated queries across all GBA biobanks
- Definition of the requirements for the donor portal as well as its design
- Strengthening of the source code by publishing as open source
- Concept for a solution to track projects connected with sample material

Software architecture

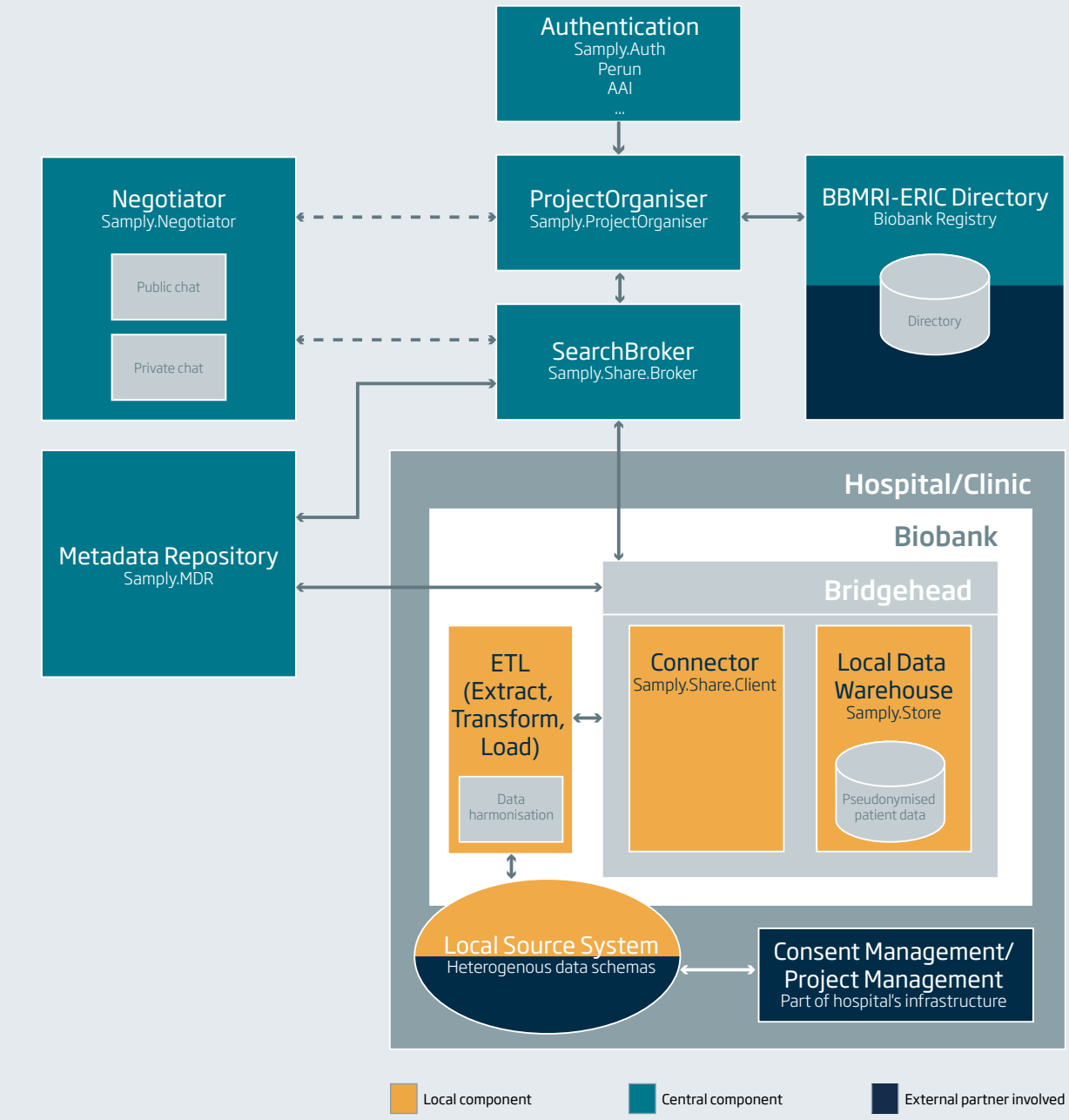


Figure 4: The local and central components of the software architecture of GBA.

WP3: The biobanking quality system

Involvement in international standardisation – DIN, ISO, CEN: GBN and members of GBA biobanks, particularly of the QM core team, are actively involved in working group 2 (WG2) of the ISO Technical Committee (TC) 276 Biotechnology. The expertise and experience bundled in GBN and its biobanks were contributed to drafting the main document, ISO/DIS 20387 Biotechnology – Biobanking – General requirements for biobanking, which was submitted for final consensus finding in February 2018 and for agreement by the ISO national mirror committees. The ISO 20387 has been available in English language from Beuth Verlag since August 2018. In addition, GBN is also involved in the preparation of the German language version of the ISO 20387 standard, the implementation guide for the ISO 20387 standard (ISO/AWI Technical Report (TR) 22758 Implementation Guide for ISO 20387) and the preliminary draft for the general requirements for the validation of sample processing methods in biobanks (ISO/CD 21899 Biotechnology – Biobanking – General requirements for the validation and verification of processing methods in biobanks). In this context, cooperation with other standardisation bodies (e. g. ISO/TC 212, technical committee for standardisation in laboratory medicine and in vitro diagnostic test systems, and SPIDIA4P, consortium for international standardisation of in vitro diagnostics) has been established to guarantee harmonisation across different standardisation initiatives. The German translation of 20387 was submitted to the national mirror committee for consideration in November 2018. The publication is expected at the end of 2018.

GBN and GBA representatives are already working together with the German Accreditation Body (DAkkS) to create the basis for an accreditation procedure in accordance with ISO 20387. The aim is to be able to start accreditation procedures directly after publication of the standard. In preparation, concrete accreditation criteria must be defined, and subject matter experts sought and named.

The content of the internal audit programme of GBN and GBA is based on the requirements of ISO 20387.

QM software system: In a multi-step process, various software products were tested, compared, and evaluated in cooperation with the respective biobank quality managers. The comparison was performed according to the following criteria: intuitive operation, possibility for presentation of processes and their visible and traceable changes, and the organisation and implementation of audits. Using these criteria, the ConSense software could ultimately be identified as the most suitable new quality management software for GBA biobanks. ConSense fulfils all our requirements and impresses with comprehensive functions as well as its price-performance ratio. The first basic training for the software was conducted in November 2018. The second training session for the audit and measures management will follow in January 2019.

An important step towards harmonisation of the quality management systems will be achieved through the centrally-organised generation of common processes and associated documents. The software is expected to help GBA biobanks to improve their local processes and additionally enables the organisation, realisation and follow-up of audits.

Quality of samples – biomarker selection/pilot ring trial: To achieve the first pillar of the quality concept designed by representatives from GBA and GBN, an extensive literature review was performed for the identification of analytical parameters in human serum and plasma, influenced by the most critical preanalytical process steps (e. g. time to centrifugation or freeze, freeze/thaw cycles or storage temperature) in biobanking. Around 550 differentially regulated analytes were screened and, based on defined selection criteria, a quality control biomarker panel of 27 metabolites was chosen. Due to the chemical variability of the metabolites in the selected quality control panel, we defined two subsets of compounds, which can be measured at moderate costs via GC-MS and LC-MS/MS. The LC-MS/MS will be implemented and the GC-MS method is currently being validated. Additionally, a small set of diagnostic quality control parameters were defined to evaluate sample transport, long-term storage, repeating freeze thaw cycles and haemolysis.

To validate and test the quality control biomarker panel developed, a pilot ring trial concept was designed, which includes the collection of liquid samples from healthy volunteers as well as from different patient groups under defined pre-analytical conditions across all GBA biobanks. The collection was approved by each of the local ethics committees of all participating GBA biobanks and around 95 percent of the samples have been collected. In addition, all samples collected and standardised will be analysed and evaluated as part of the pilot ring trial.

Tissue ring trial: Identifying critical parameters influencing sample quality during sampling, processing and storage has been the main focus of the first round of ring trials for GBA biobanks.

Fresh pig liver tissue was selected as the test material. The liver was dissected into equally sized pieces by a board-certified pathologist in Heidelberg and subsequently distributed at 4 °C to the participating GBA biobanks. Upon arrival, the liver pieces were processed

Tissue ring trial

		BB1	BB2	BB3	BB4	BB5	BB6	BB7	BB8	BB9	BB10
Section	Fissures	1	2	1	1	2	3	3	0	1	1
	Folds	1	3	2	1	3	3	3	1	1	1
	Notches	0	0	0	0	2	3	3	0	1	0
	Bucklings	1	1	0	1	3	3	2	1	1	1
	Different pieces	2	1	0	0	0	3	0	1	0	0
	Fragmentation	0	1	0	2	1	3	3	1	1	0
	Thickness	1	1	0	0	0	0	2	0	0	0
Staining	Staining residues	0	0	0	0	3	0	0	0	0	2
	Background staining	0	1	0	0	2	0	3	0	1	1
	„Over"staining	0	0	0	0	0	0	1	0	0	0
Slide	Media on slide	0	3	3	1	2	3	1	3	1	0
	Air bubbles	0	0	0	0	2	0	0	0	3	0
	Slides broken	0	3	3	0	0	0	0	0	0	0
Pos.	centred?	0	0	0	0	2	1	0	0	0	0
Score evaluation of slides		6	16	9	6	22	22	21	7	10	6
Score area calculation		3	23	21	3	4	2	20	14	20	4
Score total		**9**	**39**	**30**	**9**	**26**	**24**	**41**	**21**	**30**	**10**

3 = severe deviation 2 = moderate 1 = little 0 = none

Figure 5: HE stainings were analysed by a board-certified pathologist for different parameters such as the condition of slides and sections, staining performance, as well as areas with a score ranging from 0 (no deviation) to 3 (severe deviation). The total score characterises the quality of the HE stainings as well as the compliance with the centrally provided SOP.

according to the respective local standard operating procedures (SOPs). After different periods of storage at –80 °C (1 day and 4 weeks), the quality and quantity of the extracted nucleic acids (DNA and RNA) were determined. In parallel, tissue sections as well as extracted nucleic acids were sent to an independent reference laboratory (IBBL, Luxembourg) for the control of quality and quantity also including DNA and RNA extracted from the same material by the reference lab.

The results of this first ring trial were analysed and evaluated in feedback discussions together with each participating biobank to identify possibilities for improvement.

Liquids ring trial (DNA): A ring trial for DNA extracted from peripheral blood was designed to assess the quality of the DNA extraction procedures across GBA biobanks. To this end, whole blood samples provided by IBBL were sent simultaneously to all participating biobanks. DNA was extracted by each GBA biobank according to their local standard operating procedures and analysed for quality, integrity and DNA yield by IBBL. Using this approach, it could be demonstrated that the DNA quality, amount, integrity and stability were within the appropriate range among all participating biobanks. A more detailed analysis is currently being prepared. In addition, after performing the DNA ring trial, the different process steps were checked in a detailed analysis to identify corrective and preventive actions to further improve high-quality DNA extractions within the participating biobanks.

Audit system: Audits represent a key tool for the analysis and optimisation of internal biobank processes and the underlying management systems. All of the standards currently applied require audits to ensure compliance and ultimately improve the quality of biospecimens. Our audit programme plan is based on the audit-specific norm (DIN EN ISO 19011) and the applied standards (DIN EN ISO 17025, 17020, 15189 and ISO 9001:2015, ISO 20387). GBN intends to organise friendly audits within the network on a regular basis. For the realisation of the audits, selected GBA auditors received training in cooperation with the TÜV Süd academy in June 2018. The second part of the training in August 2018 has been biobank-specific. The auditors successfully completed the online exam for auditors. The first friendly audit took place in December 2018.

OUTLOOK FOR WP3

- Second round of ring trials for liquid and tissue samples
- Execution of a ring trial based on the collected samples employing the selected quality markers
- Evaluation of first round of audits in annual meeting of auditors in June 2019

WP4: Public accountability, public relations, public outreach

Corporate communication: The launch of the new GBN/bbmri.de website in October 2017 represented one of the key milestones of WP4. This website serves as the main information tool for the biobank community. Here, GBN shares newly developed products, offers a large image database, publishes dates for relevant conferences and workshops, and reports on progress within the project and BBMRI-ERIC. In summer 2018, the English version of the website went online. In addition, the GBN newsletter regularly informs the biobank community of relevant topics, including interviews with experts in the field. The rapid distribution of news is achieved via GBN's Twitter account, available since November 2017. A LinkedIn account was set up in December 2018 to enhance GBN's visibility in social media. Press releases con-

tributed to GBN's corporate communication, resulting in a front page report in European Hospital (3/2018) for instance, covering the ELSI workshop on incidental findings ("My genes belong to me", May 2018).

