Ethics and Biobanking: Module Handbook Version 1.0

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Acronyms

CAB Community Advisory Board

DAC Data Access Committee

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DTA Data Transfer Agreement

ELSI Ethical, legal, social issues

HIC High Income Country

ICF Informed Consent Form

LMIC Low and Middle Income Country

MTA Material Transfer Agreement

PI Principal investigator

PIL Patient Information Leaflet

REC Research Ethics Committee

Definitions

“Use” means the use of samples and or data, distributed by a biobank to a “user” or “recipient” for a purpose defined in an MTA. This may not be the use for which the samples and data were originally collected.

“Re-use” means the use of samples and or data, distributed by a “user” or “recipient” to a third party, for a purpose defined in an MTA between user and the third party The conditions under which a user may have the right to distribute samples and or data received from a biobank to a third party for re-use are set out in the MTA between the biobank and the user.

Background to this Module Handbook

Biobanks are playing an increasingly important role in biomedical research. Biobanks collect and store human biological samples and associated data for future research use. The collection, storage, use, and re-use of these samples and data raise ethical, legal, and social issues (ELSI) that must be addressed. At the heart of some of these issues are the competing interests of the various stakeholders. These stakeholders include the individuals who have donated their samples and data, the biobank, the research community, and the public who have an interest in new drugs or treatments. There is a need to balance these differing rights and interests and enable access to the samples and data while adhering to good ethical practice.

The purpose of this module handbook is to provide ethical guidance on the life cycle of a biobank. Starting with aspects related to governance of biobanks that facilitate the adherence to ethical and technical norms relevant for biobanks, the handbook explains some of the main ethical concerns and concepts such as those related to data collection and processing, consent, vulnerable populations, stigmatization and discrimination, privacy and confidentiality, return of research results, and benefit sharing. All these ethical concepts and issues are relevant for health research in general, but have specific concerns in relation to biobanks, and these are discussed. In discussing these concepts, it is assumed that the biobank per se is not collecting samples but is dependent upon researchers to provide samples to the biobank for future use. These are researchers who are willing to further science over and beyond the immediate research question that their study is addressing. In many cases, based on requirements of the drug and diagnostics developers, biobanks may reach out to clinicians and researchers to request them to provide certain types of samples for the explicit purpose of meeting these requirements. In either case, it is essential that the biobank adheres to high ethical standards.

This guidance is *in addition* to any applicable laws and policies. If any of the guidance conflicts with the national law, it is the national law that must be followed.

The handbook draws on many ethical frameworks, guidelines and other documents that are listed in Appendix 1. In addition, further readings are provided throughout the handbook.

Chapter 1 Governance of a biobank

1.1 Biobanks and importance of good governance

Biobanks are defined as repositories of systematically collected biological material(s) and associated data, often standardized and well characterized, and stored in an organized system so that they can be provided at short notice for downstream future research and/or clinical purposes[1]. The purpose and the future use of samples stored in a biobank is not often known at the time that samples and data are collected. Whoever will be given access to the samples may not be known either. Essentially participants (often already participating in a research study) are asked to provide their biological materials and data for long-term storage without knowing who will use them and for what purpose. It is therefore critical that the processes used in the management of these samples are clear and transparent and there are appropriate mechanisms in place to ensure the ethical use of these samples and data. Such processes and mechanisms are usually delineated within a framework called the governance framework that sets out the purpose of a biobank (usually to contribute to knowledge and human health), the purposes for which samples and data can be accessed, the regulations under which it operates, the roles and responsibilities of the different actors in the biobank, as well as clear lines of accountability. This is important not only to safeguard the ongoing trust of participants, but also the reputation of a biobank[2] and to increase what is sometimes called a biobank's "social license" to operate. A social license refers to the ongoing public support for a biobank. It is based in part on the public and participant trust and confidence in the biobank. Achieving a social license will involve going beyond just following the minimum legal requirements while ensuring that samples and data are used ethically and in line with participants' and societal expectations.[3]

1.1.1 Biobanks and a governance framework

Governance refers to the policies, processes and structures a biobank has adopted to control its operations, make decisions and demonstrate accountability. Governance operates within/is bound by the national and international regulatory regimes including national regulations and ethical guidelines and frameworks relevant to its function. The regulation of biobanks is generally based on multiple, and at times, overlapping laws, regulations, guidelines, and other instruments, many of which are listed in Appendix 1. There is no one governance framework that fits all biobanks. A biobank will need to establish its own governance framework and the documents in Appendix 1 can all be used as source material.

A governance framework that is appropriate to a particular biobank will depend on factors such as the purpose and scope of the biobank; whether retrospective biological materials, prospective materials, or both will be used in the biobank; the country in which the samples and data are to be collected; and the context in which it operates. The governance framework should be publicly available and include certain features, including:

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[1] Organisation for Economic Co-operation and Development (OECD), Best practice guidelines for biological resource centres. https://www.oecd.org/sti/emerging-tech/38777417.pdf, 2012

[2] Paulina Tindana and others, '*"It Is an Entrustment"* : Broad Consent for Genomic Research and Biobanks in sub-Saharan Africa' (2019) 19 Developing World Bioethics 9.

[3] For more on how good governance can improve a biobank's social license to operate, see Felix Gille, Effy Vayena and Alessandro Blasimme, 'Future-Proofing Biobanks' Governance' (2020) 28 European Journal of Human Genetics 989.

- criteria on the collection and storage of samples and data;
- criteria for decisions on access to samples and data;
- processes to track sample and data sharing;
- lines of accountability that identify key individuals and their responsibilities;
- information describing processes on all aspects of the biobank;
- mechanisms to address concerns about sample and data misuse;
- mechanisms to monitor the operations of the biobank.

The governance framework of a biobank as well as applicable laws, regulations, and other binding guidelines will guide the activities of the biobank and the typical participant informed consent practiced, A robust governance framework can also be a safeguard for broad consent if it is adopted.[4]

1.2 Recommended policies, processes, documents, and committees for biobanks

A biobank will need to develop policies and processes as part of its governance. These policies and processes are not intended to be static but should be reviewed periodically in line with changes in the law, professional guidance, and good practice. The processes should be detailed for internal use in Standard Operating Procedures and Work Instructions, on which staff must be trained to ensure compliance.

1.2.1 Policies

The exact number and type of policies will vary depending on the size, purpose, and context of a biobank. They are important to develop as they provide a framework within which the biobank will operate and a foundation on which to build processes and procedures which will comply with ethical and legal requirements. They also establish lines of accountability and provide rationale for both staff of the biobank and the public behind the biobank's processes and decision-making. Policies can also enable biobanks to adhere to international standards and give a basis on which international collaborations will be assessed.

Policies should be publicly available, with date and version. Policies should be approved by the REC.

A biobank, at a minimum, should have the following policies:

- **Consent Policy:** a consent policy defines the principles that will be adhered to when obtaining consent, including the concept of "consent process". It should provide guidelines to the PIs who provide samples to the biobank on the need to engage with communities prior to developing the consent process, the minimum acceptable criteria for consent, the elements to be included in the consent documents, and provide guidance on obtaining consent from vulnerable populations.[5]
- **Access policy**: An access policy is essential for all biobanks. It should provide clear and transparent guidelines on the conditions for access to prospective applicants seeking to use the samples and data of the biobank.

  An access policy should describe the conditions for access, the criteria for access approval, and the decision-making process. An access policy should state, at a minimum:

  - the purposes for which access to samples and/or data can be obtained;
  - the information requirements from applicants, including security safeguards, geographical location, name of the applicant and their institution, and other relevant information;

[4] See module on consent for more information.
[5] See also module on Informed Consent.

- the review and decision making process for deciding on access[6];
- the privacy and security requirements that must be met;
- constraints, and requirements related to benefit sharing and return of research results (if any), and
- any additional requirements if the samples and/or data are shared with an institution in a different country.

Samples are a finite resource and there are justifications for putting limits on the sharing and use of samples that may not apply to data. The access policy should make clear any additional requirements regarding access to samples.

- **Privacy policy**: A privacy policy is a statement on how a biobank protects a participant's data protection rights. The exact details of a policy will vary depending on the national data protection requirements. It should, however, at a minimum describe:

  - how the biobank collects, uses, stores, and shares the participants' data;
  - the rights of participants and how the biobank respects their rights;
  - the lawful basis on which the biobank is processing the data and sensitive personal data;
  - the duration of data retention;
  - the security measures taken by the biobank to protect the personal data;
  - the individual responsible for privacy and data protection within the biobank and their contact details.

  The policy must be written in language that is understandable by participants and the public.[7]

- **Conflict of Interest policy:** The purpose of this policy is to support transparency and integrity of the decision making in the biobank, and ensure that decisions are made free from external, including financial, influences. This policy is directed towards the advisory and decision-making personnel of the biobank. A policy on conflicts of interests defines who the policy concerns, what the biobank means by conflicts of interests, and how it manages them.
- **Data management policy**: The data management policy (or a data management plan) describes the rules, processes, and procedures that the biobank must follow for managing the data and samples throughout their entire life cycle. This is a process that covers collection, storage, use, re-use, and sharing of the data. The data management policy will ensure that data is processed in a consistent manner and in line with ethical, legal, and industry security standards. A data management policy can be important in demonstrating compliance with data protection law. It is also important for maintaining data quality, privacy, security, and for facilitating data access.
- **Communication and engagement policy**: Providing ongoing information to and communication with a biobank's participants and other stakeholders including the public is important for transparency and accountability and can help sustain community and public support for the biobank, which is important for sustainability.[8] Through these mechanisms, a biobank can identify and mitigate ethical or social risks associated with its operations and the research undertaken using its samples. Communication about the activities of the biobank can pre-empt some of the

[6] See also Data Access Committees
[7] See also module on "privacy and confidentiality".
[8] See also module on "engagement".

information needs of the participants and help maintain trust.
Biobanks should have a strategy in place to communicate with and engage with participants and the wider public. A communication policy can describe the stakeholders with whom a biobank intends to engage and the mechanisms that will be used.

