Recommendation

For the Assessment of Research-related Human Biobanks by Ethics Committees

Recommended by the Permanent Working Party of the German Medical Ethics Committees
Version 2.0 approved by the General Assembly on 10.06.2016

The following recommendation is intended for Ethics Committees which are involved in the approval of research proposals in the context of human biobanks. It specifies the requirements and criteria for the ethical and legal assessment of human biobanks to be set up or that are already being operated. The recommendation covers all kinds of biobanks hosting human biological material, irrespective of size, focus or other particular features. However, some of the proposed requirements are to be adapted to the specific characteristics of the respective biobank.

The recommendation is to be interpreted in connection with the text template "for the use of human biological materials and related data in biobanks", Version 3.1. from 21.06.2019. This text template contains fundamental requirements being indispensable part of donor-information and consent forms.

Introduction

Today, biobanks have been recognized as very important resources for medical research. When establishing or operating a biobank, the interests of medical research and the freedom of research have generally to be balanced with the interests and rights of donors, in particular with their right to self-determination.

1. Definition and scope of the recommendation

A "biobank" in the sense of this recommendation collects and stores human biological material and related data for medical research purposes. Medical research comprises basic research as well as applied research addressing the detection of diseases (diagnostics), their prediction (prognosis) and their treatment (therapy) and avoidance (prevention).

A "biobank" in the sense of this recommendation equally comprises cooperation or networking between several or multiple collections of human biological material, or collections of such materials that have common procedural rules and governance.

2. The role of ECs in the set up and operation of biobanks

a. Assessment of the biobank

Irrespective of legal obligations, from an ethical point of view, the establishment of a research-related biobank by public or private organizations/bodies generally needs to be assessed by an independent competent ethics committee. The same applies in case of relevant changes of the scope or the legal owner of a biobank, or in case of a transfer of the collected bio-samples into another organization.

b. Assessment of applying research-projects

Prior to releasing human biological materials and/or related data for a medical research project, the biobank has to require an ethics vote of the ethics committee in charge of the respective project, at least in cases where such a vote is mandatory (e.g., according to professional law of

physicians and/or the Declaration of Helsinki). In addition, the right of the biobank to consult its local ethics committee remains unaffected. #1

3. Required documents for the establishment of a biobank

To assess the establishment of a research-related biobank by public or private organizations/ bodies, the ethics committee requires:

- Information on the scope, governance, procedures, means of documentation, and financial plan of the biobank;
- Information on the kind, mode of collection, mode and duration of storage, implemented measures for QM and QC, intended use and security measures regarding human biological materials and related data;
- Information for donors (patients/participants) and corresponding consent-document(s).

4. Assessment criteria for a biobank

a. Donor-information documents and consent form

Pre-condition for the acquisition and storage of human biosamples for research purposes is the informed (or broad) consent form, signed by the donor after comprehensive written and oral consultation. For the content of the written information and the consent form please refer to the text template *"for the use of human biological materials and related data in biobanks"* in its current version. If the biological material is used for genetic analyses, this fact should be particularly addressed in the information and consent documents as well as in the oral consultation.
Qualified physicians or qualified staff (personnel) trained in bio-banking, able to provide supplementary information and to answer all remaining questions should perform consultation of donors. #2

The signed consent forms (both by donor and informing physician/qualified staff) must be stored by the biobank or the institution having obtained the written consent at least for the time interval the biosamples and related data will be stored or used for research purposes. Donors must receive the information document and a copy of the signed consent form.
If the consent also comprises biosamples and data to be collected during future hospital visits/ study follow-up visits, donors must be unambiguously informed about this fact.
Where the consent comprises invasive procedures in the frame of future hospital visits/study follow-up visits, these visits must have been scheduled in advance; otherwise new consent must be obtained.
In general, the consent of the donor may also be obtained for unlimited storage and usage of his/her biological materials for medical research, as long as this has been explicitly mentioned in the consent form and consultation. In any case, all permissions end with the withdrawal of a donor's consent.

When the scope and intended purpose of a biobank change, or any relevant conditions (frame) under which the consent previously has been obtained, renewal of the consent is required – except (i) a disproportionate effort has to be made **and** (ii) the scientific interest and potential benefit of such changes outweigh the interests of the donor or any other person concerned.
Pre-existing collected biological materials and related data available from a deceased individual may be transferred into and stored in a biobank only, if such materials and related data are fully anonymized or if the scientific interests outweigh the individual interests of the respective individual or any other (related) person concerned.

#1: This is a matter of debate; a more stringent view even argues that the biobank must consult its local ethics committee in case an applicant/ applying research project does not provide an ethics approval.

#2: In case an additional intervention is required to obtain biological materials, consultation **must** generally be performed (and consent obtained and signed) by a qualified physician.

b. Intended use of the donated human biological materials

The collection and storage of human biosamples for research purposes or for quality control from the perspective of the potential donor always requires a clearly assigned purpose on an individual basis. Therefore, the purpose for the collection, storage and intended usage of human biological materials and data by a biobank should be specified as accurately as possible. For example purposes might be the realization of a specific clinical study, or research focused on a specific disease or well defined disease-entities.