To ensure the proper presentation of GBN at meetings, a booth system has been designed. GBN's presence at the 2017 and 2018 National Biobank Symposia, the annual meeting of the German Society of Pathology in May 2018 and the Europe Biobank Week in September 2018 raised awareness for GBN's activities and allowed a more personal exchange with the various stakeholder groups. Accompanying information materials have been produced in German and English.

Communication with donors of samples and data: Biobanks rely on constant support from patients and healthy individuals, who voluntarily donate biological materials. In order to raise awareness, GBN has developed a donor communication campaign consisting of posters, brochures and its own website specifically targeting interested biomaterial donors (www.biobanken-verstehen.de). Key elements of the website include success stories of research projects that have led to important findings in medical research. The posters and flyers were distributed to the GBA biobanks and their hosting university hospitals. So far, nine biobank locations are already using the campaign and have distributed approx. 150 posters and 8,000 flyers; four more sites are preparing the campaign. One of the positive side effects of this campaign is that the biobanks are now able to use their own success stories for marketing purposes. In addition, promotion of the patient campaign has led to intensified communication between clinical partners and the respective biobanks.

Public events such as the "Long Night of the Sciences" have been actively attended in Berlin (2017) and Leipzig (2018) to inform the general public about the importance of biobanking. All of the different materials designed for these events, including the flyers, posters, etc. are available to every GBA biobank in order to support participation at similar local events. In that manner, the BioMaterialBank Heidelberg used the experiences from the "Long Night of the Sciences" as a best practice example for their presentation and interactive programme at the Heidelberg "Researcher's Night" in September 2018.

Figure 6: Two poster motifs from the donor communication campaign.

OUTLOOK FOR WP4

- Generation of an explanatory video for biomaterial donors
- Development of an information campaign aimed at researchers (based on the results of the potential user survey, see chapter 4)
- Maintenance and improvement of all GBN communication strategies and products

WP5: Ethical, Legal and Social Issues (ELSI)

The main objective of work package 5 is to identify and discuss critical societal, legal and ethical issues that arise in the context of biobanking. Within the Stakeholder Dialogue Forum, these issues are discussed directly with those affected, such as biomaterial donors as well as experts from the relevant fields. This year's forum topic "My genes belong to me!" looked at the question of how to deal with incidental findings in the context of biobanking and research projects. On 3 May 2018, lawyers, biobank staff, biomaterial donors and researchers discussed how and if the results of research projects can and should be reported to the relevant biomaterial donors. The event received extremely positive evaluations from the participants (Figure 8). Those who evaluated the event stated unanimously that they would participate in a second Stakeholder Dialogue Forum.

Cooperation with the biobank task force of the Permanent Working Party of Research Ethics Committees in Germany: To this day, many paediatric departments, networks, and registries collect biomaterials of diseased children/adolescents primarily on the basis of narrow consent for specific disease entities. However, the need for novel targeted therapies for paediatric patients requires the collection of biosamples and related data from children and adolescents under the conditions of "broad consent". Representatives from GBN and GBA, paediatric clinicians and the biobank task force of the

Figure 7: The Stakeholder Dialogue Forum "My genes belong to me!" in May 2018.

Evaluation of the Stakeholder Dialogue Forum

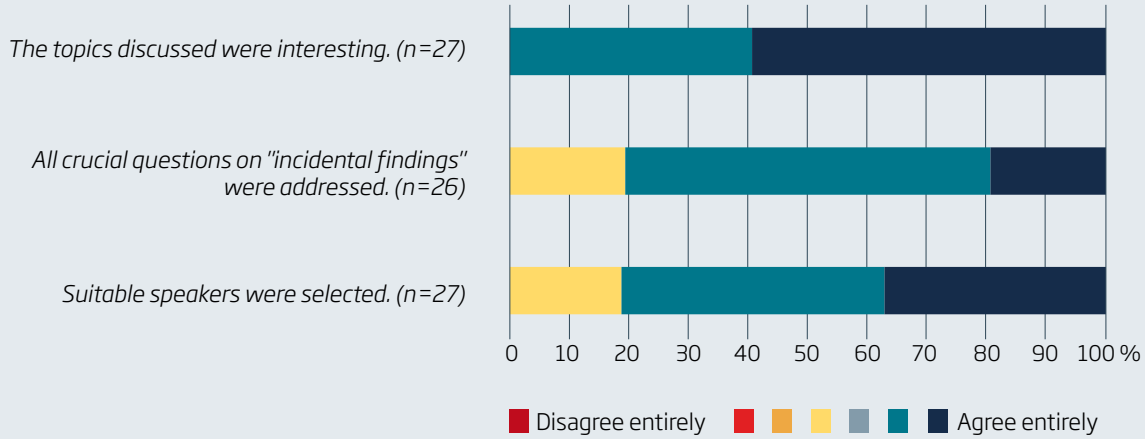


Figure 8: Stakeholder Dialogue Forum "My genes belong to me!" – results of the evaluation of the event.

"Permanent Working Party of Research Ethics Committees in Germany" have therefore developed a framework for an age-adapted master template "for the broad use of biological materials and related data donated by diseased children/adolescents treated or monitored in a hospital".

Here, the complex ethical situation of minors donating biomaterials was considered by a comprehensive bundle of precautions/limitations concerning procedural methods and rules. As only people who have reached the age of majority can give legally-valid consent, the parents or legal guardians sign the broad consent form after being informed by the treating paediatric physician. In addition, the child's right to change his/her decision at any time without any reprisal must be secured and, as a rule, children should be contacted again to obtain consent when they reach the age of majority.

Members of the Permanent Working Party of Research Ethics Committees in Germany agreed furthermore to form an "ELSI help desk" and routinely answer ethical and legal questions posed by GBA biobanks.

OUTLOOK FOR WP5

- Publication of a position paper from the first Stakeholder Dialogue Forum
- Organisation of a second Stakeholder Dialogue Forum together with biobank staff, patient representatives, lawyers and researchers

WP6: Counselling biobanks, and education and training

Online education modules: Based on the requirements compiled in the questionnaire (Figure 10) and the first on-site meeting, a GBN-/GBA-internal WP6 working group consisting of experts for pathology, clinical chemistry, data management, and two representatives from GBN, deduced more than 53 learning objectives and discussed these intensively. These learning objectives were compared with the existing modules 7 and 8 of the Bioresource Center (BRC) education platform of the Office of Biobank Education and Research (OBER) at the University of British Columbia, Vancouver, Canada (biobanking.org/webs/education). While analysing the modules, the extent to which the existing content was sufficient to cover the newly-generated learning objectives was listed. Gaps identified and necessary additions were systematically documented.

Preliminary calculations revealed that the existing modules of OBER only cover approximately 30 percent of the learning objectives deduced by the WP6 working group. Thus, far more educational content needs to be prepared than was initially assumed. Due to limited resources (personnel, financing, time) and the small overlap, the WP6 working group will focus on the 15 GBA learning objectives selected that refer to the topics of the on-site training and the ring trials. The Scientific and Ethical Advisory Board approved this decision.

In addition, the WP6 team decided to implement the online modules in ILIAS (www.ilias.de, in English: docu.ilias.de/goto_docu_cat_580.html), which several universities in Germany use. ILIAS is a very flexible learning platform allowing the import of all relevant formats that will be engaged. Furthermore, there is technical support for ILIAS at one of the GBA sites (University of Göttingen).

On the national level, preliminary contact was made to the German umbrella association for technicians (DVTA – Dachverband für Technologen/-innen und Analytiker/-innen in der Medizin Deutschland e.V.), which is interested in learning more about the online learning modules being developed in WP6.

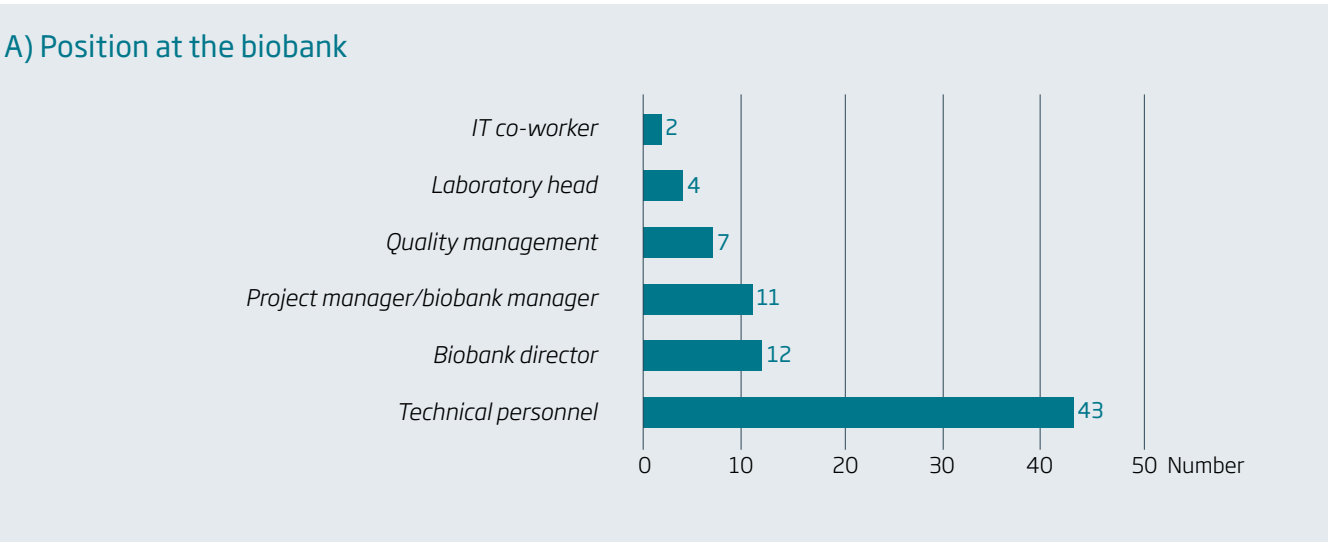


Figure 9: Results of the education survey among biobank employees: (A) Participants in the survey grouped according to their position at the biobank. (n=79)

Training: The starting point for the education measures for the technical personnel at biobanks has been the first on-site training conducted in Göttingen in January 2018. A total of 16 technicians from nine different GBA biobank sites attended the meeting. Here, they considered the advantages and disadvantages of different storage equipment and discussed biobanking-related issues in their daily work. The topic of the second training in June 2018 originated from the results of the ring trial on tissue samples. The aim of the training was to improve the quality of frozen tissue sections among all GBA biobanks. In the practical part of the training, 14 technicians from nine GBA biobanks were trained in correct use of the rotation and slide microtomes, tissue microarrays as well as staining of the tissue slides generated. All technicians then received individual feedback on their slide