- **Return of results policy**: During research, results may arise that may be of importance to participants. International policies on the return of results are still evolving, but there is an emerging consensus that biobanks should at a minimum have a policy on return of results. This policy should be communicated to participants at the time of consent, making it clear if the biobank will return results, what results will be returned, and the process it will follow for the return of results. This policy should also adhere to any national requirements on the return of results, notably, if there is the requirement that genetic results be communicated to participants by a genetic counsellor.[9]
- **Cost recovery policy**: Biobanks cannot charge for samples and data. Biobanks can, however, charge a cost for accessing the samples and/or data to recoup some of the expenses associated with establishing and maintaining the biobank. This can support the financial sustainability of the biobank. Prospective applicants wishing to access bio samples must be informed of the cost recovery policy, and the principles used for determining the cost should be publicly available.[10]
- **Benefit-sharing policy**: The main benefit for the participants and the public in research performed with biobanked samples and data is the advancement of research and improvements in the health and wellbeing of society. Other benefits can accrue in the process of research. The purpose of a benefit-sharing policy is to state how any benefits may be ethically and equitably shared. This must be communicated to participants at the time of consent.[11]
- **Training policy**: It is important that all staff are adequately trained in the legal and ethical responsibilities of the biobank and on all procedures. This includes training on data protection and security, as well as good ethical conduct of biobanks/ ethical principles governing the working of the biobank. A training policy can set out the training requirements for all staff and the approach to verifying competence.

1.2.2 Processes

Processes are high-level descriptions of a sequence of linked activities, each then usually detailed in a standard operation procedure (SOP), designed to achieve a given result. Processes, but not necessarily SOPs, should be made publicly available. These include

1. Recruitment, initial and ongoing training, and competence evaluation.
2. Project management
3. Reception, handling and shipping of samples and data
4. Sample tracking and inventory management
5. Sample access management (distribution)
6. Equipment choice, installation, commissioning, maintenance, performance evaluation, back-up and decommissioning
7. Sample and data processing

[9] See also module “return of results and incidental findings”.
[10] See also module “economic sustainability of the biobank”.
[11] See also module “benefit sharing”.

8. Infrastructure design, maintenance and verification
9. Security assurance for IT systems, physical access and disaster management

1.2.3 Committees

Biobanks establish various committees as part of the overall governance framework. The purpose of these committees is to ensure that the biobank adheres to the policies. Information about each committee should be publicly available. The committees may vary according to the purpose, size, and context of the biobank and should only be created where necessary.
There is only one committee which is required, the Data and sample access committee. This may be two separate committees, one for data, one for samples and data. Some biobanks also have ethics committees; while others consider ethics is a management responsibility, knowing that there is always an external REC to which management can refer if needed.

- **Data and sample access committee.** An important function of a biobank is the sharing of samples and data. The Data and sample access committee (the Access committee) manages access requests in line with the strategy of the biobank, the terms of the informed consent form, and any other conditions set out in the access policy, to promote sample and data sharing, to mitigate risks to the participants, and to ensure the proposed use complies with ethical, legal, and privacy considerations.
  There is no uniformity as to the composition, processes, or frameworks under which the Access Committee operates. These will depend on the purpose and context of the biobank.
  An Access Committee is not an REC. The focus of an REC is protection of participants. Access Committees do not conduct an ethical assessment of the access request. They are not concerned with the primary sample and data collection; their focus is on the re-use of samples and/or data.
  The composition, functioning, and purpose of an Access Committee should be set out in a Terms of Reference (ToR). This ToR should detail the skills and competencies required by Access Committee members. These skills and competencies may vary but they generally include individuals with expertise in data privacy, data security, ethics, patient advocacy, and the subject matter of the data being accessed.[12]

Other biobank committees may include:

- **Ethics** Committee: An in-house Ethics Committee provides advice on ethical issues related to the biobank. It is not an REC and does not perform the duties of an REC. Rather, the focus of an ethics committee is to provide ethical support and guidance to the biobank, in relation to its procedures and processes. It can also provide advice to the biobank if ethical concerns are raised following storage of the samples. This can include supporting the ethical dimensions in the development of relevant policies.
- **Biobank Executive Committee (BEC)/Steering Group**: The BEC or Steering Group is responsible for the overall strategic direction of the biobank. It defines the strategic direction and monitors the progress of the biobank.

[12] For more on Access Committees *see* Phaik Yeong Cheah and Jan Piasecki, 'Data Access Committees' (2020) 21 BMC Medical Ethics 12.

- **Management Committee**: A Management Committee is responsible for the day-to-day management of the biobank. It supports the BEC/Steering Group and implements its decisions.
- **Participant Advisory Group**: A Participant Advisory Group or a Community Advisory Board may be established by a biobank. They will be composed of individuals who have participated in the biobank or are representatives of the community that many of the biobank's participants come from. They provide the biobank with the participant perspective and can provide input, feedback, and guidance on any aspect of the biobank. This process can ensure that the interests and perspectives of the participants are considered by the biobank.
- **Independent Scientific Advisory Committee**: An Independent Advisory Committee can be appointed to provide overall advice and direction on the operations and scientific direction of the biobank. Members appointed will be independent of the biobank. Sometimes this committee is called a Scientific and ethics advisory committee.

1.2.4 Documents

- An overarching mission, vision 'who we are' document

  A mission vision document is an overarching document that explains what the aim of the biobank is, what principles and values it is guided by, how it will implement those principles and values, how the biobank is funded and its governance structure. This document is essential not only for transparency but also is a guiding document for all those who work in/for and support the biobank. By laying out the ethical values and principles upfront, it also supports legitimacy and provides a framework by which to measure accountability. This document provides the rationale for all the policies and processes mentioned above and the templates and documents mentioned subsequently.

- Standard operating procedures

  Standard operating procedures (SOPs) are detailed instructions that interpret processes in operational terms. They will guide biobank staff on all aspects of the biobank's operation. SOPs can ensure consistency in approach to a biobank's processes. SOPs are therefore essential in maintaining sample and data consistency, as well as ensuring privacy and security of the samples and data. Each SOP should have a date and version number. Biobanks typically have a hundred SOPs. Note some biobanks use the term Work Instruction to mean the same as SOP.

- Agreements

    - Material transfer agreements & Data transfer agreements

      A material transfer agreement (MTA) and a data transfer agreement (DTA) are legally binding agreements that govern the transfer of samples and data from the biobank to another entity. They specify the terms and conditions under which the samples and data may be used, including the purpose of research, commercial involvement, proprietary claims, processes of withdrawal of consent, the time limit for which the samples and/or data will be retained, the rights and obligations of the recipients, and destruction and/or return of the samples and data. It also specifies if the recipient may transfer samples and or data to third parties and if allowed then under what conditions.

DTAs in addition should provide clear information on the purpose, collection, use and exchange of genomic and health-related data, including international transfer of data; duration of data storage; identifiability of individuals and data and limits to anonymity or confidentiality of data; communication of results to individuals and/or groups; oversight of downstream uses of data; proprietary claims.

Some countries have a template MTA or DTA that must be followed. For biobanks in a country that does not, the MTA or DTA should, at a minimum:

- specify the parties to the contract;
- describe the samples and/or data being transferred;
- detail the purpose of the transfer and that the use is restricted to this purpose;
- outline the duration of sample and/or data storage;
- identify any further restrictions on the use, re-use and transfer of the samples and/or data;
- specify who owns any resulting intellectual property rights from the use of the samples and/or data;
- describe how privacy will be protected;
- confirm that no attempt at re-identification of participants will be made;
- identify the jurisdiction that governs the MTA or DTA in the event of a dispute.

- Templates
    - Informed consent form template. The informed consent template provides a framework that the PIs can use when developing their individual consent documents. The template provides expectations of the biobank vis-à-vis ethical data collection and the obligations of data collectors and data users that must be included in the consent documents. The module on consent describes in detail informed consent, the elements of a valid informed consent, and the differing models of consent that are relevant for purposes of a biobank.
    - Confidentiality Agreement Template. In the context of a biobank, a confidentiality agreement is a legal document that binds the signatory to keep guard against disclosure of confidential information about donors who have provided their data and samples to the biobank. Usually anyone handling sensitive data in the biobank, and anyone who receives this data must sign a confidentiality agreement. Having a standard template for a confidentiality agreement ensures that everyone handling the data and samples will have signed a standard document.
    - Declaration of Conflicts of Interest template. Members of any external advisory, technical or ethical committees must not allow their personal, financial or other interests conflict, or give the impression of potentially conflicting with their duties. A Declaration of interest form identifies the various conflicts that the biobank is concerned about and acts as a reminder to the committee members to be mindful of their potential conflicts if any. Such a declaration also makes the conflicts known to everyone serving on that committee and to decide whether the conflict is real or perceived, and how those conflicts can be mitigated. In certain situations, the person declaring a conflict will recuse themselves for a particular discussion or even resign from a committee. A template allows the biobank to have a standardized form that can be provided to anyone serving on sensitive committees.

1.3 Communication and engagement

The sustainability of any biobank is in part contingent on the ongoing trust and support of its participants, but also of other partners who are important for the success of the biobank. This can include funders, regulators, staff within the local healthcare systems, the wider public, and the authorities in the provider countries. This support and trust cannot be assumed but must be fostered. A key part of this will be ongoing communication and engagement, and a biobank will need to have a communication and engagement plan in place. A variety of media can be used to communicate with stakeholders. These may include townhall or village level meetings, websites, newsletters, newspapers, radio or TV, apps, and social media. There are two types of engagement that are important for biobanks: community engagement and public engagement.

1.3.1 Community engagement

Community engagement refers to engaging with and building a relationship with the community or population who are involved in the research. For biobanks, community engagement will involve specifically targeting the community/communities from whom samples and data are collected.

There is no one-size-fit-all or template for community engagement as it is deeply contextual.[13] It will depend on the community, the purpose of the biobank, the purpose of the engagement, whether there is a pre-existing relationship with the community, and the funding available, amongst other factors. It is important that a biobank respects any cultural traditions and consults with the relevant gatekeepers (e.g., consult with the village chief, the administrative head of a district or tribal leaders) in advance of any community engagement.

Community engagement can be formal or informal. Formal structures could include the establishment of a community advisory board (CAB).[14] A biobank can consult with a CAB, obtain its input into the development of ICFs and PILs to improve language, and identify cultural considerations that could impact the research.

The purpose of community engagement could be manifold and may involve:

- identifying any cultural issues or other concerns that a community may have with the establishment of the biobank itself or with research on the samples and data;
- identifying the expectations of the community for the biobank;
- obtaining input so that the ICF, PIL, and other relevant documents are culturally appropriate;
- engaging with the development of culturally appropriate governance;
- facilitating feedback of findings;
- building a partnership with the community.

[13] The H3Africa Community Engagement Guideline does provide a useful guide on possible outlines and points to consider when developing a community engagement plan.

[14] Stephen F Morin and others, 'Building Community Partnerships: Case Studies of Community Advisory Boards at Research Sites in Peru, Zimbabwe, and Thailand' (2008) 5 Clinical Trials 147; Charles Rotimi and others, 'Community Engagement and Informed Consent in the International HapMap Project' (2007) 10 Community Genetics 186; Yang Zhao and others, 'Forming and Implementing Community Advisory Boards in Low- and Middle-Income Countries: A Scoping Review' (2019) 20 BMC Medical Ethics 73.

