Position paper: Strengthening academic biobanks and patient participation for biomedical research

An initiative of:[1]

- German Biobank Node (GBN) & German Biobank Alliance (GBA)
- BRCA Network – Help for People Affected by Hereditary Cancers (BRCA-Netzwerk e. V.)
- Federal Association for Children with Heart Disease (Bundesverband Herzkranke Kinder e. V.)
- German Restless Legs Association (Deutsche Restless Legs Vereinigung, RLS e. V.)
- Association of VHL (von Hippel-Lindau) Affected Families
  (Verein VHL betroffener Familien e. V.)

This position paper is endorsed by:

- Alliance for Chronic Rare Diseases (Allianz Chronischer Seltener Erkrankungen, ACHSE e. V.)
- Italian Association of Poland Syndrome (Associazione Italiana Sindrome Di Poland, AISP)
- Working Group of Medical Ethics Committees in the Federal Republic of Germany
  (Arbeitskreis Medizinischer Ethik-Kommissionen in der Bundesrepublik Deutschland, AKEK e. V.)
- Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC) with Stakeholder Forum Patients' and Citizens' Pillar
- Bavarian Cancer Research Center (Bayerisches Zentrum für Krebsforschung, BZKF)
- Cancer Patients Europe
- EPIONI – Greek Carers Network
- EURORDIS – Rare Diseases Europe
- FHchol Austria
- FH Europe – The European FH Patient Network
- German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and
  German Cancer Consortium (Deutsches Konsortium für Translationale Krebsforschung, DKTK)
- German Rheumatism League Federal Association
  (Deutsche Rheuma-Liga Bundesverband e. V.)
- Hellenic Cancer Federation (ELLOK)
- Ligue Huntington Francophone Belge (Belgian Francophone Huntington League)
- Long COVID Germany (Long COVID Deutschland)
- Nätverket mot Cancer (Swedish Network Against Cancer)
- Association of Medical Faculties (Medizinischer Fakultätentag, MFT)
- PRO RETINA Germany (PRO RETINA Deutschland e. V.)
- RaDiOrg – Rare Diseases Belgium
- Stefan Schwartze, MP, Federal Government's Patient Commissioner
- Sällsynta diagnoser – Rare Diseases Sweden
- UNIAMO – Federazione Italiana Malattie Rare (Italian Federation of Rare Diseases)

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Background and motivation

The donation of biosamples from ill and healthy people can make a very valuable contribution to biomedical research and safety in patient care. **Centrally organised academic biobanks**[2a], which collect, process, store and distribute human biospecimens and associated data to research projects, have become increasingly important worldwide. In Germany, academic biobanks focusing on human biosamples have developed into efficient infrastructures for medical research over the past decade. With the German Biobank Node (GBN)[b] and the German Biobank Alliance (GBA)[c], the German government has launched central initiatives to establish professional, quality-assured biobanks and to harmonise them and to promote their networking.
Many researchers collaborate with these biobanks in a very productive and trustful manner, and, based on their experience, actively recommend using the services and logistics offered by centrally organised biobanks.[i] However, as a recent GBN survey[ii] has shown, some researchers continue to store biospecimens in their own freezers, which is associated with high risks.[iii] The storage temperatures of such collections are rarely adequately monitored, and disaster-management plans and back-up solutions are usually lacking in the event of refrigeration (unit) failure. Inadequately characterised, poor quality or improperly stored and released biosamples often lead to non-reproducible research results.[iv] In addition, there is usually no long-term perspective for individual sample collections, as research interests change, project funding is limited in time and/or project leaders change location. In such cases, the biosamples collected are often no longer available for other research projects.

Non-sustained sample collections are difficult to reconcile ethically with the donors' altruistic desire to support progress in medical research.[v] Patients who donate biosamples for research have sometimes experienced severe health issues. They hope to contribute to avoid similar sufferings through intensification of medical research, thereby helping other people to benefit from the research results achieved with the donated samples and associated clinical data. Some donors also have a personal interest in donating samples. They hope to support further research into their disease to speed up diagnosis and to improve treatment – possibly even with an impact on their own therapy.[vi] Particularly patients with advanced or rare diseases have a rather strong interest in the use of their biosamples and in matching their samples and clinical data with relevant biosamples and clinical data from other biobanks.