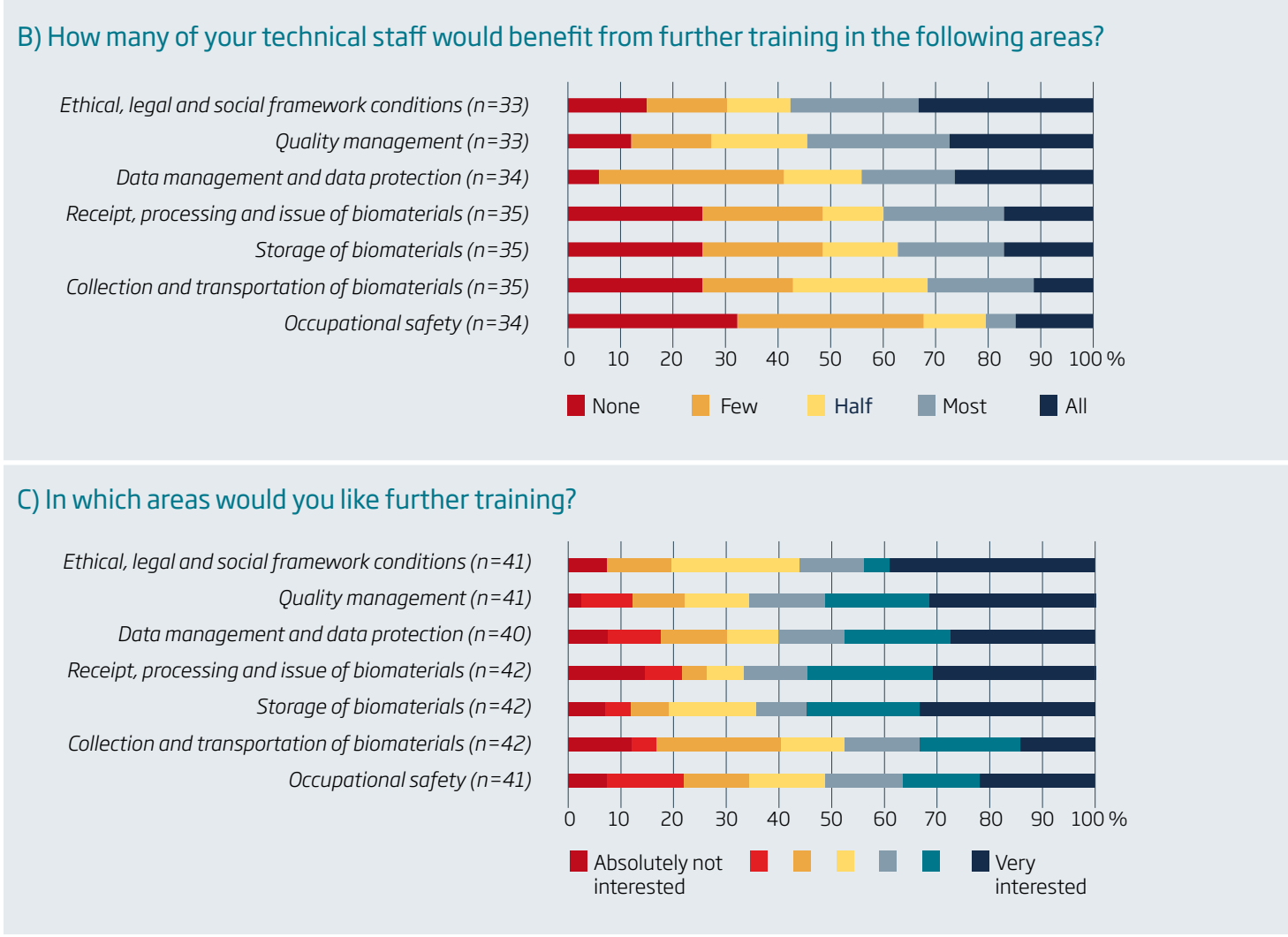


Figure 10: Results of the education survey among biobank employees: (B) Illustration of the educational needs of the technical staff on biobank-specific topics from the co-workers' perspective.
(C) Interest among technical staff regarding further training on biobank-specific topics.

Evaluation of the on-site training

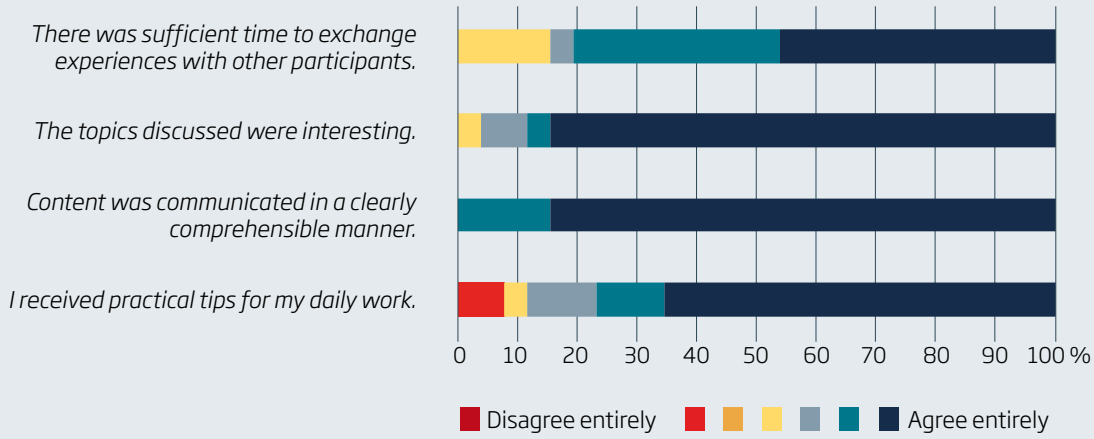


Figure 11: Evaluation of on-site training: summary of the feedback from 26 technicians regarding the first kick-off meeting and the practical training on tissue sections. (n=26)

quality, including advice for improvement. According to the evaluation, both events were very positively received by the participants (Figure 11). The third on-site training is planned for two days in January 2019 to accommodate 16 technicians. It will take place in Hanover and focus theoretically and practically on DNA isolation and measurement of its quality and quantity using different methods. Both dates were completely booked out in October 2018.

OUTLOOK FOR WP6

- Generation of educational content tailored to the needs of technical personnel
- Launch of the GBN online education platform in German
- Implementation of further on-site training for technical personnel
- Publication analysing the educational requirements of technical personnel in biobanks

3 Comparison of planned and actual project progress

Due to the lack of personnel resources, several activities of the project started with some delay. After the successful staffing of positions, temporary project delays could gradually be resolved. However, also taking into account the experiences during the proceeding project, certain revisions of the original milestone plan became necessary.

Milestones that are delayed (as of 31 December 2018) and those that have been changed are listed below:

WP1: The milestone 1.5.1.6 '2nd survey with defined stakeholder group' which was due at the end of 2018, is slightly delayed. This second survey aiming to address the stakeholder group of potential users of GBA biobanks had to undergo peer assessment at the local universities. Different regulations at GBA sites resulted in launch of the survey at different times. Some biobanks started the survey in December 2018 but the launch of the questionnaire will be completed in January 2019 at all GBA sites. The 'Report to Scientific Advisory Board and biobanks' (milestone 1.5.1.7) is planned to be accomplished accordingly in 2019. This delay will not affect the successful continuation of the project.

The concept of a stakeholder forum (work package 1.5.2) for all GBN/GBA stakeholders was revised at the beginning of the project. Instead of organising one common forum for all stakeholders, GBN decided to develop measures for each individual stakeholder group, thus ensuring more specific stakeholder involvement in the project. The concept is described in detail in the chapter "Chances for Success".

WP2: The IT work package is up-to-date with most of the milestones set in the beginning. Some milestones could not be reached for the following reasons:

The gap analysis (2.1.6) revealed that local conditions at the biobanks differed greatly and required adjustments depending on respective determining factors. It will remain a continuous task throughout the whole project duration as a result. Furthermore, we have extended the second deliverable of 2.1.6 ('Gaps closed') to April 2020.

For work package 2.1.7 'Define open-source licensing and resolve potential legal issues' in WP 2.1, a community manifest has been drafted which will be finalised by the end of 2018 with a delay of four months.

Milestone 2.1.8 'Interface definition (API) and evaluation of international standards' (due in August 2018) is currently delayed since the advances in the definition of HL7 FHIR resources and discussions with the BBMRI-ERIC Common Service IT led to a new evaluation of FHIR as a potentially better store. This milestone is expected to be achieved in January 2019.

For 2.1.11 'German Biobank Registry' we decided to go only for the BBMRI-ERIC directory to ensure Europe-wide visibility of the German biobanks and against a separate national registry. We have set up the German Biobank Directory based on the Molgenis solution which is synchronised daily with BBMRI-ERIC's directory. Because of technical delays in the collaboration with Molgenis, we could only start promoting the directory in summer 2018. To date, 24 German biobanks have registered their collections in the directory including all GBA biobanks.

The German and EU data protection concept (2.2.1) for the project was finalised on time, however the milestone 'Adaption of local data protection concepts' (2.2.2) was due in the end of August 2018. So far, the local data concepts have been approved at seven of the eleven sites. Four biobanks are still waiting for approval from their local data protection officers. Since the biobanks depend on the decision of their local data protection officers, we cannot foresee the scope of the delay.

The milestones 2.3.2–2.3.4 have been successfully implemented, for 2.3.5 'Integrate (further) existing terminologies' we are currently engaged in discussions with national and international groups to update the mapping to international accepted terminologies. Therefore, we decided to postpone this milestone to April 2020.

Work package 2.3.6 'local MDR instances' was cancelled since the central MDR now supports biobank specific metadata definition based on dedicated namespaces, thus making local MDR instances unnecessary.

The 'Tool for distributed sample search and project mediation' (2.4.3) has been developed and implemented at all GBA biobanks. Some sites still need to upload data since local data protection authorities caused delays. A first prototype of the Negotiator (for project mediation) is part of this tool and has already been developed. The Negotiator will be added to the SearchBroker to enable private or public chat functions for mediation of the researcher with the chosen biobanks. The first milestone of the work package 2.4.6 'Tool for evaluation/question researchers for satisfaction' is therefore delayed. As soon as all modules are integrated, we will present the tool for distributed sample search with a tangible prototype to researchers and undergo a thorough evaluation process by this user group.

Concerning the project proposal and follow-up management (2.4.4) due in October 2018, we are currently discussing possible alignments with the German Medical Informatics Initiative (MII). Therefore, the finalisation of this concept will be delayed.

Milestone 2.5.2 'Advanced ID management for cross-biobank sample and data linkage' was not required and thus cancelled, as each GBA biobank already possesses a working ID management system compliant with the requirements defined in the GBA data protection concept. Since milestone 2.5.3 'Linkage capability for sample-related research data' was essentially connected to 2.5.2, this was put on hold too. Here, a new strategy will be developed while conceptualising the donor portal (WP2.6).

WP3: The milestone 3.1.4 'Maintenance of generic QM manual' was postponed until the end of the project to ensure continuous updates of the QM manual which was published open access on zenodo.org in October 2018.

The project plan for WP3 concerning the work packages 3.2 'Quality of samples' and 3.3 'Sample quality concept' has been revised during the development of the concepts for the ring trials. As the ring trials for liquid and tissue samples involve completely different tasks and periods, these ring trials were separated in the project plan into two subcategories (3.3.1 and 3.3.2). Additionally, the pilot ring trial planned for testing the biomarker selection study was integrated directly into the respective task 3.2 'Quality of samples'. The milestone 3.4.1.5 'Friendly audits of biobanks – Intervention – Evaluation of measures – Further audits' is currently delayed by six months; the first friendly audits started in December 2018. The long development phase of the ISO 20387 norm was a reason for this delay, as well as the lack of personnel at the beginning of the GBN/GBA project, affecting the development of the audit programme plan (milestone 3.4.1.1) and placing the auditor training (milestone 3.4.1.4) towards the end of August 2018. This delay has no negative effect on the progress and success of the project.

WP4: All milestones within WP4 could be achieved to schedule. There are no deviations from the milestone plan.

WP5: All milestones within WP5 could be achieved to schedule. With respect to the original concept and time planning, milestone 5.5 has been postponed to the end of the project.

WP6: When outlining the project plan, a German adaption of 80 to 90 percent of the content available on the OBER platform was originally expected. However, as the content of the OBER platform differs tremendously from the identified educational needs of the technical personnel in Germany, far more content has to be generated than initially anticipated. Therefore, we decided to invest more time than initially planned in the development of an education platform that will be truly tailored to its users' needs. The key task WP6 2.5 'Content adaption, generation and implementation' scheduled for April 2018 will be achieved in the third quarter of 2019 and all milestones depending on completion of this task will be postponed accordingly for the same period of time. The delay also impairs the task 6.2.1 'Setting up the contract with the Canadian Office of Biobank Education and Research (OBER, Vancouver)' since the degree of using content from OBER will have an impact on the contract. Contract negotiations began in autumn 2018 and we expect to finalise them in January 2019.

With regard to the practical training, WP6 is ahead of schedule since the number of practical on-site training sessions was increased from one to two in 2018. The overwhelmingly positive response among the participating technicians as well as their superiors was the reason for this change in the milestone plan.

4 User involvement

Users of biobank samples and data represent a crucial stakeholder group whose perspectives and needs the GBN/GBA project has to meet. As such, user involvement is considered in various stakeholder activities by GBN/GBA. The services for GBA biobanks have already been evaluated by academic users, an evaluation of the IT developments by the same stakeholder group will follow soon. At present, an analysis of the perceptions and needs of different stakeholder groups for future cooperation is underway.

In this chapter, we describe the results of our activities to identify the users' needs regarding (already active) academic users, potential users and industry.

Academic users

To support the biobanks in implementing the needs of their users, GBN designed an online questionnaire to ask biobank users about their experiences, satisfaction with the offered services and their general feedback at regular intervals. This online survey was developed by a working group in cooperation with a professional specialist for survey design. The aim was to create a general template that can be adapted by each individual biobank, but with a core set of common questions for comparison.