Community engagement can demonstrate that the biobank respects the culture and traditions of the community and thus helps foster a relationship between the biobank and the community. Community engagement can also support the biobank as it can lead to a consent process and governance that is demonstrably informed by and supported by the community. It is also an opportunity to identify and mitigate any research-related concerns or anxieties and thereby pre-empt potential problems.

Community engagement can also involve feedback of findings to the community. This feedback is important as it demonstrates respect and acknowledges the community's important contribution to the research. Community engagement can thus be a mechanism for building rapport with the community, and sustaining their support, while also providing a safeguard for broad consent.[15] Community engagement thus is not only important for the biobank itself, but it is increasingly seen as an important component of the ethical conduct of research.[16]

1.3.2 Public engagement

Public engagement is focused on engaging with those who may not be directly involved in the research itself. Like community engagement, the approach to public engagement is context-specific, depending on the public or publics a biobank may want to engage with, and the purpose of that engagement. Public engagement can keep the public informed and updated about the research activities of the biobank.

When developing a public engagement plan, a biobank must keep in mind that the "public" should not be seen as a monolithic entity, but rather composed of differing "publics", each of which may have their own interests in the biobank.[17] These differing publics may be researchers, the healthcare system, regulators, or the wider public. Each may require different mechanisms of engagement.

[15] See module on consent.

[16] Some resources on practical experiences with community engagement are: Angela Beaton and others, 'Engaging Māori in Biobanking and Genomic Research: A Model for Biobanks to Guide Culturally Informed Governance, Operational, and Community Engagement Activities' (2017) 19 Genetics in Medicine 345; KM Haldeman and others, 'Community Engagement in US Biobanking: Multiplicity of Meaning and Method' (2014) 17 Public Health Genomics 84; Amaya M Gillespie and others, 'Social Mobilization and Community Engagement Central to the Ebola Response in West Africa: Lessons for Future Public Health Emergencies' (2016) 4 Global Health: Science and Practice 626; Irene Jao and others, 'Involving Research Stakeholders in Developing Policy on Sharing Public Health Research Data in Kenya: Views on Fair Process for Informed Consent, Access Oversight, and Community Engagement' (2015) 10 Journal of Empirical Research on Human Research Ethics 264; Paulina Tindana and others, 'Community Engagement Strategies for Genomic Studies in Africa: A Review of the Literature' (2015) 16 BMC Medical Ethics 1; Morin and others (n 13); Paulina O Tindana and others, 'Grand Challenges in Global Health: Community Engagement in Research in Developing Countries' (2007) 4 PLOS Medicine e273; P Tindana and others, 'Developing the Science and Methods of Community Engagement for Genomic Research and Biobanking in Africa' (2017) 2 Global Health, Epidemiology and Genomics e13; Megan M Campbell and others, 'Exploring Researchers' Experiences of Working with a Researcher-Driven, Population-Specific Community Advisory Board in a South African Schizophrenia Genomics Study' (2015) 16 BMC Medical Ethics 45; Haldeman and others; Rotimi and others (n 13).

[17] Ulrike Felt and Maximilian Fochler, 'Machineries for Making Publics: Inscribing and De-Scribing Publics in Public Engagement' (2010) 48 Minerva 219; Sara Chandros Hull and David R Wilson (Diné), 'Beyond Belmont: Ensuring Respect for AI/AN Communities Through Tribal IRBs, Laws, and Policies' (2017) 17 The American Journal of Bioethics 60. Sonja Erikainen and others, 'Public Involvement in the Governance of Population-Level Biomedical Research: Unresolved Questions and Future Directions' (2021) 47 Journal of Medical Ethics 52

1.4 Sustainability of the biobank

Biobanks are an important resource. Participants have given their samples and data in good faith that they will be used for the purposes given at the time of consent. There is an ethical obligation to ensure the sustainability of the biobank and it is important that biobanks develop a sustainability plan.

Biobanks may be funded through grants, but other mechanisms should be considered to ensure their economic sustainability. It is unethical (and generally illegal) to receive payment for samples and data. However, biobanks can charge for the costs associated with providing access to the samples and data. This can include the costs of the infrastructure, staffing, consumables, other equipment, as well as the cost of collecting and maintaining the resource. Biobanks should develop a cost recovery plan, taking into consideration these various factors.

In considering the pricing structure, biobanks can introduce differing cost recovery regimes depending on the recipient of the samples and/or data, whether the recipient is commercial, and the country in which they are based , i.e., a higher price can be charged to a commercial entity than an academic entity, and a higher price can be charged for an institution in a high income country (HIC) than a lower and middle income country (LMIC). Costs recovered from distribution of samples are usually insignificant compared to the costs of operating a biobank. Taking that with the generally low rates of use of samples has led many biobanks to charge only the direct costs of packing and shipping, at least to academic users.

1.4.1 ISO Accreditation

The international Organization for Standardization (ISO) has several standards that relate to biobanks. They include:

- ISO 20387:2018 (Biotechnology — Biobanking — General requirements for biobanking) on general requirements for the competence, impartiality and consistent operation of biobanks. Also allows biobanks to obtain accreditation for their activities, thus formalizing their competence.
- ISO/TR 22758:2020 (Biotechnology - Biobanking - Implementation guide for ISO 20,387) which provides support for implementing the requirements of ISO 20387:2018.

Biobanks are encouraged to work towards accreditation.

Chapter 2 Data Access and Data Protection

2.1 Data Access, sharing & dissemination

The core purpose of biobanks is making samples and data available for research to increase scientific knowledge and reproducibility, develop new and better treatments and improve health care decisions. Providing access to these samples and data, however, can impact on the rights and interests of participants, including their right to privacy,[18] right to autonomy,[19] and right to non-discrimination.[20] This is a core tension that biobanks must navigate: how to encourage and optimize the use of the resource for research that is for the public good, while protecting the rights and interests of participants.

Biobanks must put in place measures to help balance these competing rights and interests. Samples and data must be shared in a manner that minimizes risk to the participants and their community and maximizes the benefit for society. A clear and publicly accessible Access Policy must set out the conditions for obtaining access to the samples and data. The detailed procedures based on the policy must ensure that the use of the samples and data is in line with the consent, and that sample and data use ensure ongoing protection of participants' right to privacy. The procedures must also avoid stigmatizing and discriminating against participants and should guard against re-identification. The procedures must make clear the responsibilities of the users of the samples and data and the conditions of sample and data access. Samples and data can only be shared with those who agree to uphold these conditions of use in legally binding agreements. Biobanks should recognize and be committed to follow "the FAIR principles[21] to enable the reusability of their data. In addition, biobanks should follow the CARE principles, where applicable, which describe how data should be treated to ensure indigenous rights over its use are respected.[22]

As a condition to making the samples and data available for research, the access policy must require that the dissemination of research results by the researchers who accessed the samples does not result in stigmatization of or discrimination against the participants or their community. This is important for public accountability.

Embargos on sharing can be ethically permissible if they are justified, e.g., time needed for data analysis, preparation of results, and/or issues related to intellectual property. The time limit of any such embargos must be proportionate and minimized as far as possible.

[18] See module on privacy and confidentiality, and module on data protection and biobanking.
[19] See module on consent.
[20] See module on stigmatization and discrimination.
[21] Mark D Wilkinson and others, 'The FAIR Guiding Principles for Scientific Data Management and Stewardship' (2016) 3 Scientific Data 160018.
[22] Stephanie Russo Carroll and others, 'Operationalizing the CARE and FAIR Principles for Indigenous Data Futures' (2021) 8 Scientific Data 108.

2.2 Data protection

2.2.1 Background

The introduction of data protection regulations across the world (which govern the *processing* of *personal data* – see definitions below) has strengthened the protection of personal data. While these regulations are important, they are not the only regulations that apply to research. Researchers must still follow all other applicable legislation and ethical guidance.

Data protection regulations generally set out the principles and conditions that must be met in the processing of personal data, as well as the rights of data subjects. Data protection regulations are general legal frameworks, as they apply to the processing of personal data in all sectors, i.e., the same rules apply to the processing of personal data in the banking sector as by social media.

They are in general strict, and if applied as stated, can limit the use of personal data for research purposes. However, most data protection regulations provide some exceptions to the strict processing requirements if the processing is for research. Some also have extra provisions in place for the processing of genetic data. The exact exceptions vary from country to country, so it is important that biobanks be aware of the specific national data protection requirements that apply.

The discussion in this section will reflect on data protection regulations generally and not those of a specific country, though the European regulations, GDPR, are frequently referred to. There are likely to be differences, requirements and more detail in national frameworks than what is stated here. If there is no data protection regulation available, it may be used to guide the processing of personal data in your biobank so that personal data is processed in line with good practice.

2.2.2 Definitions

- "Personal data" means any information relating to an identified or identifiable natural person ('data subject') such as name, identification number, location data, online identifier or other factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person[23].
- "Processing" means any operation or set of operations which is performed on personal data or on sets of personal data. This includes the collection, recording, organization, structuring, storage, use, dissemination etc. of personal data.
- "Anonymization" of personal data means rendering personal data anonymous in such a manner that the data subject is not or is no longer identifiable. Anonymized data is usually not covered by data protection regulations
- "Pseudonymization" means the processing of personal data in such a way that the data can no longer be attributed to a specific data subject without the use of additional information, as long as such additional information is kept separately and subject to technical and organizational measures to ensure non-attribution to an identified or identifiable individual" (GDPR Article 4(3b)). Pseudonymized data is usually covered by data protection regulations. This type of data is also referred to as "coded" or "de-identified".
- "Special categories" of personal data include health data, genetic data, and data revealing racial or ethnic origin. So, all kinds of data that a biobank will be processing.

[23] https://gdpr-info.eu/art-4-gdpr/

2.2.3 Application of data protection regulations to biobanking

The goal of data protection is not the restriction of the use of personal data or restricting data sharing. Rather it is about ensuring that personal data is used and shared in a manner that protects privacy rights (see section on privacy and confidentiality above).

Data protection regulations do not apply to anonymized data, if re-identification is not possible. Data protection regulations also do not apply to the sample itself. Generally, they apply only to the data from a sample that is identifiable, which includes pseudonymized data. There are some exceptions to this rule (e.g., Italy explicitly applies the GDPR to biological samples in its national framework), but generally it is the data from the samples only that falls under data protection regulations. For confirmation, consult your national data protection regulation.[24]

Since biobanks also process special categories of personal data such as health related and genetic data, there are additional rules and processes that must be followed for this type of data.

There is discussion and uncertainty in the literature as to whether genetic data can be considered anonymous under data protection law.[25] Biobanks should refer to the applicable national law for the scope of the data protection regulations and make an assessment based on the criteria set out.