The donation of biosamples and data, a cornerstone of biomedical research today, cannot be overstated. It requires a great deal of trust in the institution to which these valuable resources are given. Sample donors have a right to responsible and quality-assured handling of their donated biosamples and associated clinical data, their swift scientific use and the prudent and efficient use of public and private funds.

Centrally organised academic biobanks, but also many patient associations, do not understand why public funds are repeatedly used to finance project-related individual “biobanks” in newly purchased freezers. Although centralised facilities already exist in many places, new biobanks are often set up for larger research initiatives. This not only has a negative impact on the funding situation of existing

[2] See the glossary at the end of the document, which explains the terms marked with letters. References and bibliographical references are numbered and are also found at the end of the document.

biobanks, but also counteracts the standardisation and networking efforts of the GBN. A national fragmentation of the biobank landscape is the detrimental consequence of uncoordinated funding measures.

The particular relevance of professional, centrally organised biobanks is highlighted by the increasing molecular subtyping of almost all cancers. In the era of personalised medicine, large quantities of high-quality and comparable samples and data are crucial. Especially for rare diseases, centrally organised biobanks and biobank networks play a pivotal role, as often only very few of such samples are available at different locations in Germany, Europe and worldwide.

Due to the interests described above, patients are important stakeholders of academic biobanks. Patient representatives are well connected in their respective patient communities and have collective experiential knowledge and broad expertise. Despite recommendations, e.g. from the German Federal Ministry of Education and Research (BMBF)[vii], patient organisations and their representatives are not yet regularly involved as consortial partners in biobank-related research projects. Because of their great relevance to patients, particularly biobanks may profit from participatory (research) approaches.

In the position paper presented here, representatives of GBN/GBA and patient organisations have jointly developed solutions to strengthen both centrally organised academic biobanks and patient participation in biomedical research projects and funding programmes (with biobank relevance).

Issues

Quality-assured, centrally organised academic biobanks (such as the GBA biobanks) need to be used more effectively than in the past. This could include a transfer of existing sample collections under the umbrella of quality assurance and sustainable use provided by centrally organised biobanks. In principle, such biobanks should be involved in an advisory capacity as early as possible, especially in newly planned biomedical research projects. Through quality-controlled biobanking of newly acquired samples, centrally organised academic biobanks can ensure a more efficient and sustainable use of human biosamples and associated data in the long term. Optimised processing and storage of human biosamples is also a prerequisite for current (e.g. omics technologies and single-cell sequencing) and future analytical methods. The use of quality-assured, centrally organised biobanks should therefore be anchored in the funding guidelines of the BMBF, the Federal Ministry of Health (BMG), the German Research Foundation (DFG) and other funding institutions, especially for newly set up clinical trials and/or research networks.

This would better exploit the potential of these already established biobanks and accelerate the cultural change in academic research towards increased sharing of samples and data.[viii] Increased use of centrally organised academic biobanks allows researchers to access existing samples and associated data from different projects/studies in a transparent and regulated manner and ensures the sustainable use of biosamples beyond the end of the respective funding periods. To achieve this, using a "broad consent" [d] is largely favourable, because study-specific consents usually make it much more difficult to reuse the collected (project) samples.[ix]

In addition, a more effective networking of national research initiatives is of great interest. As core elements of the biomedical research infrastructure, it is imperative that centrally organised academic biobanks are consistently integrated into future and current initiatives, such as the Network of University Medicine (NUM), to avoid a repeated establishment of similar structures with scarce funding.

The GBN can take the lead in coordinating national initiatives to collect and analyse human biosamples. This also ensures harmonised, streamlined and therefore more efficient sample processing and organisational processes in university medical biobanks (which will, among other things, avoid repeated assessments and audits). GBN also enables German biobanks to be closely linked to the European biobank network BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium)[e], thus increasing cross-border exchange and participation in international research projects to make even more effective and sustainable use of the collected biosamples and associated data.

To make biomedical research, and particularly biobank research projects, more patient-relevant and -oriented, patient representatives should be involved in the whole process from the very beginning. This includes the identification of research needs, the co-design of calls for proposals, the co-evaluation of patient-relevant work packages and, subsequently, direct participation in patient-relevant work packages as well as the appropriate financial compensation for patient representatives. The approach to systematically implement patient participation in research has already proven successful in projects within the National Decade against Cancer and the German Rheumatism League. When research results are published, there is a need for a generally understandable version to be disseminated through patient community channels and used for public relations by biobanks.