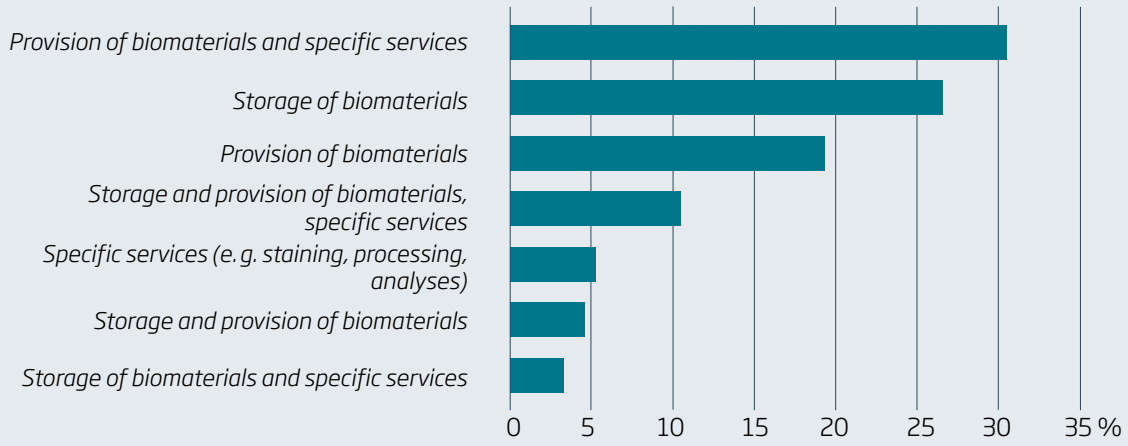
Within the survey, biobank users were asked about their professional background, how they got in contact with the biobank, and the impact of the biobank services on their project. Furthermore, they were asked to share recommendations for improvement and to indicate their level of satisfaction with the biobank services as well as to list outcomes such as publications. The questionnaire was conducted in autumn 2017 as a web-based application and customised for the respective GBA biobanks (also available in English). The user survey was sent to more than 530 users of all eleven GBA biobank sites with a return rate of 36 percent in 2017. GBN evaluated the biobank users' satisfaction in aggregated results. Especially interesting findings from the user survey were that (1) the majority of users not only requested samples but also a variety of specific services like the staining of tissue sections and the extraction of nucleic acids, and (2) the majority of users first learned of the biobank and its services through colleagues. The feedback from GBA biobanks about the user survey has been extremely positive as structured user feedback helps them to further improve their services.

During the initial developments within IT, important stakeholder groups representing the users of the IT products including academic researchers and patients were identified and characterised by usability methods. The results of a workshop with biobank managers and IT experts in September 2017, as well as the feedback from the Steering Committee, allowed to determine practical aspects and the technical requirements of each GBA biobank. These findings built the foundation of the IT frameworks' design and were necessary to determine how each of the biobanks could implement the tool for distributed sample search (see chapter 2).

Through the ongoing cooperation with BBMRI.uk, where researchers' recommendations have already been thoroughly considered, we have gained valid information on the user's requirements of a web-based biosample search tool. GBA's distributed search pilot will be evaluated by biobank users in a first round when the tangible prototype is finished (see chapter 3).

For this purpose, the researchers participating in the user satisfaction survey at each GBA site will be asked for their recommendations to further improve the search tool.

A) Which biobank services did the user use during his/her project?



B) How did the user first hear about the biobank?

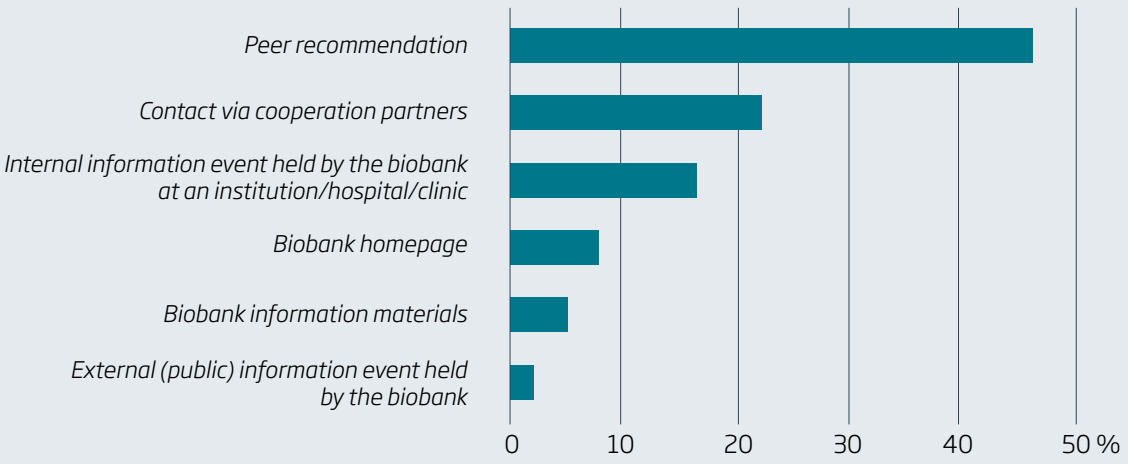


Figure 12: Results of the survey among biobank users: (A) Presentation of the biobank services used. (B) How users first heard about the biobank. (n=200)

OUTLOOK

- Until the end of the funding period, GBA biobanks will regularly query the user satisfaction and GBN will evaluate the aggregated results
- First evaluation of the distributed sample search tool by researchers

Potential academic users

The group of potential users of biobank services and data has proven to be the most difficult to reach. However, it is essential for biobanks to understand why researchers might decide against a collaboration in order to tailor their services to the researchers' needs.

Therefore, an anonymous online survey has been developed to profile the group of potential users of biobank services, to learn about their approach to acquisition, storage and use of biomaterials and to identify concrete reasons why researchers might hesitate to contact their local university biobanks. The questionnaire has been developed by the stakeholder working group in cooperation with a professional specialist for survey design. After pretesting, a tailored version of the questionnaire was created for each GBA site to be distributed by the biobanks among researchers active at medical faculties. Due to the different local regulations, the biobanks had to launch the survey independently, the first biobank launching it in mid-December 2018.

The survey offers the opportunity not only to gain valid information about the needs and preferences of scientists who have not been in contact with the respective biobank yet, but also to advertise the local biobank and to inform about available biobank services.

OUTLOOK

- The survey for potential biobank users will be conducted at all eleven GBA biobank sites
- Survey results will be used to develop strategies to motivate potential users to cooperate with the biobanks for the acquisition, storage and use of biomaterials
- The results will also provide an information basis for the planned campaign targeting researchers and other potential users of biobanks

Industrial users

The pharmaceutical and diagnostics industry forms another group of users and potential users of biobank services. Currently, only a small fraction of GBA biobanks cooperates with the pharmaceutical and diagnostics industry for the acquisition, storage and use of biomaterials. In order to better understand the apparent reluctance to collaborate, as well as the attitudes and needs of biobanks in this context, GBN conducted six informal interviews with the directors and managers of GBA biobanks. These discussions revealed substantial uncertainty regarding the ethical acceptance of cooperation with the industry. One conclusion was that there is a lack of guidelines on how such cooperations should be structured and organised. Therefore, GBN aims to develop harmonised procedures for cooperation with industry.

In a preliminary workshop with representatives from various pharmaceutical companies working together within the Association of Research-Based Pharmaceutical Companies (Verband forschender Arzneimittelhersteller, VfA), GBN discussed needs and requirements for possible collaborations with academic biobanks.

Based on the information gained from the informal interviews and the workshop with industry representatives, GBN has launched a series of GBA-internal workshops to discuss ethical issues related to the cooperation with industry from a biobank perspective. The goal of these workshops is to develop and publish recommendations with regard to industry cooperations for (GBA) biobanks. It became clear during the first workshop held in June 2018 that some unresolved issues need to be tackled in a next step. Workshops with the aim to resolve the critical points and the formulation of a common position on this topic are planned for the coming year.

In order to better understand the attitudes and requirements of pharmaceutical and diagnostic companies, GBN is currently preparing a series of interviews with representatives from various industries. The preparatory work for this interview study has been initiated (recruitment of participants, design of the study, etc.). The first interviews are scheduled for July 2019.

OUTLOOK

- Additional workshops with GBA biobanks are planned with the aim of defining recommendations for cooperation with industrial partners
- Interviews will be conducted with representatives from the pharmaceutical and diagnostic industry and results fed back to the GBA community

5 Publications

GBN/GBA publications in 2018

Ebert L, Habermann J, Duhm-Harbeck P, Ingenerf J, Ulrich H, Kroll B, Kern J, Tas D, Stampe F, Maqsood S, Ückert F, Ataian M, Proynova R, Holub P, Schüttler C, Prokosch HU, Knell C, Sahr S, Illig T, Breu M, Jahns R, Linde J, Nussbeck SY, Engels C, Hummel M, Lablans M. **Harmonizing European and German Biobank Request Workflows: BBMRI-ERIC and GBA – a Synergy!** Europe Biobank Week 2018. Antwerp.

Hartfeldt C, Klingler C, Schmitt S, Specht C, Hummel M. **Die Bedeutung von Stakeholder Engagement: Befragungen der Nutzer und Nicht-Nutzer von Biobanken.** 7. Nationales Biobanken-Symposium 2018. Berlin.

Hartfeldt C, Schmitt S, Meinung B, Hummel M, Schirmacher P, Kiehntopf M. **German Biobank Alliance – Ring Trial Concept as part of the Quality Management System for Biobanks.** Biospecimen Research Symposium 2018. Luxembourg.

Hartfeldt C, Schmitt S, Rufenach C, Porst R, Hummel M. **German Biobank Alliance: Implementation of a User Satisfaction Questionnaire and its Evaluation.** Europe Biobank Week 2018. Antwerp.

Hartfeldt C, Kiehntopf M, Heiling S, Meinung B, Schuster C, Geithner K, Weis N, Schirmacher P, Specht C, Hummel M, Schmitt S. **GBN/GBA-Aktivitäten im Qualitätsmanagement: QM-Software, Auditsystem, Ringversuche.** 7. Nationales Biobanken-Symposium 2018. Berlin.

Hartfeldt C, Schuster C, Meinung B, Schmitt S, Weis N, Rufenach C, Hummel M, Schirmacher P, Kiehntopf M. **German Biobank Alliance: An Audit Concept for Continuous Improvement of Biobanks.** Europe Biobank Week 2018. Antwerp.

Hartung ML, Herpel E, Baber R, Rufenach C, Nussbeck SY. **German Biobank Alliance: Implementation of an educational program for technical personnel in biobanks.** 7. Nationales Biobanken-Symposium 2018. Berlin.

Hartung ML, Herpel E, Baber R, Rufenach C, O'Donoghue S, Watson PH, Nussbeck SY. **German Biobank Alliance: Implementation of an educational program for technical personnel in biobanks.** Europe Biobank Week 2018. Antwerp.

Heiling S, Geithner K, Ritzmann H, Meinung B, Winter T, Dorow J, Baber R, Geiger J, Jahns R, Anton G, Illig T, Habermann J, Rose M, Schirmacher P, Brandts C, Nussbeck SY, Gieger C, Hummel M, Kiehntopf M. **German Biobank Alliance – Ring trial concept "Liquid" as part of the Quality Management system for Biobanks.** Europe Biobank Week 2018. Antwerp.

Huth V, Lesch W, Jahns R, Rufenach C, Schütt A, Hummel M. **Information campaign to empower donors and promote biobanks in the public.** Europe Biobank Week 2018. Antwerp.

Kern J, Tas D, Ulrich H, Schmidt EE, Ingenerf J, Ückert F, Lablans M. **A Method to use Metadata in legacy Web Applications: The Samply.MDR.Injector.** GMDS Jahrestagung 2018.

Kern J, Breu M, Dolch C, Ebert L, Engels C, Johansen M, Kiel A, Knell C, Kroll B, Linde J, Prokosch HU, Schüttler C, Stampe F, Tas D, Ulrich H, Hummel M, Lablans M. **Die föderierte Suche des German Biobank Node.** 7. Nationales Biobanken-Symposium 2018. Berlin.

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Chances for success

The achievements of GBN and GBA – the overwhelming majority of milestones and deliverables could be achieved on schedule – lay a very solid basis for successful work in the remaining funding period and beyond.