2.2.4 Key individuals in data protection law

The following are the key individuals in data protection law, though the exact titles and descriptions may vary. In the context of biobanks, the data subject is the participant, and the data controller is the biobank.

Data controller: This is the person or legal entity who is deciding the purpose and the means of the processing (i.e., the purpose of the biobank and how the aims of the biobank will be achieved). This is the person or legal entity who is responsible for ensuring that the principles of data protection are met. In the biobank context, it may be the manager of the biobank or the employer of the manager.

Data processor: This is not directly employed by the data controller but processes personal data under the direction of the data controller. They may be consultants, for example. The data controller is generally responsible for ensuring that the data processor meets the principles of data protection.

Data protection officer: This is an individual within an organization appointed to advise and promote compliance with the data protection law.

Data subject: This is the person to whom the personal data relates. In the biobanking context, it will be the research participant.

Data recipient. The researcher who receives data from the biobank is the data recipient. There is a duty on the biobank to ensure the recipient commits to adhering to certain data protection provisions.

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[24] Santa Slokenberga, Olga Tzortzatou and Jane Reichel, *GDPR and Biobanking - Individual Rights, Public Interest and Research Regulation across Europe* (Springer 2020) <https://www.springer.com/gp/book/9783030493875> accessed 21 July 2020.

[25] Mahsa Shabani and Luca Marelli, 'Re-Identifiability of Genomic Data and the GDPR: Assessing the Re-Identifiability of Genomic Data in Light of the EU General Data Protection Regulation' (2019) 20 EMBO reports.

Supervisory authority: This is a national independent body established to monitor and enforce compliance with the law.

2.2.5 Principles of data processing

The principles below are the principles that generally can apply in the processing of personal data. The exact formulation and scope of these principles vary according to the national legislative framework, and biobanks must consult the applicable national regulations.

1. **Lawfulness, fairness, and transparency**: Personal data must be processed lawfully, fairly, and transparently in relation to the data subject. Lawful means that there must be a legal basis for the processing of the personal data based on one of the grounds set out in the regulation. The processing of special categories of personal data is generally not permitted unless it falls within one of the permitted grounds. Some data protection regulations have scientific research as one of the permitted grounds.
2. **Purpose limitation**: Personal data should be collected for specified, explicit, and legitimate purposes and not further processed in a manner that is incompatible with those purposes. This means that the purpose must be clearly set out. Some data protection regulations have special provisions for scientific research within this provision.
3. **Data minimization**: Only the data that is necessary for the specific purpose should be collected and processed. It is essential that only the minimal amount of data that is required to achieve the objectives of the data processing is used. Some data protection regulations have special provisions for scientific research within this provision.
4. **Accuracy**: Personal data must be accurate and, where necessary, kept up to date. Processes should be in place to ensure that all personal data that is collected is accurate.
5. **Storage limitation**: Personal data should be kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the personal data are processed. Once the objective of the processing has been achieved, the data should be deleted. Data that is rendered anonymous does not fall under data protection law. However, to anonymize the data, one must still have a lawful basis to do so. Some data protection regulations have special provisions for scientific research within this provision.
6. **Integrity and confidentiality**: Personal data should be processed in a manner that ensures appropriate security, including protection against unauthorized or unlawful processing and against accidental loss, destruction, or damage, using appropriate technical or organizational measures. It is essential that both organizational and technical measures are put in place to secure the data. The data protection regulations do not specify the exact security measures that must be introduced. The focus is on the security risks that you generally need to guard against.

2.2.6 Consent & data protection regulations

Consent is generally a lawful ground for the processing of personal data and processing of special personal data. In some countries, consent is the *only* lawful ground for the processing of genetic data for research. It is important that biobanks first consult the national data protection regulations to determine the possible lawful grounds for the processing of personal data for the biobank.

But consent as a lawful basis for the processing of personal data is not necessarily the same as the ethical principle of consent.[26] Consent under data protection law is generally defined as being a *freely given, specific, unambiguous* indication of the data subject's wishes.

In some jurisdictions broad consent is not considered to meet the requirements of consent under data protection law due to the lack of a specifically defined purpose. In such countries, biobanks wishing to use broad consent for prospective collections can proceed to obtain the consent of participants under a broad consent framework, provided that in addition they can identify a legal basis that supports this framework. For example, the European GDPR provides for the use of broad consent if it is in "keeping with recognized ethical standards for scientific research"[27]. In Germany for example, this includes an effective governance such as oversight by ethics committees, effective organizational measures to safeguard confidentiality and comprehensive information for participants and public transparency[28].

Biobanks seeking the use of retrospective samples and data through a waiver of consent will also need to identify a lawful basis other than consent.

2.2.7 Data subject rights

Data subjects have rights that the Data Controller must protect. These rights can vary according to the national framework but can include:

(1) **Right to be informed**: The Data Subject has the right be informed about what their personal data will be used for.
(2) **Right to access**: The Data Subject has the right to access personal data that the Data Controller has about them. The Data Controller should have in place a process to facilitate this.
(3) **Right to rectification**: The Data Subject has the right to have inaccurate personal data corrected and incomplete data completed.
(4) **Right to erasure**: The Data Subject has the right to request that their data is erased.
(5) **Right to restriction of processing**: The Data Subject can request that the Data Controller stop processing their personal data.
(6) **Right to data portability**: The Data Subject has the right to move their data from one Data Controller to another.
(7) **Right to object**: The Data Subject can object to the processing of their personal data where the lawful basis of processing is not consent.
(8) **Rights in relation to automated decision-making and profiling**: The Data Subject has the right to object to a decision based solely on automated processing.

Some data protection regulations do provide exceptions to some of these rights if the processing is for research.[29]

[26] Edward S Dove and Jiahong Chen, 'Should Consent for Data Processing Be Privileged in Health Research? A Comparative Legal Analysis' (2020) 10 International Data Privacy Law 117.
[27] https://gdpr-info.eu/recitals/no-33/
[28] https://pubmed.ncbi.nlm.nih.gov/35643273/
[29] Ciara Staunton, 'Individual Rights in Biobank Research Under the GDPR' in Santa Slokenberga, Olga Tzortzatou and Jane Reichel (eds), *GDPR and Biobanking: Individual Rights, Public Interest and Research Regulation across Europe* (Springer International Publishing 2021) <https://doi.org/10.1007/978-3-030-49388-2_6> accessed 20 May 2022.

2.2.8 Safeguards for data subjects when processing is for research

As discussed throughout, data protection regulations often have exceptions to some of the strict processing requirements if the processing is for research purposes. If an exception is invoked in relation to research, data protection regulations often state that appropriate safeguards must be established. Guidance on what are considered "appropriate safeguards" is limited, but biobanks can look to other ethical principles for guidance.[30]

2.2.9 Data protection impact assessment (DPIA)

Countries in the EU and EEA and possibly others require a DPIA when the processing is likely to result in a high risk to the rights and freedoms of the data subjects. As part of a DPIA, you will need to carry out a risk assessment of your processing activities to identify and minimize risks to data subjects. Biobanks generally process health data and genetic data, and it is quite likely that they will be high risk and require a DPIA. Prior to establishment biobanks should consult their national law to determine if a DPIA is required.

2.3 Data sharing in the context of International collaborative research

International collaborative research is important in research, and sample and data sharing are a part of that. Currently there is bias and a lack of representation in global datasets, with datasets generally representative of Caucasian populations. As a result, the clinical and health outcomes will be less relevant for populations from diverse clinical ancestry.[31] International collaborative research that provides access to underrepresented populations is thus important.

In the past, international research was often exploitative. Samples and data were collected and taken from local populations for research in laboratories in high income countries. This practice, often referred to as "parachute research", meant that samples and data were not used for research to the benefit of the local population and not subject to local oversight or governance.[32] This has resulted in some mistrust in collaborations[33], and in increasingly strict contractual conditions on the collaboration.

It is essential that any international collaborative research is non-exploitative, is for the benefit of the local population from which the samples came, and works toward remedying global health inequity. Biobanks must be mindful of any power imbalances that may exist when providing access to samples and data. International collaborative research can help address health research inequalities by including capacity building as part of the research. The type of capacity building should be proportionate to the research.

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[30] Ciara Staunton and others, 'Appropriate Safeguards and Article 89 of the GDPR: Considerations for Biobank, Databank and Genetic Research' (2022) 13 Frontiers in Genetics <https://www.frontiersin.org/article/10.3389/fgene.2022.719317> accessed 20 May 2022.

[31] Segun Fatumo and others, 'A Roadmap to Increase Diversity in Genomic Studies' (2022) 28 Nature Medicine 243.

[32] Billie-Jo Hardy and others, 'South Africa: From Species Cradle to Genomic Applications' (2008) 9 Nature Reviews Genetics S19.

[33] NS Munung, BM Mayosi and J de Vries, 'Genomics Research in Africa and Its Impact on Global Health: Insights from African Researchers' (2018) 3 Global Health, Epidemiology and Genomics <https://www.cambridge.org/core/journals/global-health-epidemiology-and-genomics/article/genomics-research-in-africa-and-its-impact-on-global-health-insights-from-african-researchers/201362D87E263FA7CC475B176EDCE7A7> accessed 22 September 2021.

2.3.1 Transborder flow of personal data

If it is intended to share samples and/or data with researchers outside the provider country, this must be specified in the informed consent. This also must be included in the research protocol and approved by an REC. Biobanks must be aware that there are often local restrictions on the cross-border sharing of samples and data. This may include that such sharing can only occur if there is a PI from the provider country, if there is REC or some other national approval, or other restrictions. Biobanks must ensure that any cross-border sharing of samples and data is in line with requirements as specified in applicable data protection regulations. There should be appropriate attribution of the sample and data collectors.

The transborder flow of personal data especially between well-resourced and less resourced countries can become complicated if the data protection regulations in the two countries are not compatible.

At a higher level than that of the biobank, simple solutions need to be found that are safe and respectful of fundamental rights that do not conflict with other countries' laws or with regulations of international organisations.[34] Such solutions could include an equivalence of regulations in the recipient and donor country, adequacy of safeguards in the recipient country, or contractual clauses between donor and recipient (such as an MTA) that require protections to participants data as per international guidelines, but none of these solutions is ideal.

A framework for the responsible sharing of data and conduct of research that is acceptable to all stakeholders including those in less developed countries may be more promising[35]. Such a framework would rest on the following principles:

- Respect Individuals, Families and Communities
- Advance Research and Scientific Knowledge
- Promote Health, Wellbeing and the Fair Distribution of Benefits
- Foster Trust, Integrity and Reciprocity

and would include elements of transparency; accountability, engagement; data quality and security; privacy, data protection and confidentiality; risk-benefit analysis; recognition and attribution; education and training; sustainability; and accessibility and dissemination[36].