Closer links with the patient community can help centrally organised academic biobanks to achieve more direct or indirect involvement in biomedical research projects – for example, if patient representatives recommend the inclusion of such biobanks within a grant reviewing process. In addition to an increased participation in projects, an appropriate reimbursement of biobank services granted by funding bodies also plays an important role in the sustainable financing of biobanks: e.g., for project consulting, planning of logistics, and the quality-controlled processing and storage of samples. Nevertheless, further measures are required by the responsible federal states and funding institutions to secure the funding of centrally organised academic biobanks in the long term. Their budgets, which are currently allocated to faculties, university hospitals and non-university research institutions, are often insufficient as basic funding. Consequently, the federal states should increase the basic funding accordingly. Moreover, the funding institutions should also increase the programme lump sums to ensure that centrally organised biobank infrastructures receive an appropriate share within research projects that collect biosamples.

In the medium term, health insurance companies should also contribute to the financing, because in the future, the quality-assured storage of selected biosamples will play an even more important role in patient care. Patients with, e.g., familial, immunological or oncological diseases often depend on having access to their own samples and those of their family members over years and decades for their own predictive and therapeutic assessment and, on this basis, for their medical choices. So-called longitudinal collections, which are built up over a long observational period, may facilitate earlier diagnosis (e.g. identification of novel biomarkers) and thus lower treatment costs in the long term. This underlines the close relationship between research and healthcare, and indicates that corresponding billing codes for biobanking in the context of healthcare should be generated in the standardised rating scale.

Approaches

The federal states and funding agencies recognise **biobanking and patient participation as cross-cutting issues** for successful biomedical research.

This is achieved by ...

- **... including the cooperation with centrally organised and quality-assured academic biobanks (such as the GBA biobanks) as a criterion in funding calls[x]:**
  - Applicants must check whether the samples required for their research project are already available in biobanks.[xi] For this purpose, reference is made to the existing biobank and sample search tools[f]: directory.bbmri.de, samplelocator.bbmri.de, and bbmri-eric.eu/bbmri-sample-and-data-portal/.
  - The biobanking of new prospective collections is preferably carried out under the roof of centrally organised academic biobanks.
  - Biobank representatives are involved in the tendering and evaluation of biomedical funding programmes in which biosamples are collected.

- **... creating better conditions and incentives for the sharing of samples and data in the academic context:**
  - Biosamples and associated data should preferably be collected under a "broad consent" framework.
  - Biosamples and associated data collected as part of a biomedical funding programme should be available for re-use in other research projects within a reasonable time after the funding has ended (e.g. as stipulated in the User Manual of the Medical Informatics Initiative[xii]).
  - Specific calls will be issued regularly for research on existing broad consent sample collections and associated datasets.
  - Appropriate training is provided for all stakeholders (researchers, donors, patient representatives, medical and administrative staff) on the sharing and joint use of samples and data.

- **... specifically promoting the involvement of donors/patients through participatory research approaches:**
  - Donor/patient representatives should be involved from the outset in the planning, tendering and co-evaluation of patient-relevant work packages in biomedical research projects.
  - Donor/patient representatives should be appropriately involved in participatory research projects, for example in a patient advisory board or as collaborators.
  - Funding agencies should provide adequate funding for donor/patient involvement activities.
  - Researchers must publish the results of their biomedical research (within reasonable time limits and unsolicited) in a recipient-oriented way – donors should be informed about the (general, not individual) results obtained with their biosamples and data.

- **... ensuring sustainable funding of centrally organised and quality-assured academic biobanks:**
    - Funding agencies provide fixed reimbursement rates in grants and use of funds statements: for consulting, planning of logistics and the quality-controlled processing and storage of biosamples by biobanks.
    - Funding agencies will increase the programme lump sums to ensure that centrally organised biobank infrastructures receive an appropriate share of research projects planning new biosample collections.
    - The responsible federal states will increase the basic funding.
    - Funding agencies (GKV-Spitzenverband) support the remuneration of academic biobanks for the selective storage of samples (e.g. for diagnostic or prognostic purposes) and for the release of biobank samples (study samples or samples obtained with broad consent) in the context of patient care by the health insurance funds. For this purpose, billing codes in the standardised rating scale are required.
    - Sustainable funding of the German Biobank Node (GBN) is ensured as an umbrella organisation and coordinating centre for further training, quality assurance (proficiency tests) and IT networking of biobanks as well as the central link to the European biobank network BBMRI-ERIC.