To establish a consortium consisting of heterogeneous partners with a very ambitious work programme is a major endeavour and challenge. However, due to the high degree of motivation and excellent work of the GBN team at the headquarters along with the GBA partners, the overwhelming majority of milestones and deliverables could be achieved on schedule. Any changes from the original work plan are described and explained in detail in chapter 3.

These achievements lay a very solid basis for successful work in the remaining funding period and beyond. The GBN headquarters now has a well-recognised infrastructure and has evolved as a central coordination and contact platform far beyond GBA. Among others, it includes close cooperation with the German Medical Informatics Initiative (MII), the German Centres for Health Research (DZG) and the German National Cohort (NAKO). This cooperation leads to more harmonised and synchronised developments across the various consortia, which in turn enables considerably faster and more cost-efficient infrastructures. Examples here are (1) the integration of DZG into the audit programme thus harmonising QM activities, (2) opening the IT infrastructure by integrating other infrastructures such as DZG, (3) the involvement of biobank stakeholders and public engagement by sharing our patient information campaign, and (4) collaboration with MII on concepts for patient empowerment strategies – all examples are overarching topics, not limited to a certain initiative and GBN/GBA has taken a leading role in many aspects. New opportunities arise from these developments which are discussed in the chapter "Outlook".

The original concept for the stakeholder management was based on a common stakeholder forum consisting of representatives from various GBN/GBA stakeholder groups discussing the developments and products within the project. This concept was revised at the very beginning of the project. Instead of one common forum for all stakeholders, GBN decided to analyse the individual stakeholder groups separately. Different methodological approaches were chosen depending on the topic we wanted to analyse. The method of online surveys was selected to specifically ask certain stakeholders for their opinion, for example users of the biobanks (user satisfaction), technical personnel in biobanks for educational needs, and staff of the GBA biobanks evaluated the GBN products; the survey for potential academic users of samples is forthcoming. For users from industry we chose individual interviews, for the patient empowerment concept we conducted a focus group with patient representatives, and for researchers we will evaluate the IT tool using usability methods such as "Think Aloud Testing" or "Walk Through Studies" combined with semi-structured interviews. The existing Stakeholder Dialogue Forum as described in WP5 is predominantly used to address stakeholder groups that only have indirect contact with biobanks – such as biomaterial donors, patients or the general public, to discuss ethical questions in a broader context. In our opinion, this change of the stakeholder concept has helped the individual work packages tremendously to align their activities accordingly and will ensure the user-tailored development of our products and services.

The establishment of a biobank IT network is quite an endeavour, especially considering the federated structure in Germany. However, we already successfully tested all required IT components essential for communication within our network. This proof of principle is meanwhile translated into a first installation of a SearchBroker which allows federated queries across several GBA biobanks employing real-world patient data. This achievement is one of the hallmarks of our project demonstrating real-time feedback of potentially available samples and data derived from various biobanks. Of course, there is still much work to be done, but our IT basic and core teams are highly motivated to realise the next steps of our ambitious work programme.

For collaborative projects across various biobanks, comparable quality of biomaterials (and their data) is of utmost importance. The quality system developed within GBN/GBA which is based on three pillars (quality management, quality assessment/ring trials, and auditing) is key to achieve this goal. However, results from the first ring trials as well as internal audits revealed that there is still a need for further harmonisation of critical process steps, particularly in the pre-analytical phase, as well as for implementation of valid measures for quality assurance. The friendly audit programme will provide further insights into how this harmonisation process can be moved forward in detail across all GBA biobanks. Our project's future work programme will thus guarantee that all GBA biobanks operate according to agreed and harmonised quality criteria. In addition, this process will be further supported by application of a biomarker panel, currently under validation in a GBA pilot ring trial, for quality assessment and quality control of relevant aspects in the biobanking workflow.

Public outreach and engagement have already been very successful. However, this needs to be continued and extended within the GBA biobanks and beyond. We will use the experience gained in the first part of the project to adapt and intensify our activities. Similarly, ELSI issues can also be regarded as a continuous process, which mainly needs adaption. In cooperation with MII, we will explore new ways to gain patients' consent on a considerably broader scale. This also involves new elements and tools to inform patients regarding the need for biomedical research and the importance of the contribution of individual patients. Education and training has already been prepared for intensification in the next period. This includes on-site training and online education in cooperation with OBER (Canada), which also requires significant extension.


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Outlook

In addition to continuing and intensifying the work initiated within the current funding by the Federal Ministry of Education and Research (BMBF), extension of this development to further areas is of central importance. Also biobanks at many sites need to be upgraded to create modern research facilities.

Continue the German Biobank Node (GBN)

GBN is indispensable as a linking, coordinating and competence pooling authority for the concerted further development of the German biobanks. GBN has already firmly established itself and been accepted in this position, and prevents resources from being wasted in parallel developments. At GBN's central office, experts for all relevant areas of biobanking work with the biobanks to ensure that new steps and measures are coordinated and harmonised across all locations. This broad expertise at the GBN central office is fundamental to future endeavours – also in terms of the coordination with other national research initiatives, such as the German Medical Informatics Initiative (MII), the German Centers for Health Research (DZG) and the German National Cohort (NAKO), as well as BBMRI-ERIC on the European level. The latter plays a special role in the successful integration of German research initiatives into European funding structures (Horizon 2020, Innovative Medicines Initiative, etc.).

Expand the IT infrastructure

(Networked) IT systems for biobanks will be of central importance to two developments: (1) due to the rapid advances in the molecular subclassification of diseases, the compilation of sufficient case collectives will in future only be possible across sites, and (2) biobanks will increasingly be consulted as sources of (molecular and diagnostic) data on certain diseases. The latter point also includes the generation of research data from existing biomaterials as well as the return of research data to the biobanks. The outcome is a pool of very high-quality data that can sustainably accelerate biomedical research. There have already been successful activities in this direction in a number of European countries (Finland, Norway, Netherlands, etc.).

In order to cater to these requirements, the work begun in Germany must now be continued and intensified. Particularly the cooperation of GBN and the biobanks with MII is important here. Discussions between GBN and the heads of the four MII consortia have revealed that in none of the consortia biobanking has been taken into consideration sufficiently yet, despite having clearly acknowledged the importance of biobanking. It also emerged in the discussions that no financial resources have been earmarked in the MII funding for the inclusion and further development of biobanks – also with regard to the IT requirements of biobanks. It moreover became clear that the different sites in the MII consortia have divergent appreciations of biobanking and engage in activities on very different levels.

To create synergies between GBN, the GBA biobanks and the MII consortia and DZG, and to avoid (potentially incompatible) parallel developments, intensive coordination and productive cooperation that cater to the needs of the biobanks and their stakeholders are vitally important.

Measures

- Close cooperation/networking with MII and other national consortia/networks
- Raise MII biobank sites to the same level of development as GBA biobanks
- Connect local biobanks to the data integration centres (DIZ)

Refine tools for biosamples and data searches

For biomedical research and the further development of precision medicine, it is essential for researchers to quickly be able to locate and use well-characterised, high-quality biomaterials and associated data. Systematic searches and queries to individual biobanks are time-consuming and often unsuccessful. Searches across all biobanks on the feasibility of a project can help in both academic and pharmaceutical or diagnostic research contexts. The first stage of the GBN/GBA federated search provides the basis for this: the tool developed and installed enables real-time searches using a combination of different parameters (currently age, gender, demographic data, ICD-10 code, material types, etc.). Initially, only the number of biomaterials available at different biobanks matching the search criteria are displayed within a matter of seconds. The second step in the search allows the researcher to contact the relevant biobanks, refine their query and ultimately gain access to samples and data. A tool ("Negotiator") has been developed to support and accelerate this process that can be used after a successful search to contact the biobanks.

The combination of sample information with the clinical data available in the DIZ of the MII will greatly enrich these searches. The biobanks together with the MII use and access committees will form a well-organised governance structure which allows rapid access to biomaterials and their data. This will take the support of biomedical research and precision medicine to the next level.

Measures

- Empower more biobanks to become members of the national (and European) IT network for federated sample and data search
- Facilitate free access to the federated search (first step; feasibility query) for all academic and non-academic researchers
- Integrate German biobanks into BBMRI-ERIC's European federated search

Expand the quality system

High-quality biomaterials and their clinical and demographic information are essential to generate new knowledge along with the results of biomedical research. The past has shown that the insufficient quality and/or characterisation of biomaterials often leads to non-reproducible data. Various studies estimate the resulting annual financial losses in the double-digit billions. However, not only the huge financial losses but also the delay in the development of new treatments must be avoided in the future through the stringent quality control of biomaterials. Modern, well-structured and quality-oriented biobanks play a decisive role here.

As part of the ongoing BMBF funding for GBN and the GBA biobanks, extremely important steps have been taken to assure the quality. Thus GBA biobanks have already successfully conducted the first ring trials for the processing of tissue samples and DNA isolation from blood samples. In addition, extensive literature research has enabled the identification of quality biomarkers for liquid biosamples; validation of these biomarkers is currently being prepared. GBN has already published a handbook for quality management. Using centralised quality and process management software (ConSense) and a checklist developed for DIN ISO 20387, GBN has moreover established the basis for an extensively harmonised quality standard. Furthermore, the first "friendly audits" with specially trained auditors began at the GBA biobanks in December 2018.

For biomedical research to be successful, this quality initiative for biobanks launched in Germany under GBN's leadership must be consistently pursued. In the European comparison, the ongoing funding has given German biobanks a major development boost and this must be continued and sustained in the long term through further measures.

Measures

- Expand the quality standards to other national biobanks and all MII sites
- Far-reaching accreditation initiative for all German biobanks
- Develop quality biomarkers to assess the suitability of biomaterials for different applications (omics technologies, single-cell assays, etc.)
- Set up a national ring trial and auditing system for quality assurance

Establish further training opportunities for biobank staff

The work at biobanks places special demands on employees and these are not taken sufficiently into account in any training course at present. This was confirmed in a survey conducted by GBN in the GBA biobanks. Interest in GBN and GBA training courses was extremely high. It will only be possible to successfully implement further developments in biobanking with the accordingly qualified employees – appropriate further training opportunities are a key requisite for this.

Measures

- Establish comprehensive structured training offers for biobank employees in all work areas
- Train technical staff in the various biobank-specific processes
- Project management for the professional processing of queries

Consider ethical, legal and social aspects

Ethical, legal, and social aspects (ELSI) are of utmost importance to the biobanks' work: compliance serves to protect both the biomaterial donors and the researchers. In recent years, important milestones in biobanking could be reached in Germany through GBN's involvement in the biobanking working group of the Permanent Working Party of Research Ethics Committees in Germany (AK-EK) as well as in MII's consent working group. Among others, this includes the publication of master templates for implementation of the EU GDPR in biobanks as well as for industrial biobanks and for broad consent for biomaterial donations from minors. In addition, the members of the AK-EK biobanking working group have successfully been convinced of the benefits of an "ELSI help desk" to continuously respond to ethical and legal questions from biobanks.

Measures

- Support biobanks in implementation of the AK-EK recommendations
- Expansion of the "ELSI help desk"
- Accompanying ELSI research on the comprehensibility of patient information and broad declarations of consent for the donation of biomaterials and data (in collaboration with patient representatives)

Intensify public outreach activities

Only effective communication can help biobanks and biobank networks to achieve greater visibility in the long term. In the current BMBF funding phase, GBN has instigated measures for a number of different target groups: GBN supported the GBA biobanks in the formulation and dissemination of "success stories" – reports on research successes made possible by biosamples and associated data from the biobanks. Particularly the general public – and thus potential biomaterial donors – forms an important target group for the public outreach work of GBN and GBA. After all, biobanks and biomedical research depend on people making their biomaterials and data available for research purposes. For this reason, GBN has launched a patient campaign at several GBA locations, which uses posters, flyers and a website to provide clear information on the biobanks' work and their significance to research that is also comprehensible for laypersons. It remains essential to provide information and proactively implement public outreach measures to

maintain and even increase sample donors' willingness to donate. A campaign for researchers to make clear the value of centralised biobanks and the high quality of their biosamples is currently being prepared.

Measures

- Intensify (multimedia) public outreach work and involve other national biobanks and biobanks at MII sites in public outreach work
- Set up patient portals together with MII which offer information about the use of biomaterials (development in collaboration with patient representatives)
- Regular press work

Intensify stakeholder management

Stakeholder management constitutes a strategic pillar in sustainable organisational management. In order to include the perspectives of relevant stakeholders in activities, GBN has conducted several surveys during the ongoing BMBF funding phase that not only focused on the interests of academic researchers as an important target group, but also on the needs of commercial partners (pharmaceutical and diagnostics industry). The findings are currently being evaluated to determine recommendations for the biobanks.