[34]

[35] https://www.ga4gh.org/framework/

[36] Ibid above

Chapter 3. Ethical issues and concerns

3.1 Consent

3.1.1 Consent in the context of health research

2.1.1 Background

Informed consent is a fundamental principle of modern biomedical research. Freely given informed consent must be obtained prior to research on humans.[37] First stated as a key principle in the Nuremberg Code, the importance of informed consent has been reiterated in all subsequent codes, guidelines, and other texts on ethics in research (e.g., Declaration of Helsinki) as it is an expression of our right to autonomy and demonstrates respect for persons.[38] All individuals capable of giving consent have the freedom to decide whether they want to participate in research.

The ICF and PIL are important in protecting the autonomy of participants. These documents provide mechanisms through which information is provided to participants, enabling them to make informed choices about their involvement in the research. The information must be provided to participants in a language that is clear and understandable to them. The discussion in this section pertains to the ethical principle of consent. Please refer to the module on data protection for discussion on consent as a lawful basis for the processing of personal data.

3.1.2 Elements of consent

There are four elements to a valid consent:

1. It must be given by a person who has capacity to consent.
2. The consent must be voluntary.
3. The consent must be informed.
4. Participants must be able to withdraw their consent.

3.1.2a Capacity

In the context of an informed consent, the concept of 'capacity' can be broken down into the following – the person can understand what is written either by reading or having it explained by a trusted third party; can understand the consequences of taking part in the said activity i.e. can understand what the consequences and the risks described in the ICF are, and what the benefits mean to them; can understand that they can say 'No' or withdraw their consent at any time; and understand they can ask questions at any time. Generally, a person is considered to have the capacity to consent to research if they are 18 or older. This age, and the circumstances in which a person under the age of 18 can consent to research, can vary according to the relevant national law. It is important to remember that the legal age to consent to medical treatment is often not the same as the legal age to consent to research.

Some adults (aged 18 or older) lack the capacity to consent either because they are mentally challenged or have other disabilities which preclude their understanding. They are usually considered vulnerable

[37] Ezekiel J Emanuel, David Wendler and Christine Grady, 'What Makes Clinical Research Ethical?' (2000) 283 JAMA 2701; Ezekiel J Emanuel and others, 'What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research' (2004) 189 The Journal of Infectious Diseases 930.

[38] Evelyne Shuster, 'Fifty Years Later: The Significance of the Nuremberg Code' (1997) 337 New England Journal of Medicine 1436.

participants and there are extra protections in place for these individuals (see next section on vulnerability). If capacity is in doubt, an assessment of capacity must be done in line with applicable national law and/or national guidance. If an adult is deemed to lack capacity, a legally authorized representative may be able to provide consent on their behalf, if provided for by national law. The assent of the person who lacks capacity on whom the research is to be conducted should also be obtained where possible in line with national law.

3.1.2b Voluntary

A participant's decision to participate in research must be voluntary and free from undue influence. Factors impacting voluntariness may be intrinsic to the participant (e.g., they may be part of a vulnerable population) or extrinsic to the participant (e.g., power imbalance between the participant and the researcher or others in a close relationship putting pressure to participate). Not all factors can be assumed to be undue influence but must be assessed considering the context.

At times participants are compensated for their involvement in research. Concerns have been expressed that compensating participants for their involvement in research could be an inducement to participate. However, paying a participant can be ethical if appropriately estimated to compensate them for their time, expense, and the inconvenience of being involved in research.[39] Any proposed compensation must be submitted for approval by an REC in advance.

3.1.2c Informed

Participants must be informed about the purpose of research, potential risks to them, and measures to mitigate these risks, as well as the potential benefits of the research. This information should be provided in a PIL, but other forms of media (e.g., video, computer game, comic book) can be developed and used.[40] The information must be provided in a language the participant can understand. Participants must be afforded the opportunity to ask questions of the study team and have sufficient time to consider their involvement in the research. Should they decide to participate, participants should sign and date an ICF. The PIL and the ICF should be reviewed and approved by the REC.

3.1.2d Withdrawal of consent

Participants can alter their consent or withdraw their consent at any time. Participants must be informed about their right to withdraw their consent during the consent process and how they may withdraw their consent.

Participants must also be informed at the time of consent about any limits that there may be on their ability to withdraw their consent during this time. For example, if the samples and/or data have been anonymized they must be informed that it will not be possible to identify their samples and/or data. Participants must also be informed if it is not possible to withdraw samples and/or data that have been distributed to a user, or data that needs to be retained for audit purposes.

The options for withdrawal should be presented to participants at the time of consent. The options may be:

[39] Martin Wilkinson and Andrew Moore, 'Inducement in Research' (1997) 11 Bioethics 373.
[40] Some examples of other media are: Biobanking and Beyond - YouTube. Genome Adventures - Blog (weebly.com)

- No further use: the biobank will no longer use the samples and data in future research but will continue to use them for research that has been initiated.
- No further contact: participants will no longer be contacted by the biobank but the use of their sample and data will continue.

3.1.3 Consent in the context of biobanks

Even though biobanks themselves normally do not collect samples or data but act as their repositories, they have a responsibility to ensure that the samples and data stored have been collected and managed in an ethical manner. The manager of the biobank is responsible for ensuring that informed consent has been obtained by the members of the study team in an ethical manner, respecting all elements mentioned above. The study team must be appropriately trained and have sufficient knowledge and skills to be able to use the ICF to discuss the proposed collection of samples and data, the purpose of the establishment of the biobank, the potential risks to the individual, the potential benefits, and other factors that may be relevant. The ICF and PIL are important tools in promoting transparency and accountability of the biobank.

In the biobank context the following information should, at a minimum, be provided in the PIL and ICF:

- the purpose of the biobank;
- the potential risks associated with the collection, storage, use, and re-use of samples and data;
- governance arrangements of the biobank and how access to the samples and data will be provided;
- duration of storage;
- if consent to access participants' medical records is to be obtained;
- the right to withdraw at any time, and any limits on that withdrawal;
- the possibility that participants may be re-contacted by the biobank & the likely purpose of the re-contact;
- whether any individual results will be fed back to participants;
- whether a commercial entity can be given/apply for access to samples and data; and
- safeguards that will be maintained for samples and data, and how participants' privacy will be protected.

3.1.4 Types of consent models for biobanks

The informed consent process has undergone some development with the emergence of research performed with biobanked samples and data. There are different models that can be used by biobanks:

- Specific informed consent
- Broad consent
- Tiered consent
- Dynamic consent.

Some countries have specific rules on consent. Before determining the most appropriate model to be used, biobanks must first consider the consent models that are legally and ethically permitted in the country where they are intending to collect samples and data. Whichever consent model is used, biobanks must remember that informed consent is an ongoing process and not one that begins and ends with the signing of the ICF.

3.1.4a Specific consent

Specific consent is consent for a specific research project when the purpose of the research is known at the time of collection and participants are informed about the potential risks and benefits of that research. The samples and data may be stored for future use but can only be used for the research purposes for which consent has been obtained. Use of the samples and data beyond this use requires participants to be re-contacted and re-consented for a new research project, which is cumbersome and, in many cases, impossible. Alternatively, a waiver of consent (if legally available) might be obtained from an REC.

3.1.4b Broad consent

The ease with which samples and data can be used and re-used with no additional *physical* risk to participants has led to changes to the specific consent paradigm.[41] Although there is no extra physical risk, the re-use of samples and data does raise risks related to privacy, stigmatization, and discrimination.[42]

Broad consent is a consent model that has been developed to enable participants to give their consent to future unspecified research or broad categories of research.[43] There is no one accepted definition of broad consent, but it generally refers to a process whereby participants consent to the use of their samples and data for future research, within defined but broad parameters.

With broad consent, future research uses may not be known. Thus, it will not be possible to specify the potential risks and benefits of the research. Participants must nevertheless be informed about the purpose of the biobank; the potential risks associated with the collection, storage, use, and re-use of their samples and data; governance arrangements of the biobank; and how access to the samples and data will be provided.

The broader the consent (i.e., the more unspecified the use), the more safeguards (e.g., community engagement) that are required to mitigate the broadness of the consent. What is important is that the future research is approved by an REC which will determine whether the use of the samples and/or data in research is in line with the original consent provided. It is also important that the biobank has appropriate checks and balances to ensure that the samples are managed ethically and access to samples by third parties is scrutinized by a data access committee. It is for this reason that broad consent has been referred to as "consent to governance", as participants are granting the biobank the use of their samples and data for future unspecified purposes, on the promise that the future research is subject to oversight.[44]

[41] David M Secko and others, 'Informed Consent in Research performed with biobanked samples and data: A Deliberative Approach to the Debate' (2009) 68 Social Science & Medicine 781.
[42] Jane Kaye and others, 'Data Sharing in Genomics — Re-Shaping Scientific Practice' (2009) 10 Nature Reviews Genetics 331; Francesca Forzano and others, 'ESHG Warns against Misuses of Genetic Tests and Biobanks for Discrimination Purposes' [2021] European journal of human genetics: EJHG.
[43] David Wendler, 'Broad versus Blanket Consent for Research with Human Biological Samples' (2013) 43 The Hastings Center report 3.
[44] Barbara A Koenig, 'Have We Asked Too Much of Consent?' (2014) 44 The Hastings Center Report 33; Paulina Tindana and Jantina de Vries, 'Broad Consent for Genomic Research and Biobanking: Perspectives from Low- and Middle-Income Countries' (2016) 17 Annual Review of Genomics and Human Genetics 375.

Concerns have been raised about broad consent, including that it is not fully informed.[45] There has also been resistance to its use in some regions, in part due to previous exploitative research practices.[46] It is worth noting that, having considered the ethical acceptability of broad consent, and through engagement with REC members across the African continent, the H3Africa Framework for Best Practice for Genomics Research and Biobanking in Africa views broad consent as a "best compromise".[47] This is provided that it is supported by community engagement and accompanied by a mechanism such as a data access committee that supports accountability and equity in the use of the resources.

3.1.4c Tiered consent

In response to concerns about the use of broad consent, tiered consent has been proposed as an ethically preferable alternative model as it provides participants with more options.[48] Under a tiered consent model, participants are presented with a range of consent preferences, which can include the use of their sample in a specific study, use for a particular illness, and use in future unknown research. Participants can tick boxes to indicate what they consent to (and what they do not consent to). As participants have more options, a participant's right to autonomy is respected.[49] While a tiered consent is ethically more robust, tracking and monitoring compliance with the participants' choices can be expensive and problematic. Tiered consent may also create obstacles to research if the initial consent or its limitations are vaguely worded.