Glossary

[a] Centrally organised academic biobanks

Centrally organised academic biobanks – such as the biobanks of the German Biobank Alliance (GBA) – process and store blood, tissue and other human biosamples. Samples are collected both as part of patient care for diagnostic purposes and for research activities. Along with the biospecimens, associated clinical data, such as diagnosis, age or disease progression, are collected and stored in encrypted (pseudonymised) form in university hospital data integration centres.

Centrally organised academic biobanks must have an overarching governance (statutes/policy), clear rules for access to samples and data (use and access rules) and be approved by the relevant ethics committee. They operate in accordance with the international ISO standard for biobanking (ISO 20387) and therefore under strictly controlled conditions to provide biospecimens and data of very high quality. According to this definition, 'centrally organised' biobanks may also include several sub-biobanks operating in a harmonised manner under a common umbrella.

Further information: biobanken-verstehen.de

[b] German Biobank Node (GBN)

The German Biobank Node (GBN) is the umbrella organisation of academic biobanks in Germany, based at the Charité – Universitätsmedizin Berlin. The GBN was founded in 2014 and is funded by the German Federal Ministry of Education and Research (BMBF).

Further information: bbmri.de

[c] German Biobank Alliance (GBA)

Under the leadership of the GBN, academic biobanks at 36 locations and an IT development centre have joined forces in the German Biobank Alliance (GBA). The GBA biobanks have established common quality standards. Compliance with these standards is ensured by internal audits and proficiency tests. In addition, the majority of GBA biobanks are certified or accredited. GBA biobanks make their quality-assured human biospecimens and associated data available for medical research throughout Europe.

Further information: bbmri.de/ueber-gbn/german-biobank-alliance/

[d] Broad consent

Many university hospitals and research institutions offer broad consent to sample donors. This allows for a wide range of research activities to be carried out on the donated biospecimens (and associated data), including those that are unknown at the time of sample collection, in order to better support medical research. For such future research projects, sample donors will not be asked for their consent again. Rather, consent will be replaced by a positive vote by the responsible ethics committee, which will review and evaluate the project. Templates for broad consent are available from the Working Group of Medical Ethics Committees (AKEK) and the Medical Informatics Initiative (MII).

[e] BBMRI-ERIC

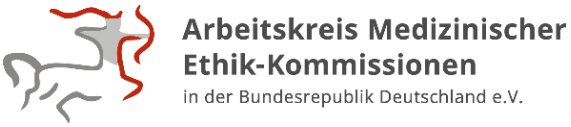
BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium) is a pan-European infrastructure of national biobank networks. The German Biobank Node (GBN) represents the interests of German biobanks.

Further information: bbmri-eric.eu

[f] Online search tools for biosamples/biobanks

The Sample Locator (samplelocator.bbmri.de) allows scientists to search for human biosamples and associated data in academic biobanks, mainly in Germany. The German Biobank Directory (directory.bbmri.de) is a centralised list of German biobanks with aggregated information on their human sample collections. It is part of the European BBMRI-ERIC directory (directory.bbmri-eric.eu). In addition to the directory, BBMRI-ERIC offers other tools on a portal (bbmri-eric.eu/bbmri-sample-and-data-portal/).

Logos of the initiators and supporters of this document



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PRO RETINA
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[i] GBN documents some of these collaborations in 'success stories' on the GBN website: https://www.bbmri.de/research/successful-projects/?L=1. Researchers recommending GBA biobanks have participated in a GBN 'testimonial campaign': https://tinyurl.com/mpy8uvru.

[ii] Klingler, C., von Jagwitz-Biegnitz, M., Baber, R., Becker, K. F., Dahl, E., Eibner, C., Fuchs, J., Groenewold, M. K., Hartung, M. L., Hummel, M., Jahns, R., Kirsten, R., Kopfnagel, V., Maushagen, R., Nussbeck, S. Y., Schoneberg, A., Winter, T., Specht, C. (2021). Stakeholder engagement to ensure the sustainability of biobanks: a survey of potential users of biobank services. Eur J Hum Genet. https://doi.org/10.1038/s41431-021-00905-x.