For strategic further development of the biobanks, the different stakeholders' requirements must also be taken into account in the future. Stakeholder management is an ongoing process – stakeholders' interests and needs are flexible and may depend on changing framework conditions.

Measures

- Continue and strengthen existing approaches to take different stakeholders' needs into account even more effectively
- Transfer the needs identified to recommendations for action for biobanks
- Continuously update the stakeholders' needs

In addition to continuing and intensifying the work initiated, further fields of action that are important for biobanking must also be taken up. The following explanations highlight the possibilities for an enhanced and closer interaction.

Establish sustainable biobanking for clinical trials and cohorts

In addition to a large number of data sets, a variety of biomaterials are also obtained during many clinical trials. The latter are particularly valuable as comprehensive structured clinical information is available for these. Unfortunately, the use of these biomaterials generally is not sustainable, as they are no longer available for further research projects when the respective trial ends. Well-structured central biobanks can provide support on two fronts: (1) existing biobank structures can be used to store biomaterials from clinical trials. New biobank structures of varying quality are currently being established for almost every clinical trial. Using the existing centralised biobanks would prevent this unnecessary waste of resources and ensure a high level of quality. (2) After the respective trial ends, centralised biobanks guarantee sustained use of the biomaterials and associated data in cooperation with local ethics committees. Since biobanks have no own scientific interest in the biomaterials and data, they can in future act as “trustees” to ensure the sustainable use of these valuable materials. This would create considerable added value for biomedical research.

The biobanks must be equipped and prepared for this important task accordingly. In the case of multicentre trials, it must always be possible to find biomaterials that are stored at different locations due to distributed biobanking and to link these to clinical information. Overarching quality assurance measures are particular important here. Biobanks must be involved in the planning of clinical trials as early as possible so that information on biomaterials and their linking to clinical information is available from the start of the trial.

Measures

- Involve biobanks in clinical trials, cohorts and research networks at an early stage
- Determine use of samples and data beyond the end of clinical trials or projects
- Position centralised biobanks as "trustees" for the sustainable use of biosamples and associated data from trials, projects and research alliances

Facilitate cooperation with industry

Cooperation between pharmaceutical companies and academic biobanks is currently still difficult – it is therefore hardly surprising that a survey of GBA biobanks found that cooperations are rare. That being said, with their materials and data, academic biobanks can support and accelerate the development of drugs and diagnostic procedures. Agreements between academic biobanks and industrial enterprises can moreover prevent companies from setting up their own biobanks.

In order to be an attractive partner for companies, biobanks must meet certain criteria: their biomaterials must be simple to retrieve and linked to comprehensive clinical information, and it must be possible for samples and data to be made available quickly. If these conditions are met, it will hardly be necessary for industrial enterprises to operate their own biobanks. The highly successful cooperation of the Finnish biobanks and their national node with pharmaceutical companies shows that this concept is promising. If academic biobanks in Germany are unable to efficiently support industrial partners, commercial biobanks will rapidly fill this gap.

To be able to enter into cooperations with industrial enterprises, university biobanks must continue to evolve. Thus GBN has held intensive discussions with various companies in order to identify the requirements and needs of potential industrial partners. During an internal workshop, GBA representatives moreover discussed the framework conditions for a possible cooperation with pharmaceutical companies. This includes ethical and legal aspects as well as questions of financing and the more rapid availability of biosamples and associated data. Eventually, the successful establishment of an IT infrastructure that enables an uncomplicated and immediate search for biosamples and associated data across different biobanks is central to the cooperation with commercial partners.

What's more, a new European regulation on in vitro diagnostics will come into force in May 2022, which requires the validation of diagnostic procedures using patient materials. This not only applies to the development and validation of new and existing tests, but also to their production. The demand for high-quality biosamples will continue to grow rapidly under these new framework conditions. The academic biobanks must also prepare for this.

In order to strengthen the German biobank landscape as an attractive platform for cooperation with industrial partners, as many national biobanks as possible must be connected within the network. This requires further locations to be readied and integrated in addition to the eleven biobank sites of the German Biobank Alliance (GBA). Furthermore, close cooperation with the MII's DIZ is indispensable for the access to associated medical data. In light of the expertise available and with a view to the European network, this further expansion of the national biobank alliance must take place under the leadership of GBN.

Measures

- Create the appropriate framework conditions for efficient cooperation with industrial enterprises
- Expand the national biobank alliance under the leadership of the German Biobank Node (GBN)
- Financial support for the readying of further biobank sites
- Close association with MII

Set up new collections

In the course of the ongoing BMBF funding phase, it has become clear that joint collections of high-quality biosamples from well-characterised donors should be built up across all GBA sites in cooperation with different clinics. This could also take place in cooperation with the DZG or MII, especially with regard to the clinical data. Collections of biosamples from healthy or diseased individuals (who only suffer from one major disease) are needed as controls for certain (multimorbid) pools of patients, for instance. Cooperation with non-university clinics and specialist practices is also conceivable.

Measures

- Develop coordinated cross-location collection strategies for biomaterials from different control groups
- Initiate project-independent collections

Position biobanks as data sources

High-quality biomaterials in combination with comprehensive clinical and phenotype information are extremely valuable and very limited in number. Hence biobanks will in future increasingly offer data rather than biosamples. This is already common practice in some European countries (Netherlands, England, Finland, Norway). A number of German biobanks have also begun pursuing this approach.

The data available to biobanks can originate from one of two sources: (1) from the biobanks themselves if it is their own or an institutional collection of (molecular) data, or (2) from research projects for which biomaterials have been made available for trials. The biobanks' ability to provide information on the research data that is available must be facilitated. This can be achieved through the appropriate identification in the biobank information system, linking to the relevant data sources or, where appropriate, local storage in the biobanks. In the case of research queries, biobanks must not only be able to provide information on existing biomaterials, but also on clinical data available outside the biobank – depending on the respective query.

Biobanks of population-based trials often collect both biomaterials and the data generated from these. It must be obligatory to report data (e. g. from genetic and molecular analyses conducted as part of the trials or by biobank users) back to the biobank. The implementing institution retains ownership of the data and can, with its consent, facilitate a new research project. The biobank thus acts as the data's "trustee". This in turn allows the biobank to link data sets (e. g. phenotype data and analysis data) from several data owners in a pseudonymised system. This is hugely advantageous for potential evaluation projects. A similar system for the recording of genetic and molecular data in biobanks as well as for the surrender of associated data to biobank users is desirable.

In order to link clinical data and pure research data with biosamples and to process and make these available for research projects, biobanks in Germany must be readied accordingly. A future-oriented approach is needed in this respect so that biomedical research in Germany can keep pace with international developments. Particularly the funding bodies are called upon to facilitate the sustainable use of samples and data after funding ends by providing the corresponding guidelines for the use of funding.

Measures

- Enable the linkage and/or return of research data to biobanks
- Adapt funding guidelines to allow research data to be used once funding ends
- Ready biobanks to link sample and research data and develop standards for the disclosure of data

Conclusion

The Health Research Framework Programme recently published by the German federal government calls for "reliable and efficient life science research infrastructures as a central prerequisite for excellent medical research". The consistent continuation of funding for German biobanks is particularly essential given the immense progress made in recent years. Structures that have successfully been established such as the German Biobank Node (GBN) and the German Biobank Alliance (GBA) must be continued and numerous biobanks that are not yet GBA members must be transformed into "modern research infrastructures" in order to reinforce interdisciplinary cooperation and networking across all institutions and alliances.

German Biobank Node

The German Biobank Node (GBN) has been firmly established as the central coordinating and competence pooling infrastructure for German biobanking and the engine of successful activities. GBN also plays a decisive role on the European level in the cooperation with BBMRI-ERIC. As a centre for German biobanking with broad expertise (in the fields of IT, QM, ELSI, stakeholder management, public outreach), GBN is of utmost importance to future development.

Required measure: continue funding for the German Biobank Node

German Biobank Alliance

The funding of eleven GBA biobank sites by the Federal Ministry of Education and Research (BMBF) has resulted in rapid and concerted development: German biobanks are now also role models for modern biobanking in the international comparison. Further biobank locations can benefit from the structures created and also attain this same high level.

Required measure: fund new biobank locations and support the existing GBA biobanks to involve further sites

Medical Informatics Initiative

The work of the German Medical Informatics Initiative (MII) is particularly in the field of IT networking very similar to the activities of GBN/GBA. The GBA biobanks' IT infrastructure is already very advanced. Closer cooperation between MII and GBN/GBA would yield synergy effects.

Required measure: fund the cooperation with the MII (e. g. ready the biobanks at all MII sites; biobanks as the basis for clinical use cases)

Annexes

WP1: Central Executive Management Office

		Year 1	Year 2	Year 3
		05/2017-04/2018	05/2018-04/2019	05/2019-04/2020
WP 1.1	Day-to-day management: Operation of the Central Office			
1.1.1	Setup of central office; recruitment of staff			
1.1.2	Establishment of GBA communication platform (Confluence)			
1.1.3	Support of National Node Director in all activities			
1.1.4	Project management of all GBA work packages re. tasks, finances, reporting			
1.1.5	Central point of contact for all national GBA-related issues			
WP 1.2	Establishment of a governance structure and GBA consortium			
1.2.1	Attunement governance structure for GBA and setup of boards			
1.2.2	Development of a consortium agreement and negotiation with all partners			
1.2.3	Steering board meetings: Preparation, execution, and follow-up of decisions			
1.2.4	Scientific and Ethical Advisory Board: Preparation, execution, and follow-up of decisions			
1.2.5	Regular contact and exchange with BMBF and DLR; reporting			
WP 1.3	National hub for BBMRI-ERIC			
1.3.1	Central point of contact for BBMRI-ERIC on all levels; regular exchange of information			
1.3.2	Management Comittee and other meetings of BBMRI-ERIC: participation and transfer of decisions			
WP 1.4	Outreach to German biobank community beyond GBA			
1.4.1	Regular exchange/interaction wt community via AG Biomaterialbanks and other			
1.4.2	Co-hosting the annual Biobanking Symposium			
WP 1.5	Stakeholder involvement			
1.5.1	Interdisciplinary working group on biobank performance (structured, quantitative measurement of stakeholder satisfaction with biobank performance and interaction)			
1.5.1.1	Set up interdisciplinary GBA working group			
1.5.1.2	Define stakeholder groups			
1.5.1.3	Develop, test and revise questionnaires considering key performance indicators			
1.5.1.4	1st survey with defined stakeholder group: GBA biobanks			
1.5.1.5	Provide report to Scientific and Ethical Advisory Board and biobanks			
1.5.1.6	2nd survey with defined stakeholder group: Potential users of biobank services			
1.5.1.7	Provide 2nd report to Scientific and Ethical Advisory Board and biobanks			
1.5.1.8	3rd survey with defined stakeholder group: Industry – qualitative interviews and discussions with stakeholders			
1.5.1.9	Provide 3rd report to Scientific and Ethical Advisory Board and biobanks			
1.5.1.10	Final report on biobank performance			
1.5.2	Stakeholder Dialogue Forum ~~(qualitative interviews and discussions with stakeholders)~~			
1.5.3	Stakeholder communication			
All resources for tasks such as website, newsletter, social media, events etc. have been allocated in WP4				
Additional resources in WP5 (ELSI) ad WP6 (Education&Training) are allocated to the GBN central office				

Original work plan/milestones | Change | Delay | ▼ Deliverable | ✔ In plan | Change | Delay

Deliverable	Status	Reasons for Delay/Change
▼Central office functional	✔	
▼Communication platform established	✔	
	✔	
	✔	
	✔	
▼Governance structure in place	✔	
▼Consortium agreement signed by all partners	✔	
▼Annual schedule	✔	
▼Annual schedule	✔	
▼Annual reports	✔	
▼Regular contributions to BBMRI conferences, work programme, newsflash	✔	
▼Regular reporting both ways; active participation in projects and calls	✔	
▼Regular contributions to agenda wt GBA topics	✔	
▼Annual symposium	✔	
▼Working group established	✔	
▼User groups and key performance indicators defined	✔	
▼Questionnaire developed	✔	
	✔	
▼KPI report to SEAB and biobanks	✔	
	←	Due to different regulations at GBA sites, the launch of the survey will be completed in January 2019
▼KPI report to SEAB and biobanks	←	
	✔	
▼KPI report to SEAB and biobanks	✔	
▼Final KPI report to SEAB and biobanks	✔	
	⟳	Revision of the concept of the stakeholder forum; therefore this task was transferred to WP 5.5