3.1.4d Dynamic consent

A more recent theoretical consent model that has been developed and used in the biobank context is dynamic consent.[50] Dynamic consent uses information technology and digital technologies to enable participants to change and update their consent preferences over time, as well as receive information on the use of their data and sample in research.[51] At the time of recruitment, participants can be asked to

[45] Mark Sheehan, 'Can Broad Consent Be Informed Consent?' (2011) 4 Public Health Ethics 226.
[46] Ciara Staunton and Jantina de Vries, 'The Governance of Genomic Research performed with biobanked samples and data in Africa: Reframing the Regulatory Tilt' [2020] Journal of Law and Biosciences 1.
[47] Jantina de Vries and others, 'Regulation of Genomic and Biobanking Research in Africa: A Content Analysis of Ethics Guidelines, Policies and Procedures from 22 African Countries' (2017) 18 BMC medical ethics 8; Jantina de Vries and others, 'Addressing Ethical Issues in H3Africa Research–the Views of Research Ethics Committee Members' (2015) 9 The HUGO journal 1.
[48] Victoria Nembaware and others, 'A Framework for Tiered Informed Consent for Health Genomic Research in Africa' (2019) 51 Nature Genetics 1566.
[49] Nicki Tiffin, 'Tiered Informed Consent: Respecting Autonomy, Agency and Individuality in Africa' (2018) 3 BMJ Global Health e001249.
[50] Deborah Mascalzoni and others, 'Ten Years of Dynamic Consent in the CHRIS Study: Informed Consent as a Dynamic Process' (2022) 30 European Journal of Human Genetics 1391; Nicholas Mamo and others, 'Dwarna: A Blockchain Solution for Dynamic Consent in Biobanking' (2020) 28 European Journal of Human Genetics 609; Harriet JA Teare, Megan Prictor and Jane Kaye, 'Reflections on Dynamic Consent in Biomedical Research: The Story so Far' (2021) 29 European Journal of Human Genetics 649; Susan E Wallace and José Miola, 'Adding Dynamic Consent to a Longitudinal Cohort Study: A Qualitative Study of EXCEED Participant Perspectives' (2021) 22 BMC Medical Ethics 12; MK Javaid and others, 'The RUDY Study Platform – a Novel Approach to Patient Driven Research in Rare Musculoskeletal Diseases' (2016) 11 Orphanet Journal of Rare Diseases 150.
[51] Jane Kaye and others, 'Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks' (2015) 23 European Journal of Human Genetics 141; Isabelle Budin-Ljøsne and others, 'Dynamic Consent: A Potential Solution to Some of the Challenges of Modern Biomedical Research' (2017) 18 BMC Medical Ethics 4; Mascalzoni and others (n 32).

participate in the biobank and may be invited to select preferences on the use of their samples and data in research.

The dynamic consent interface will be demonstrated to participants, including how they will receive information, how to update their preferences on receiving information on the use of their samples and data, and how to update their consenting preferences.

The advantage of a dynamic consent model is that it enables participants to tailor their consent choices to their own preferences, and change their preferences over time, thus giving more control to participants over their future sample and data use. This is important as empirical research does indicate that some participants want more control over their sample and data use and that participants' preferences change over time.[52] The platform also enables the biobank to easily contact their participants to obtain consent for research that they may not have consented to, or to obtain consent to access to participants' medical records, for example. It is also a platform that can provide transparent information to participants on the use of their data and sample in research.

The disadvantage of a dynamic consent model is that it requires IT infrastructure and security measures to support the system, which are expensive. It will also not be suitable for participants who may not be digitally literate or do not have the necessary phone or other required infrastructure. Thus, any use of dynamic consent will also need to be supported by systems that, for example, enable participants to call a phone number to update their consent preferences and receive information to ensure that they are not excluded. Concerns have also been raised that contacting participants about new studies too frequently could lead to consent fatigue and thus a superficial or shallow engagement with the consent process.

3.1.4e Blanket consent

Blanket consent is where participants donate their samples and data without any restrictions on access or oversight.[53] It is generally not permitted and is considered unethical.

3.1.4f Informed opt-out and residual samples

Samples left over after clinical diagnosis or treatment may also be of use to researchers. In some countries these leftover samples can be used for research unless the patient takes the initiative to opt-out. This may be for specific research or more broadly defined research. This is known as an informed opt-out for the prospective use of left-over clinical samples. For it to be applicable patients must be:

- informed about the possibility of the use of their samples in research;
- provided with information on the use of their samples;
- informed about their right to withdraw from research; and
- can opt out of the use of their samples in research.

[52] Anna Middleton and others, 'Global Public Perceptions of Genomic Data Sharing: What Shapes the Willingness to Donate DNA and Health Data?' (2020) 107 The American Journal of Human Genetics 743; Pam Carter, Graeme T Laurie and Mary Dixon-Woods, 'The Social Licence for Research: Why Care.Data Ran into Trouble' (2015) 41 Journal of Medical Ethics 404; James Brian Byrd and others, 'Responsible, Practical Genomic Data Sharing That Accelerates Research' [2020] Nature Reviews Genetics 1.
[53] Wendler (n 25).

3.1.4g Waiver of consent

In addition to the prospective collection of samples and associated data for research, researchers may want to use samples and data left over from clinical use (residual samples) or previous research and for which there is no consent in place covering the intended use. The participants may not be contactable and thus it may not be possible to obtain their consent to use their samples or data in research. To be allowed to use these samples and data, a waiver of consent from an REC must be obtained.

The use of such samples and data is generally only permitted if the research has an important social value, it would not be feasible to conduct the research without the samples and data, the research poses no more than minimal risk to the participant or the community to which they belong, and the waiver of consent has been approved by an REC. Depending on the context, a waiver of consent should be supported by community engagement or a public information campaign (see section on community and public engagement).

3.2 Vulnerability

3.2.1 Consent and vulnerable populations

Vulnerability has been defined as a position of relative disadvantage, that requires a person to trust and depend upon others, or as "able to be physically or mentally hurt, influenced or attacked". While it can be argued that as human beings, we are all vulnerable, the situation or characteristics of some people and groups may limit their ability to anticipate, cope with, resist, and recover from harm that they are exposed to, making them more vulnerable to harm than others. It is contextual, and a person could have more than one vulnerability.

The Declaration of Helsinki defines vulnerable persons or populations to be those with an increased likelihood of being wronged or of incurring additional harm and requires that all vulnerable groups and individuals receive specifically considered protection, when enrolled in research. However, according to the DoH, medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

In the case of health research, vulnerable populations are likely to be those who are unable to protect their interests such as those with inadequate knowledge, understanding, resources, or legal protection. It could also be due to them being in hierarchical positions within society or within the research system itself. People suffering from stigmatized conditions, or those that are marginalized or historically have been subject to discrimination also become vulnerable when taking part in research[54]. Harm to such populations could occur in various ways, for example, through

- unfair recruitment processes (*if marginalized populations are not recruited for research even though it has social value for them, or they are recruited for research even though the research is unlikely to have social value for them)*,
- unfair allocation of risks and benefits (*when vulnerable people bear the risks of research but do not receive any benefits*)

[54] See module on Vulnerability to learn more

- consent that is unlikely to be voluntary *(person in a hierarchical social structure or a hierarchical position with the person conducting research, persons with a relative or absolute lack of freedom, persons legally not recognized to be autonomous)* or
- consent that is unlikely to be informed (*illiterate person or persons with challenged mental capacities, minors)*.

Therefore, when enrolling vulnerable persons *for sample and data collection for biobanks*, special attention should be paid not only to consent (that consent is not obtained coercively or under duress, that those unable to consent for legal or medical reasons have surrogates that can make decisions for them and so on), but also to fair recruitment procedures and a fair allocation of risks and benefits.

Biobanks should take reasonable measures to ensure that they receive samples and data from vulnerable populations *only* with appropriate safeguards and to ensure when possible that the outputs and outcomes of research benefit these populations in a fair manner. Biobanks should engage with PIs to ensure that the safeguards put in place are sufficient, and with recipients of samples to ensure as far as is reasonably possible that samples from vulnerable populations are used to develop knowledge, tools and products that will be relevant to their needs. The policies and processes, including engagement activities adopted for the management of samples and data from vulnerable populations must be publicly available.

3.2.2 Children as donors of samples to biobanks

Children may also be donors of samples to biobank collections but are considered vulnerable because their consent is generally not legally acceptable. Biobanks must consult the national legal and ethical requirements of the country in which they are collecting the samples and data of children as many countries have specific related legislation.

Generally, prior to the collection of samples and data from children, the consent of a legally authorized representative (as defined by national law) of the child must be obtained. In addition, the *assent* (i.e., the agreement) of the child should be obtained if they have sufficient maturity. The refusal of the child to store blood in the biobank must be respected, unless there are exceptional circumstances.

It is important that the language of the assent form is suitable for the age of the child. Different assent forms may need to be developed depending on the age range of children (i.e., an assent form for a child of 15 may not be suitable for a child of 9).

When the child reaches the age of majority the biobank must have procedures in place to ensure consent for the continued involvement of the now adult is in place, or a waiver must be obtained.

3.3 Stigmatization & discrimination

Achieving the full public value from biobanks is only possible if access to samples and data is provided to researchers and the research results are disseminated, and products are made available including to communities which provided the samples. This is also important for the public accountability of biobanks. When data and samples are accessed for research on stigmatized conditions, or for research on groups that are marginalized or historically have been subject to discrimination, the dissemination of these results can also further risk stigmatizing or discriminating against some communities, thus increasing their vulnerabilities. For example, research results could indicate that a certain marginalised community or

group is more susceptible to a certain genetic condition, which if not communicated with due regard to confidentiality and sensitivity can further disadvantage them socially.

Biobanks must be mindful of such risks when providing access to their samples and data for research and have procedures in place to guard against such risks. Any access decision must consider the potential risk of stigmatization and discrimination when disseminating research results, and researchers must be advised appropriately to be mindful of the labels that they use to describe the community and ensure that any such labels do not lead to further stigmatization or discrimination.

Furthermore, researchers from the institution or community where samples were collected can assist in appropriately interpreting the results.

3.4 Privacy and confidentiality

Maintaining the privacy and confidentiality of participants is essential for research, and a fundamental ethical principle. The right to privacy is also enshrined in paragraph 12 of the Universal Declaration of Human Rights and hence legally binding. In addition, it is a legal requirement under data protection law. Therefore, biobanks have a responsibility to ensure that the samples and data are collected, stored, used, and shared in a manner that respects the privacy and confidentiality of their participants. This is also important for fostering trust in biobanks.