[iii] Becker, K. F., Wipperfürth, J. Herpel, E. (2018). Präanalytik und Biobanking: Einfluss präanalytischer Faktoren auf die Gewebeprobenqualität. Pathologe, Jul, 39, (4). S. 297–302. doi: 10.1007/s00292-018-0437-7; Ellervik, C., Vaught, J. (2015). Preanalytical variables affecting the integrity of human biospecimens in biobanking. Clin Chem. Juli 61, (7). S. 914–934. doi: 10.1373/clinchem.2014.228783; Robb, J. A., Gulley, M. L., Fitzgibbons, P. L., Kennedy, M. F., Cosentino, L. M., Washington, K., Dash, R. C., Branton, P. A., Jewell, S. D., Lapham, R. L. (2014). A call to standardize preanalytic data elements for biospecimens. Arch Pathol Lab Med. Apr;138, (4). S. 526–537. doi: 10.5858/arpa.2013-0250-CP.

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[v] Lesch W., Schütt A., Jahns R (2016). Biobanken in der öffentlichen Wahrnehmung: Verständnis, Interesse und Motivation von Probenspendern in Deutschland. Gesundheitsforschung kommunizieren, Stakeholder Engagement gestalten (Lesch W. & Schütt A., Hrsg.). TMF-Schriftenreihe, Band 14, Medizinisch-Wissenschaftliche Verlagsgesellschaft mbH & Co. KG, MWV, Berlin 12/2016, S.113-121. ISBN 978-3-95466-286-9.

[vi] Ibid.

[vii] Federal Ministry of Education and Research (BMBF, 2021). Principles of Successful Patient Involvement in Cancer Research. Revised Version. https://www.gesundheitsforschung-bmbf.de/files/2021_06_01_Principles_Paper_bf.pdf; Forum Gesundheitsforschung (2023). Erklärung des Forums Gesundheitsforschung zur aktiven Beteiligung von Patientinnen und Patienten in der Gesundheitsforschung. https://projekttraeger.dlr.de/media/gesundheit/GF/Forum-GF_Erkl%C3%A4rung-Patientenbeteiligung_27-03-2023.pdf.

[viii] Joly Y., Dalpé G., So D., Birko S (2015). Fair Shares and Sharing Fairly: A Survey of Public Views on Open Science, Informed Consent and Participatory Research in Biobanking. PLoS One. 2015 Jul 8;10(7):e0129893. doi: 10.1371/journal.pone.0129893; Holub P., Kohlmayer F., Prasser F., Mayrhofer M. T., Schlünder I., Martin G. M., Casati S., Koumakis L., Wutte A., Kozera Ł., Strapagiel D., Anton G., Zanetti G., Sezerman O. U., Mendy M., Valík D., Lavitrano M., Dagher G., Zatloukal K., van Ommen G. B., Litton J. E (2018). Enhancing Reuse of Data and Biological Material in Medical Research: From FAIR to FAIR-Health. Biopreserv Biobank. 2018 Apr;16(2):97-105. doi: 10.1089/bio.2017.0110. Epub 2018 Jan 23.

[ix] Jahns R., Geiger J., Schlünder I., Strech D., Brumhard M., von Kielmansegg S**.** (2019). Broad donor consent for human biobanks in Germany and Europe: a strategy to facilitate cross-border sharing and exchange of human biological materials and related data. Journal Lab. Med. doi: 10.1515/labmed-2017-0064.

[x] German Cancer Aid, for example, formulated the following in a call for proposals: “Whenever possible, an affiliation or collaboration is recommended with the following structures: Interaction with a Biobank Network (e.g. the German Biobank Alliance (GBA), Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), Biobanking working group of the TMF (Technology, Methods, and Infrastructure for Networked Medical Research).” Deutsche Krebshilfe (2021). Program for the Development of Interdisciplinary Oncology Centers of Excellence in Germany. 9th Call for Applications. https://www.krebshilfe.de/fileadmin/Downloads/PDFs/Foerderung/CCCs_9th_Call/Ausschreibung_und_Leitfaden_9._Call_30.09.21.pdf.

[xi] To this end, the DFG has published a guideline: German Research Foundation (DFG, 2021). Guide for quality-promoting aspects in medicine and biomedicine. https://www.dfg.de/resource/blob/175534/bacd3a442799a949eebb9c82f7e8e304/leitfaden-qualitaetsfoerdernde-aspekte-en-data.pdf.

[xii] Medizininformatik-Initiative, AG Data Sharing (2020). Übergreifende Nutzungsordnung zum Austausch von Patientendaten, Biomaterialien, Analysemethoden und -routinen im Rahmen der Medizininformatik-Initiative. https://www.medizininformatik-initiative.de/sites/default/files/2020-12/MII_Nutzungsordnung_v1.1.pdf.