WP2: Biobanking IT Network for Germany and BBMRI-ERIC

		Year 1	Year 2	Year 3
		05/2017-04/2018	05/2018-04/2019	05/2019-04/2020
WP 2.1	Biobanking IT framework			
2.1.1	Search and recruit staff			
2.1.2	Set up a GBA-wide agile development process			
2.1.3	Interact/coordinate with national initiative on medical informatics			
2.1.4	Interact/coordinate with BBMRI-ERIC			
2.1.5	Conceptualising framework			
2.1.6	Identify local gaps in GBA biobanks; fill gaps to meet concept requirements			
2.1.7	Define open-source licensing and resolve potential legal issues			
2.1.8	Interface definitions (API) and evaluation of internatl. standards			
2.1.9	Sustainability: Document and release source code of tools			
2.1.10	Interoperability testing			
2.1.11	German Biobank Registry (Deutsches Biobankenregister)			
WP 2.2	German and EU data protection			
2.2.1	Global GBA data protection concept			
2.2.2	Adaption of local data protection concepts			
WP 2.3	Semantics & meta data repository (MDR)			
2.3.1	Stakeholder and requirement analysis and semantics concept			
2.3.2	Set up MDR			
2.3.3	Create common dataset consented by all GBA biobanks; integrate into MDR			
2.3.4	Mapping of local terms against GBA vocabulary			
2.3.5	Integrate existing terminologies			
2.3.6	~~Local instances of MDR~~			
2.3.7	Intuitive, enhanced GUI			
2.3.8	Collaboration with other initiatives			
WP 2.4	IT support for sample & data request management			
2.4.1	Stakeholder and requirement analysis for sample and data requests			
2.4.2	Definition of sample and data requesting process			
2.4.3	Tool for distributed sample search and project mediation			
2.4.4	Follow-up concept			
2.4.5	Follow-up tool			
2.4.6	Tool for evaluation/question researchers for satisfaction			
WP 2.5	Pseudonymisation and ID management for sample and data tracking			
2.5.1	ID management for participating (and future) biobanks			
2.5.2	~~Advanced ID management for cross-biobank sample and data linkage~~			
2.5.3	Linkage capability for sample-related research data			
WP 2.6	Donor empowerment and contact as well as consent management			
2.6.1	Stakeholder and requirement analysis for consent and contact management			
2.6.2	Electronic documentation of patient consent			
2.6.3	Donor portal			
2.6.4	Informing donors about research done			
2.6.5	Engine for (re-)contacting donor			
2.6.6	Interface for additional data from donor			
WP 2.7	Feedback about the use of biobank samples			
2.7.1	Definition of uses cases			
2.7.2	Centrally run system			
2.7.3	Backflow of metadata on research data			
2.7.4	Mapping and distribution of metadata to local samples/systems			
2.7.5	Mapping of metadata to MDR; extension of MDR terminology/ontology			
2.7.6	Include metadata on research results in decentral queries			
2.7.7	Concept for feedback of research results and data			

Original work plan/milestones | Change | Delay | Cancelled | ▼ Deliverable | In plan | Change | Delay

Deliverable	Status	Reasons for Delay/Change
▼Teams recruited	✔	
▼Development cycles, meeting equipment, harmonised toolset installed	✔	
	✔	
	✔	
▼First concept version ▼Finalised & consented	✔	
▼Implementation gaps for each bank identified ▼Gaps closed	⟳	Transformation into a continuous task
▼Developing partners and their technology transfer departments agree	←	Not finalised yet, delayed by four months
▼Programmers' API defined & documented	←	Additional evaluation of FHIR as a potentially better store, achievement expected in January 2019
▼Public availability of well-defined source code allows adoption even beyond GBA	✔	
▼Interoperability tests against API defined & executed successfully	✔	
▼Operation by core team ▼Automated update of biobank data	⟳	Decision in favour of BBMRI-ERIC directory, collaboration with Molgenis
▼GBA-wide data protection concept finalised	✔	
▼Local DP concepts written/adapted ▼local DP officers agree	←	Four biobanks still waiting for approval from their local DP officers, delay continues until the task is completed at all sites
▼Semantic MDR concept finished	✔	
▼Development prototype setup ▼MDR production instance running	✔	
▼Common data elements defined and integrated into MDR	✔	
	✔	
▼All identified ontologies integrated (as far as legally possible)	⟳	Ongoing discussions with national and international groups to update the mapping to international accepted terminologies
▼Local MDR instances established	⟳	Central MDR, local MDR instances unnecessary
▼GUI for user-friendly mapping of biobanking purpose ontology elements	✔	
▼APIs for MDR queries ready to use by others	✔	
▼Requirements and use cases defined	✔	
▼Process defined	✔	
▼Tool ready to distribute searches and mediate projects	←	Tool already implemented, delay in loading data at some sites caused by local regulations in data protection
▼Concept done	←	Current discussion of possible alignments with MII, finalisation of the concept delayed
▼Tool ready to process follow-up	✔	
▼Questionnaire pre-run	←	Prototype for evaluation not ready yet
▼Pseudonymisation tool ready to run	✔	
▼~~Cross-Biobank ID Management in place~~	⟳	Not required, each GBA biobank already possesses a working ID management system compliant to the requirements defined in the GBA data protection concept
▼Linkage of research data via pseudonyms possible locally ▼cross-biobanks	⟳	Originally connected to 2.5.2, put on hold; a new strategy will be developed according to the WP2.6 concept
▼Requirements and use cases defined	✔	
▼First consent form documented digitally at local biobanks	✔	
▼Web portal for donors ready	✔	
▼Individual page in portal for donor	✔	
▼Contact management in place	✔	
▼Electronical forms for donors	✔	
▼Sites agree on governance for specific use cases	✔	
▼System chosen and set up	✔	
▼APIs developed and distributed: central system ready to accept data	✔	
▼Distribution to local systems and mapping to samples possible	✔	
▼MDR contains terminology for feedback of metadata from research data	✔	
▼First decentral request transferred	✔	
▼Concept finalised	✔	

WP3: The Biobanking Quality System

		Year 1	Year 2	Year 3
		05/2017-04/2018	05/2018-04/2019	05/2019-04/2020
WP 3.1	Quality management system and DIN/ISO/CEN			
3.1.1	Participation and involvement in BBMRI and DIN ISO expert groups			
3.1.1.1	Support of standardisation activities (DIN)			
3.1.2	Analysis of QM status quo in GBA biobanks			
3.1.3	Refinement and harmonisation of existing QM manuals according to generic QM manual developed in GBN WP3 with respect to CEN and DIN ISO activities			
3.1.4	Maintenance of generic QM manual			
3.1.5	Stakeholder questionnaires (biobanks and biobank users)			
3.1.5.1	Development of stakeholder questionnaires (biobanks and biobank users) together with WP1			
3.1.5.2	Distribution of questionnaire to stakeholders and definition of key performance indicators, first survey			
3.1.5.3	Analysis of results			
3.1.5.4	Evaluation of implementation status of generic QM manual developed in GBN WP3			
3.1.5.5	Start second survey			
3.1.5.6	Analysis of results			
3.1.6	SOP guided workflows by QM software tools			
3.1.6.1	Development of workflows			
3.1.6.2	Selection of respective software tools			
3.1.6.3	Implementation of tools			
WP 3.2	Quality of samples			
3.2.1	Synopsis on already known QC biomarkers (NCI Biospecimen, ISBER, ESBB) with regard to (1) Critical process steps (time to centrifugation, time to freeze, long term storage,freeze thaw cycles, cold/ warm ischemia ...); (2) Different materials (DNA, serum ...); (3) Disease status and (4) Purpose			
3.2.2	Selection of quality control biomarkers			
3.2.3	Pilot ring trial			
3.2.3.1	Development of the concept together with GBA biobanks			
3.2.3.2	Preparation at local GBA biobanks (ethics, study realisation)			
3.2.3.3	Collection of samples			
3.2.4	Analysis of samples of the pilot ring trial (3.2.3)			
WP 3.3	The sample quality concept			
3.3.1	GBA ring trial (RT) - liquids			
3.3.1.1	Development of the concept together with GBA biobanks			
3.3.1.2	Selection of ISO DIN 17143 accredited reference laboratories			
3.3.1.3	Development of RT timeline			
3.3.1.4	Realisation of RT			
3.3.1.5	Analysis of results			
3.3.2	GBA ring trial (RT) - tissue			
3.3.2.1	Development of the concept together with GBA biobanks			
3.3.2.2	Selection of ISO DIN 17143 accredited reference laboratories			
3.3.2.3	Development of RT timeline			
3.3.2.4	Realisation of RT			
3.3.2.5	Analysis of results			
3.3.3	Corrective and preventive actions (CAPA) ensuring a standardised level of sample quality across GBA biobanks			
3.3.4	Refinement and adaption of critical process steps in generic QM manual			
3.3.5	Second round of selected ring trials			
WP 3.4	The audit system			
3.4.1	Development of an audit programme for GBA biobanks according to DIN ISO 19011			
3.4.1.1	Development of audit programme plan			
3.4.1.2	Definition of quality measures (see WP 3.2 and 3.3)			
3.4.1.3	Development of a training and education programme for GBA auditors → communication with WP6			
3.4.1.4	Training of auditors and development of (internal) audit programme procedures			
3.4.1.5	Friendly audits of biobanks - Intervention - Evaluation of measures - further audits			
3.4.2	QM indicators/KPIs for comparison of biobank performance and achievement of GBA goals and progress			
3.4.2.1	Definition and selection of QM indicators to be included in standardised annual QM reports			
3.4.2.2	Survey of KPI in GBA biobanks			
3.4.2.3	Analysis of results			
3.4.3	External audits			
3.4.4	Involvement of GBA auditors in BBMRI activities			

Original work plan/milestones | Change | Delay | ▼ Deliverable | ✔ In plan | Change | Delay

Deliverable	Status	Reasons for Delay/Change
▼Annual reports, active contribution	✔	
Publication of international biobanking standard ▼Milestone 1: Identification of existing gaps and needs based on reviewed standards (M8) ▼Milestone 2: Development of project related national standardisation input for international standardisation (M36)	✔	
▼Report to SEAB and biobanks	✔	
▼Implementation or adaption of QMS in all GBA biobanks	✔	
▼Open access publication ▼Updates	⟳	Continuous updates of the QM manual required
▼Distribution of questionnaire to GBA biobanks	✔	
▼Report to QM core team (D)	✔	
	✔	
▼Report to SEAB and biobanks	✔	
▼Report to QM core team (D)	✔	
▼Final report to SEAB and biobanks	✔	
	✔	
▼Selection of tools and cordination with GBA biobanks	✔	
▼Implementation of respective tools	✔	
▼Gap analysis	✔	
▼List of QC markers	✔	
	⟳	Integration of the pilot ring trial in 3.2
▼RT concept available/timeline developed	⟳	Integration of the pilot ring trial in 3.2
▼Approval of local ethic committees	⟳	Integration of the pilot ring trial in 3.2
▼Standardised collection of samples/selection of reference methods	⟳	Integration of the pilot ring trial in 3.2
▼Validation of QC biomarkers	⟳	Integration of the pilot ring trial in 3.2
	⟳	Revision during the development of the concepts for ring trials
	⟳	Ring trial liquids and tissue involve different tasks: separation in two subcategories
▼RT concept available	✔	
▼List of reference laboratories	✔	
▼Draft and timeline of ring trials	✔	
	⟳	Time plan adapted to new concept
▼Report to biobanks/workshop with biobanks	⟳	Time plan adapted
▼RT concept available	✔	
▼List of reference laboratories	✔	
▼Draft and timeline of ring trials	✔	
	⟳	Time plan adapted
▼Report to biobanks/workshop with biobanks	⟳	Time plan adapted
▼List of individual recommendations for the respective biobanks	✔	
▼Regular updates of QM manual	✔	
▼Report of second ring trial results to biobanks	✔	
▼Audit programme outline	✔	
▼Audit checklist	✔	
	✔	
▼Workshops with qualifications (participation confirmation)	✔	
▼Report of audit results to SEAB and biobanks	←	Lack of personnel at the beginning of the project caused delay of six months
▼List of key performance indicators	✔	
	✔	
▼Report of results to SEAB	✔	
▼Report of results to SEAB and GBA biobanks	✔	
	✔	