The potential risks to privacy and confidentiality must be considered in advance of sample and data collection, and measures must be put in place to mitigate these risks. This is known as privacy by design. Risks to privacy and confidentiality can depend on the context in which the samples and data are used. For example, combining data with multiple data sets brings about increased risk of re-identification.

In addition to the individual's information, samples and data can contain genetic data, and this data can reveal information about a participant's family and the community or population that they come from. Biobanks therefore must consider these other potential privacy risks.

Risks to privacy and confidentiality can be internal to the biobank (e.g., unauthorized staff member obtains access to the personal information of a participant) or external to the biobank (e.g., cyberattack). Internal and external risks must be identified and measures introduced to mitigate these risks.

3.4.1 Measures to mitigate risks to privacy

Biobanks must put in place processes to guard against unauthorized access to and use of the samples and data. These processes should be included in the data security plan for the biobank.

Biobanks also must put in technical means to guard against internal and external unauthorized access to the samples and data. Systems for logging access to samples and data must be put in place. In addition, data must be encrypted, and meet high standards (current standards?) of security.

Individuals with responsibility for privacy and security must be identified and given the time and resources necessary to fulfill the roles. Their responsibilities include keeping up to date with the latest standards in privacy and security as well as possible training of staff.

Biobanks shall require all staff to undergo training on privacy, security, and confidentiality. This training should include information on the importance of protecting privacy and confidentiality in the use of samples and data, the legal and ethical requirements in the protection of privacy, the processes and procedures put in place by the biobank to protect privacy and confidentiality, the security measures to be followed, and their individual role in the protection of privacy and confidentiality.

3.4.1a Anonymization of samples and data

Anonymization of samples and data means cutting all links between samples and data on one side and personal information on the other. Anonymization can help protect participants' privacy, but there are downsides. Anonymization renders it impossible to link the data with a participant's future medical records and other externally derived information. It also means that a participant cannot be re-contacted to obtain their consent to further research uses and any results or incidental findings cannot be fed back to a participant. Anonymization also means that a participant cannot withdraw consent for the use of their

samples and data. Furthermore, due to advancements in genetic research, it may not be technically possible to anonymize samples and genetic data.

3.4.1b De-identification of samples and data

To circumvent the disadvantages of anonymization while still respecting individuals' privacy and confidentiality, a process known as pseudonymization could be used. A code unique to the participant, but not based on his personal data, is allocated to the sample and data at the time of collection. The correspondence table between these codes and the personal data is separately maintained and access to this information is restricted to those that require this information. This access must be justified, e.g., genetic counsellor requires the information to feedback genetic results to a participant.[55] Biobanks must be mindful that de-identification of samples and data alone is insufficient to protect the privacy and confidentiality of participants. Biobanks must also put in place processes to guard against unauthorized access to or use of the samples and data.

Access to samples and data for research purposes must only be allowed if the recipient guarantees provisions on privacy, confidentiality, and security.[56] Biobanks must only share coded or anonymized samples and data. The MTA or DTA must contain provisions on the protection of privacy and confidentiality, including relevant legal provisions on data protection, and the requirement that the recipient will not attempt to re-identify the individual.

[55] See module on return of results and incidental findings.
[56] See module on access, sharing, and dissemination, and module on governance of biobanks.

Chapter 4 Post research Responsibilities towards Participants

Biobanks not only have responsibilities to manage data obtained from participants in a responsible, respectful, legal and ethical manner as mentioned above, but they must take responsibility for the management of the outcome of the research conducted on samples that were shared by them. Below are two of

4.1 Return of research results

There are differing types of results that can be returned to participants during research: summary results; results from tests conducted at baseline; return of individual research results. They will be each dealt with in turn. It is not the remit of the biobank (which itself does not conduct research) to return research results, but to have policies in place that require researchers who provide samples to, or obtain samples from, the biobank to do so according to agreed principles. Such obligations can be set out in the MTA. Biobanks themselves should have policies in place that facilitate this return, acting as benevolent mediators between the participants and the researchers.

4.1.1 Summary results

Summary, or aggregate, results of the research that do not identify or single out an individual and are in line with the guidance in this document should where possible be disseminated, with a lay summary. This can be on a biobank's website, and/or other forms of communication that have been decided through community engagement.

4.1.2 Baseline test results

A biobank may require participants to undergo tests as inclusion/exclusion criteria, or during baseline for additional information to be added to the participant's biological sample and/or data. There is the risk here of therapeutic misconception, which refers to a participant's mistaken belief that research is designed to benefit them rather than produce generalizable study results.[57] It should be made clear to participants that these are not health checks but rather studies conducted to annotate the sample and/or data. Participants, however, may want the results of these tests.

A procedure must be put in place in advance of the collection of these tests to establish if and how test results will be returned to participants and by whom. This process must be communicated to participants at the time of consent.

4.1.3 Individual research results

Sometimes a study plans to carry out certain analyses as part of the research that are likely to have clinical relevance to the individual participants. There is emerging consensus that individual results, if they have been validated should be returned to participants if they so wish.[58] However, there is ongoing

[57] Paul S Appelbaum, Charles W Lidz and Thomas Grisso, 'Therapeutic Misconception in Clinical Research: Frequency and Risk Factors' (2004) 26 IRB: Ethics & Human Research 1; Gail E Henderson and others, 'Clinical Trials and Medical Care: Defining the Therapeutic Misconception' (2007) 4 PLOS Medicine e324.

[58] Bartha Maria Knoppers and others, 'The Emergence of an Ethical Duty to Disclose Genetic Research Results: International Perspectives' (2006) 14 European Journal of Human Genetics 1170.

debate on what results should be returned and the process for the return of these results. Most results obtained in research cannot be used to make clinically relevant decisions and, in most situations, it is ethically appropriate to inform participants that the unvalidated test results will not be returned back.

There is guidance on the return of genetic results available from organizations such as the European Society for Human Genetics, H3Africa, the American College of Medical Genetics and Genomics (ACMG) and GA4H,[59] and checklists have been developed[60] that biobanks can draw from. In any case a biobank should have in place a policy on the return of individual results.

4.1.4 Incidental Findings

These are findings that are not being looked for as part of the research process but are a byproduct of research processing (especially whole genome analysis) and may have relevance or significance for the participant. There has been a lot of debate on how incidental findings should be managed, given that they are usually not validated. The emerging consensus is that such findings should be returned ONLY if they have clinical significance, have been validated, are actionable and the participant wants to receive them. As stated above, a policy must specify the process for managing IFs.

4.1.5 Policy on return of results

In developing a policy on the return of individual results including IFs, a biobank should take into consideration the following:

Planning: A return of individual results policy must be considered in advance of the collection of samples and data and included as part of the protocol for review by an REC. Which results will be returned to participants and the process for dissemination must be communicated to participants. This policy can change as research and the biobank evolve, but substantial changes must be approved by an REC. For already established biobanks, they should now consider the development of such a policy.

Applicable laws: Some countries have specific regulations on return of individual research results.[61] This may be that participants have a right to have individual results returned or that genetic results must be returned by a genetic counsellor. There is also a right of access to personal data in many countries under data protection law (although there may be an exemption in some jurisdictions if the use of the personal data is for research). Some countries also have genetic discrimination laws in place to guard against the use of genetic information to discriminate.[62] In developing a policy on return of results, a biobank must ensure that it is in line with any applicable laws in the provider country, and the biobank's country.

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[59] Zandra C Deans and others, 'Recommendations for Reporting Results of Diagnostic Genomic Testing' (2022) 30 European Journal of Human Genetics 1011; David T Miller and others, 'ACMG SF v3.2 List for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing: A Policy Statement of the American College of Medical Genetics and Genomics (ACMG)' (2023) 25 Genetics in Medicine <https://www.gimjournal.org/article/S1098-3600(23)00879-1/fulltext> accessed 6 October 2023.

[60] Danya F Vears and others, 'A Practical Checklist for Return of Results from Genomic Research in the European Context' (2023) 31 European Journal of Human Genetics 687.

[61] Adrian Thorogood, Gratien Dalpé and Bartha Maria Knoppers, 'Return of Individual Genomic Research Results: Are Laws and Policies Keeping Step?' (2019) 27 European Journal of Human Genetics 535.

[62] Yann Joly and others, 'Looking Beyond GINA: Policy Approaches to Address Genetic Discrimination' (2020) 21 Annual Review of Genomics and Human Genetics 491.

Returning individual results: Researchers may lack the necessary skills to return results to participants, thus the return of individual results policy must identify the personnel who will return the results and explain them to the participants. The central figure in this process is usually the principal investigator. For genetic results, genetic counsellors have an important role and should be involved in their return; their role may also be a legal requirement. There are limited numbers of trained genetic counsellors in many settings. In identifying appropriate individuals to return results, a biobank must be mindful of the realities of the specific context in which the results will be returned. In the absence of genetic counsellors, an REC can approve a plan on ethically managing the return of individual genetic results.

REC review: A return of results policy must be submitted to an REC for approval along with the information to be provided to participants on the return of results. Any substantive changes to a policy must be approved by the REC. If a biobank is not returning results, this should be ethically justified in the protocol.

Consent: During the informed consent process, participants must be asked, potentially with options, whether they wish individual research results to be communicated to them. Participants must be informed that this return of individual results can only occur if their biological materials have not been anonymized. The consent process should describe the potential impact that the return of results may have on them. This can include the benefits and utility of the information as well as the risk that can arise in the return. This utility must be widely understood as it is not just clinical utility but also personal utility e.g., can inform reproductive decisions.[63] If a biobank is not returning results to participants, this must be communicated at the time of consent.

Information to be returned: Biobanks should identify the results that they will return. The American College of Medical Genetics and Genomics has guidelines on the type of genetic results that should be returned that a biobank may wish to follow.[64] Biobanks may decide to only return actionable results. However, what is actionable can depend on the healthcare setting or other socio-economic factors. For biobanks that have collected samples and data from differing regions, what is actionable can vary. It is important that biobanks have one policy in place on the results that they will return.

Validity: A policy must specify the process for validating the results before they are communicated to participants.

Funding: The process for return of results must be adequately funded. This needs to be included in the budget for the biobank.

Community engagement: Community engagement can have an important role in the development of any policy on the return of results and should be used throughout the development of the policy.

[63] Jennefer N Kohler, Erin Turbitt and Barbara B Biesecker, 'Personal Utility in Genomic Testing: A Systematic Literature Review' (2017) 25 European Journal of Human Genetics 662; Lonna Mollison and others, 'Parents' Perceptions of Personal Utility of Exome Sequencing Results' (2020) 22 Genetics in Medicine 752; Erin Turbitt and others, 'The PrU: Development and Validation of a Measure to Assess Personal Utility of Genomic Results' (2023) 25 Genetics in Medicine 100356.
[64] Miller and others (n 54).

4.2 Benefit sharing

The HUGO Ethics Committee defined benefit as "a good that contributes to the wellbeing of an individual and/or a given community".[65]

Benefits derived from research using samples and data may be shared at two separate and independent levels: first at that of the participants, second at that of the provider institute and country. A biobank is an intermediary in benefit sharing, neither generating benefits from research directly, nor receiving a share of those benefits.

4.2.1 Sharing of benefits with participants

Those who participate in health research accept risks (though minimized) and may receive individual benefits such as return of results, access to clinical care, or access to therapy for the disease being researched. But such benefits should not be promoted to participants as a reason to participate. They are positive, possible secondary effects but not the main reason.

Concerns have been expressed that benefit sharing whether at the level of the participant or at that of the provider institution can lead to undue inducement to participate in research.[66] But others have pointed out that research participants are motivated to participate in research due to altruism (and there is considerable research to back up this claim), and there is no evidence that benefit sharing diminishes the altruism of research participants.

4.2.2 Sharing of benefits with provider institutions and countries

Current ethics guidance encourages researchers, sponsors and funders to do more, by sharing benefits to ensure that research collaborations are fair to the researchers and the country in which research, at least the collection of samples and data, is taking place.[67] In the context of health research undertaken in low resource settings, the CIOMS guidelines provide guidance on "fair distribution of benefits" (and burdens) of research, to research communities such as making available any intervention or product or knowledge that is an outcome of the research supported by that community as well as additional benefits such as strengthening the health system or capacities of researchers. The ethical basis for this wider "sharing of benefits" rests on the understanding that those carrying out the research (researchers from richer countries, and sponsors), derive benefits whether it is an academic accolade, a career advancement, gaining intellectual property or financial gains. It can also provide a mechanism that can reduce exploitation, counter power imbalances, counter the effects of commercialization, and can be important in achieving justice. [68],[69] In this way, benefit sharing can be used as a tool to remedy some of the inequity in international collaborative research.

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[65] HUGO Ethics Committee, 'Hugo Ethics Committee Statement on Benefit Sharing' (2000) 58 Clinical Genetics 364.
[66] Angela Ballantyne, 'Benefits to Research Subjects in International Trials: Do They Reduce Exploitation or Increase Undue Inducement?' (2008) 8 Developing World Bioethics 178.
[67] H3Africa framework. Cornelius Ewuoso, Allan Sudoi and Dorcas Kamuya, 'Rethinking Benefit Sharing in Collaborative Human Genetic Research from an Afrocommunitarian Perspective' (2022) 13 Frontiers in Genetics
[68] Dorcas M Kamuya and others, '"When They See Us, It's like They Have Seen the Benefits!": Experiences of Study Benefits Negotiations in Community-Based Studies on the Kenyan Coast' (2014) 15 BMC Medical Ethics 90.
[69] Ballantyne (n 63).

Benefits may be monetary or non-monetary, for the community of participants or the community of researchers or for health systems. Non-monetary benefits can include capacity building (such as training of personnel from the community), knowledge exchange, technology transfer, or feedback of individual findings to the participants. Monetary benefits can include funding of local initiatives, or a percentage of revenues.[70] As in the case of health research, any intervention or product developed using samples from a biobank must be relevant to the health needs of the communities that provided the samples, and provisions may be put in place to make these products available and accessible to these communities within a reasonable time frame (subject to regulatory approvals etc.) A list of potential benefit sharing measures is given in the annex to the Nagoya protocol.

One concrete form of benefit sharing is the commitment by the researcher to include the provider institution in the research as a research collaborator or to entrust one specific part of the project, typically the product validation, to the provider institution.

The costs associated with benefit sharing can be a concern. Discussions on benefit sharing might include researchers, sponsors, representatives of the community, the local or national governments, civil society and scientific and ethics experts[71]. A benefit-sharing plan can be approved by the REC.

4.2.3 Benefit sharing and biobanks

If the biobank is directly involved in sample collection, it can ensure that participants are aware of the known benefits being shared with them, however limited they may be. If the biobank is sourcing samples from third parties, it could in theory review the ICF and PIL and evaluate the source in relation to the efforts made to share benefits with the participants.

If the biobank is collecting samples and data for a known use and user / requester, it can ensure that appropriate benefit sharing is negotiated directly between provider and recipient/researcher institutions. The biobank is in no position and usually does not have the resources to be involved.

But often biobanks store samples and data for future use not knowing at the time of collection either the use or the user. This may be the case for prospective collections or for samples collected for a specific research project but excess to needs and made available for other research projects.

The only case in which a biobank can meaningfully and realistically be involved in establishing benefit sharing with provider institutions is the case of prospective collections managed by the biobank. The researcher end-user is unknown, but the biobank is in direct contact with the provider. The biobank cannot make undertakings for the future researcher who might be an academic, a start-up, big pharma, or a contract researcher. It is up to the biobank to negotiate with the provider some form of benefit sharing, funded by the biobank or its funding agency, such as capacity building. Providers may not receive percentages of hypothetical future profits but at least receive something tangible immediately.

[70] HUGO Ethics Committee recommends that profit-making entities dedicate a percentage (e.g., 1–3%) of their annual net profit to healthcare infrastructure and/or to humanitarian effort.
[71] CIOMS guideline 2

ANNEX 1

Research ethics committees (RECs) are independent bodies tasked with reviewing research proposals that involve human participants. Their function is to review research protocols to balance the risk and benefits of the research and ensure that the research adheres to the research ethics guidelines and applicable laws. An REC may be local, regional, national, or institutional. RECs are multidisciplinary and must have the appropriate expertise to review an ethics application. For research generally, as part of their review, RECs examine the study design, the balance of risk to the participants and the social value of research, the ICF and PIL, and other relevant aspects, to ensure that the research is scientifically valid and ethically sound.

In the context of a biobank, the collection and use of biological samples and data is subject to approval by an REC. This must be obtained in advance of sample and data collection. REC review may also be required for research that requires the future use of samples and/or data from the biobank. In addition to assessing the risks and benefits of the proposed research, the REC will determine whether the use of the samples and/or data is within the scope of the informed consent of the participant. If it is outside the scope of informed consent, the REC can require the re-contact and re-consent of the participants.[72]

Any amendments to any ethics related biobank documents must be approved by an REC. At the institutional level this includes amendments to the policies listed above and at the study or collection level amendments to the biobank protocol, ICF and PIL.

[72] See module on informed consent.

10. Biosecurity

Biobanks that handle pathogenic samples have a responsibility for biosecurity and biosafety. Biobanks have a responsibility to those who are handling the samples (i.e., its workforce), and to the wider public not to release pathogenic agents.

The International Health Regulations are the legally binding international agreement designed to prevent the spread of disease, as revised and adopted by the 58th World Health Assembly (WHA) on 23 May 2005. The purpose and scope of the IHR (2005) are "to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade." Biosafety and biosecurity are two of the technical areas assessed by the monitoring and evaluation framework of the International Health Regulations.

Although interlinked, biosecurity and biosafety are distinct concepts. The WHO defines biosafety as "containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents or their inadvertent release" and biosecurity as "principles, technologies and practices that are implemented for the protection, control and accountability of biological materials and/or the equipment, skills and data related to their handling".[73] Thus biosafety is about the processes a biobank can put in place to prevent accidental or unintentional release of biological agents, whereas biosecurity is focused on preventing unauthorized access, loss, theft, misuse, diversion or release.

The WHO's *Laboratory Biosafety Manual* (4th edition) describes the requirements for the safe handling and storage of samples that include risk assessment, facility design, working practices and procedures, transport and biosecurity. ISO 35001 is also an international standard for any organization that tests, stores, transports, works with, or disposes of hazardous biological materials.

The procedures a biobank will need to introduce will depend on the biosafety level (BSL) of the agent, with BSL-1 being the lowest and BSL-4 being the highest.

[73] World Health Organization. Laboratory biosafety manual. Fourth edition. Geneva, World Health Organization, 2020.

Appendix 1: Relevant documents & resources

ACMG SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG)

Belmont Report

BBRMI ELSI Helpdesk

CARE Principles for Indigenous Data Governance

Centre for Disease Control, Ten Guiding Principles for Data Collection, Storage, Sharing, and Use to Ensure Security and Confidentiality

Council of Europe Convention for the protection of individuals with regard to the processing of personal data (Convention 108+)

Council of Europe Recommendation CM/Rec(2016)6 of the Committee of Ministers to Member States on research on biological materials of human origin

Council for International Organizations of Medical Sciences International Ethical Guidelines for Health-related Research Involving Humans (CIOMS Guidelines)

Global Alliance for Genomics and Health: Accountability Policy

Global Alliance for Genomics and Health: Consent Clauses for Genomic Research

Global Alliance for Genomics and Health: Consent Policy

Global Alliance for Genomics and Health: Data Access Committee Guiding Principles and Procedural Standards Policy

Global Alliance for Genomics and Health: Data Privacy and Security Policy

Global Alliance for Genomics and Health: Framework for responsible sharing of genomic and health-related data sharing

Global Alliance for Genomics and Health: Model consent clauses for rare disease research

Global Alliance for Genomics and Health: Policy on Clinically Actionable Genomic Research Results

H3Africa Ethics and Governance Framework for Best Practice in Genomic Research and Biobanking in Africa

H3Africa Guidelines for Community Engagement

H3Africa Guideline for Informed Consent

H3Africa Guideline for the Return of Individual Genetic Research Findings

HUGO Ethics Committee Statement on Benefit Sharing

International Agency for Research on Cancer Common Minimum Technical Standards and Protocols for Biobanks Dedicated to Cancer Research: IARC Technical Publication No. 44

ISBER Best Practices: Recommendations for Repositories (4th edition)

Nuffield Council on Bioethics, The collection, linking and use of data in biomedical research and health care: ethical issues

OECD Guidelines on Human Biobanks and Genetic Research Databases

OECD Best Practice Guidelines for Biological Resource Centers

OECD Recommendation of the Council concerning Access to Research Data from Public Funding

OECD Recommendation of the Council on Health Data Governance

Te Mata Ira Guidelines for Genomic Research with Māori

The Trust Code - A Global Code of Conduct for Equitable Research Partnerships

UNESCO International Declaration on Human Genetic Data

UNESCO Universal Declaration on the Human Genome and Human Rights

World Economic Forum White Paper Genomic Data Policy Framework and Ethical Tensions

World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects (Declaration of Helsinki)

World Medical Association Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks (Declaration of Taipei)