WP4: Public Accountability, Public Relations, Public Outreach

		Year 1	Year 2	Year 3
		05/2017-04/2018	05/2018-04/2019	05/2019-04/2020
WP 4.1	Corporate communication			
4.1.1	GBN website			
4.1.1.1	Project management for development of new website wt agency			
4.1.1.2	Definition of structure/design adaptions/extension from GBN to GBA			
4.1.1.3	Programming (Front End, Back End) – agency			
4.1.1.4	Content development			
4.1.1.5	CMS training			
4.1.1.6	Import of contents			
4.1.1.7	Testing with stakeholder groups and bug fixing			
4.1.1.8	Launch			
4.1.1.9	Continuous updates			
4.1.2	GBN newsletter (quarterly edition)			
4.1.2.1	Integration of GBA in concept (year 1)/planning of topics for one year			
4.1.2.2	Generate content/layout/integration into website of newsletter Q1-Q4			
4.1.2.3	Evaluation of user behavior and adaption of content to interests for future issues and website			
4.1.3	Press releases			
4.1.3.1	Event related press releases/contributions in newspapers, magazines, TV			
4.1.4	Scientific conferences			
4.1.4.1	Booth system (concept, design, production)			
4.1.4.2	Presentations at scientific conferences			
4.1.5	Social media			
4.1.5.1	Set up social media accounts (LinkedIn, Twitter)			
4.1.5.2	Continuous contributions			
4.1.6	Picture database			
4.1.6.1	Establish picture database as a resource for biobanks			
WP 4.2	Communication with patients/donors of samples and data			
4.2.1	Patient website			
4.2.1.1	Project management			
4.2.1.2	Structure and design adaptions (according to design system)			
4.2.1.3	Programming (Front End, Back End)			
4.2.1.4	Content development			
4.2.1.5	Import of contents			
4.2.1.6	Testing wt stakeholder and bug fixing			
4.2.1.7	Launch			
4.2.1.8	Content updates			
4.2.2	Biobank tool kit			
4.2.2.1	Generic text modules (provide texts in tool kit and support local biobanks)			
4.2.2.2	Generic film modules (provide film modules and support local biobanks)			
4.2.2.3	Generic flyer (support local biobanks in adapting the flyer)			
4.2.2.4	Picture database			
4.2.2.5	Infographics			
4.2.3	Public events			
4.2.3.1	Long night of sciences, Researchers' Night, etc.			

Original work plan/milestones | Change | Delay | ▼ Deliverable | ✔ In plan | Change | Delay

Deliverable	Status	Reasons for Delay/Change
	✔	
▼Design finalised	✔	
▼Programming finalised	✔	
	✔	
▼User training	✔	
	✔	
	✔	
▼Website online	✔	
▼Website updates	✔	
▼Annual editorial plan	✔	
▼Newsletter delivered (4x p.a.)	✔	
▼Statistics report and user feedback	✔	
▼Annual press review	✔	
▼Booth system in use	✔	
▼Presentations at scientific conferences	✔	
▼Social media accounts set up and running	✔	
	✔	
▼Picture database available	✔	
	✔	
▼Design finalised	✔	
▼Programming finalised	✔	
	✔	
▼User training	✔	
	✔	
▼Website online	✔	
▼Website updates	✔	
▼Provide text modules to local biobanks	✔	
▼Provide film modules to local biobanks	✔	
▼Provide flyer template to local biobanks	✔	
▼Picture database available	✔	
▼Infographic available	✔	
	✔	

WP5: Ethical, Legal and Social Issues (ELSI)

		Year 1	Year 2	Year 3
		05/2017-04/2018	05/2018-04/2019	05/2019-04/2020
WP 5	Establish regular ethical discussion platform with research community, ethic boards, patients and legislators			
5.1	Preparation, realisation and follow-up of workshops involving all relevant stakeholder groups; #1 on national implementation of GDPR ; follow-up workshops depending on current developments, e. g. consent of minors, consent of incapacitated individuals			
5.2	Regular ELSI discussion forum at the annual biobanking symposium			
5.3	Continued close cooperation with Biobank Task Force of the Working Party of the German Medical Ethics-Committees			
5.4	Continued contribution to the tasks of the BBMRI Common Service ELSI according to BBMRI work plan			
5.5	Integration of ELSI themes in Stakeholder Dialogue Forum (with respect to WP 1.5.2)			
5.6	Regular information on current ELSI developments on both GBN website & GBN newsletter			

WP6: Education, Training, Counselling

		Year 1	Year 2	Year 3
		05/2017-04/2018	05/2018-04/2019	05/2019-04/2020
WP 6.1	Counselling			
6.1.1	TMF working group "Biomaterialbanks" (AG BMB)			
WP 6.2	Education			
6.2.1	Set up contract with the Canadian Office of Biobank Education and Research (OBER), Vancouver			
6.2.2	Survey of educational needs of stakeholder 'BB technical personnel'			
6.2.3	Defining learning objectives for technical personnel			
6.2.4	Analysis of pre-selected existing online modules available from Canadian Office of Biobank Education and Research			
6.2.5	Content adaptation, generation and implementation acc. to stakeholder and national needs; setup of the exam			
6.2.6	Validation, testing and bug fixing			
6.2.7	Translation of content into German language			
6.2.8	Validation, testing and bug fixing			
6.2.9	Launch incl. setup of registration process and waiving of fees			
6.2.10	Continuous updates			
WP 6.3	Training			
6.3.1	On-site training for technicians			

Original work plan/milestones | Change | Delay | ▼ Deliverable | ✔ In plan | Change | Delay

Deliverable	Status	Reasons for Delay/Change
▼Position papers as result of workshops	✔	
▼Annual ELSI forum for biobanking community	✔	
▼Implementation of generic concepts in GBA biobanks*	✔	
▼Products of Common Service ELSI*	✔	
▼Stakeholder Dialogue Forum report	Change	Continuous task including the original concept of the Stakeholder Forum
▼Regular updates on ELSI topics	✔	

** Deliverables/milestones are dependent on working focus and results of other organisations and therefore can not be predicted in detail here*

Original work plan/milestones | Change | Delay | ▼ Deliverable | ✔ In plan | Change | Delay

Deliverable	Status	Reasons for Delay/Change
▼Meeting reports and individual biobank advice	✔	
▼Contract between GBA and Canadian Office of Biobank Education and Research (OBER)	Delay	Revision of the education strategy, contract negotiation planned to be finalised in January 2019
▼List of educational needs for technical personnel in biobanks	✔	
▼Catalogue of educational objects	✔	
▼List of gaps	✔	
	Delay	Revision of the education strategy, delay for 16 months
▼Pre-selected modules for technical personnel in English	Delay	Revision of the education strategy, delay for 16 months
	Delay	Revision of the education strategy, delay for 16 months
▼Pre-selected modules for technical personnel in English	Delay	Revision of the education strategy, delay for 16 months
▼German content modules online available for GBA technical personnel and other German biobanks	Delay	Revision of the education strategy, delay for 16 months
▼Module updates/extensions	✔	
▼On-site training course for technicians	Change	Additional on-site training sessions required

External Scientific and Ethical Advisory Board (SEAB) recommendations for the German Biobank Node and German Biobank Alliance

SEAB meeting in Berlin on 21 September 2018

General comments on 2018

The SEAB congratulates GBN and GBA for their extraordinary achievements and the work completed over the past year. Everything delivered as part of this project is outstanding and unprecedented in Europe and the rest of the world. The members of the SEAB believe that the achievements in Germany make GBN/GBA a role model for Europe. Furthermore, the products generated are of high importance for the development and support of biobanks in Europe, primarily via the BBMRI-ERIC network.

Specific comments on 2018

WP1 – Coordination and stakeholder activities

Concerning all of the stakeholder work, we especially encourage the continuation and intensification of the very important interaction with industry, which has already been initiated. At the same time, we also recommend reaching out to ethics committees and clinicians as further, very important stakeholder groups. Following the User Satisfaction Survey addressing biobank users, we propose adding a question regarding the impact of biobank services on achieving the research project aims.

GBN's products are very useful to the biobank community and meet their needs exactly, hence it is very important to continue this work. This also includes common position papers, which could be highly significant to biobanking at the national level in Germany. With regard to the interaction with industry, the development and provision of a contract template and a common pricing strategy would be greatly beneficial to the whole community. A harmonised pricing strategy within GBA (and beyond) would moreover ensure transparency for patients and help to gain their trust. Together with the politicians and lawyers, we encourage you to further their involvement and to continue inviting these stakeholders to relevant occasions and events – as was the case during the successful workshop held in May 2018.

WP2 – IT network

The SEAB is impressed with the live online search for biomaterials and data across six different GBA biobanks. Having witnessed this live search, we highly recommend intensive outreach activities not only in Germany but also on the European level to broadly demonstrate what has been achieved. We therefore strongly encourage you to give such a live online presentation in London during the next BBMRI-ERIC Management Committee meeting (8–9 October 2018). This should be mirrored on the national level through the active involvement of non-GBA biobanks in the alliance. Start marketing and communicating your activities and achievements to the community now and not just at the end of the project.

Concerning the competition with commercial IT platforms, we suggest you benchmark your system by comparing the differences, relative advantages and disadvantages. One unique advantage of GBN/GBA is that its biobanks are embedded in academic environments and their host institutions would be reluctant to enter patient data in another privately-owned platform. Since the project is driven by both sides – by researchers as well as by the biobanks – we recommend further intensifying the focus on the users' needs, including socio-technical aspects. Also reflect on how to handle the different IT interfaces of the users, especially the researchers and clinicians. Consider the role of bio-

banks as an entry point for a researcher into the IT network by performing overarching searches for samples and data. This digitalisation will support your role to be a science enabler or even a science driver.

WP3 – Quality management system
The SEAB is very positive about GBN's support for GBA biobanks with the conducting of "friendly audits" as a first step on their way to accreditation according to the recently published ISO 20387 norm. Concerning the quality assurance for biomarkers, we encourage GBN to allocate sufficient funding to complete the work programme of the liquid and tissue samples.

WP4 – Public relations and communication
The GBN website is very well designed and informative. We recommend that you provide a list of all products available to the community to increase their visibility and accessibility.

WP5 – Ethical, legal and social issues (ELSI)
We urge you to publish a position paper as a follow-up from the ELSI workshop ("My genes belong to me!") on incidental findings held in May 2018. Due to the complexity of this topic, no definite solution could be found on how to translate research findings into medically relevant information and what role biobanks should play in this process. We suggest establishing a small working group to discuss this topic again and reach a consensus. You should also consider the regulations in Switzerland and in the United States during this process.

WP6 – Education and training
We agree with Dr. Nußbeck's idea of prioritising e-learning according to the content and experiences of the quality work package, especially the ring trials. This will maximise the impact since it corresponds to the practical work of biobank-related technicians.

Sustainability

Focusing on the future of the project and the sustainability, it is essential to start planning now with a focus on the products with the highest value and impact. The SEAB expressed its willingness to review this sustainability concept and to share its opinions and advice.

With respect to sustainability, it should be ensured that the project continues at the national level without interruption, especially in terms of the IT developments, so that the developments can be finished and operations can be rolled out by GBN. Outreach work and the involvement of non-GBA biobanks should not dilute the efforts at this point; they can be involved at a later stage.

In order to reach out to the community, you should start planning communication of the most important activities to maximise further use of your products. This could be documents or some sort of workshop. You need to explain to non-GBA biobanks how to proceed, how to implement solutions and to motivate them to get involved.

One particular suggestion is a document describing the "lessons learned" while setting up your national IT network, but also including European experience from the BBMRI-ERIC (ADOPT) Colon Cancer Data Collection. This would be most informative for future developments, ensuring your work and experience are documented for posterity.

The SEAB especially welcomes the collaboration with the German Medical Informatics Initiative (MII) and recommends fostering this cooperation by developing a work plan defining the next steps for joint activities. Clearly state the common ground with the MII and also indicate the differences. This especially holds true for GBN's advanced IT development, which covers important aspects that are also relevant for MII. The close cooperation with MII is of great importance for GBN since political decisions might also be influenced by demonstrations of the added value derived from this interaction.

The final and most important point relates to the sustainability of the GBN/GBA project after the funding period ends. Regarding decisions to be made, we encourage you to engage with funders and ministries immediately. One opportunity to do so could be created by inviting them to the national annual biobanking symposium in December 2018. Politicians and other responsible persons should also be invited to this event – it is very important to reach out to them at this stage, too.

So once again, congratulations on everything that has been achieved!

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