On the other hand, the openness of future medical questions and challenges also requires the establishment of biobanks with broad usage of biosamples and data and is legitimate considering the aspects (i) opening new vistas for medical research, and (ii) optimization of public health care. However, the unpredictability of the future use – as a pre-condition for the legal validity of the donor's broad consent – must be compensated by procedural methods; in this regard, ethics committees are of particular importance for the assessment of biobanks (set up and operation) as well as for the assessment of individual research projects (*see point 2 above*).

In addition, the donor has to be informed unambiguously on the broad scope of the intended use of his/her biosamples and related data. The donor may be allowed to exclude certain research fields and/or procedures from the intended use of his/her biological materials and/or data.

c. Data protection and pseudonymization

c1) Storage of individual-identifying data

As a general rule, individual-identifying data should never be transferred to a biobank, but rather be stored in the institution (hospital/treating physician) where the (health) data were obtained and collected. Such an approach is preferred, because in this manner, individual-identifying data are protected by medical confidentiality, and any access for third parties is regulated and restricted by criminal law.

c2) Pseudonymization of biological materials and related data for storage & use

As a general rule, human biological materials and individual-related data shall always be stored in an at least double pseudonymized manner in order to sufficiently secure donor's privacy. #3 Handling of pseudonymized data should always involve a custodian (e.g., the data protection officer of the respective institution/university); in addition, pseudonymized data should be hosted by at least two independent bodies, each with separated responsibilities. #4 In single cases with lower data protection standards specific justification/explanation is required.

Anonymisation has always to be sought for in case individual-related data are not or not any more required for accomplishing the scientific/research question, and there are no conflicting rights of the donor.

c3) Pseudonymization for release and use of biological materials and related data

As a general rule, for medical research projects biosamples and individual/person-related data shall always be released and used in an at least double coded/pseudonymized manner. The codes/pseudonyms employed when transferring biosamples and/or related data must be different from those employed for storage.

Researchers must be bound by material transfer or data access agreement (MTA/DAA) not to attempt to identify individuals of whom biosamples and/or data have been received and utilized.

Biosamples and related data must be transferred only in a double pseudonymized/coded manner, and only to projects and institutions applying appropriate data protection safeguards.

#3: This procedure shall hinder re-identification of the donor by third parties, but will eventually not avoid or oppose to a persistent cognition of the donor's identity by the treating physician.

#4: This procedure accomplishes the principle of "informal separation of rights", describing a means of distributing data on separate data-stores/data-repositories with independent separate administrators in a manner that from each of the data subsets alone re-identification of an individual concerned is impossible (TMF Guidelines on Data Protection for Medical Research – Generic Models, Version 2).

The transfer of human biological materials and/or related data to a non-EU country may only take place, where that third country ensures a level of measures and procedures to protect privacy that adheres to current EU-regulations (GDPR). If this is not the case, the biosamples and/or related data must be anonymized prior to transfer. In any case, the pseudonymization keys must remain in the EU.
Wherever possible, individual/person-related data should be altered in order to reduce the risk of re-identification (e.g., replacement of date specifications, use of imaging data or documents with garbled identifiers only).

c4) Reversal of double pseudonymization/conditions of re-identification

A relinking of pseudonymized biosamples and/or individual/person-related data with the donor him-/herself is only permitted in case that safety and/or security of donors or research-projects (follow-up studies) are concerned. For the researchers, however, double pseudonymization must be safeguarded under all circumstances.
Biobank staff has to be bound by professional discretion in case they do not underlie medical confidentiality.

d. Duration of storage and the right of withdrawal

For medical research purposes, biosamples and individual-related data – dependent on the respective consent – may be stored either for a limited time period or equally for unlimited time.

Donors may withdraw consent in oral or written form at any time with or without justification, and without any reprisal. Withdrawal must be documented by the body/person/institution receiving this information. If the donor requests anonymisation of his/her biosamples and related data, the respective pseudonymization-key must be deleted. If the donor requests destruction of his/her biosamples and deletion of all related data, the pseudonymization-key must be deleted only **after** destruction of the biosamples. However, data cannot be removed from completed studies and/or published research results.

e. Use and release of biological materials and data for research projects

It must be ensured that any misuse of human biological materials and/or individual-related data is impossible; in addition, transparent access rules for researchers to both, biosamples and related data must have been implemented and this implementation should be acknowledged and controlled.

e1) Application
The user/handling guidelines of a biobank should make sure, that prior to any release/ transfer and use of biosamples and/or related data an assessment of the intended research-project by a competent ethics committee is required; otherwise the access requesting researcher must provide justification, why an ethics-assessment is eventually not required or not appropriate.
In any case, the biobank finally decides if and to what extent a transfer and use of biosamples and/or related data will be granted. The access- and prioritisation-rules of the biobank should be laid down transparently in the user/handling guidelines, being part of the documents to be submitted to and assessed by the ethics committee in charge of the biobank.
Prior to any release/transfer of human biological materials and/or related data the biobank has to make sure that the consent of the respective donor is valid and fully covers the purpose of use described in the intended research-project.

e2) Granted rights of usage
As a general rule, together with the release/transfer of biosamples and/or related data the applicants' rights of usage should be time-limited, project-specific, and non-transferable.
Duplication or transfer of biosamples and/or data to third parties is only permitted if this is

indispensable to accomplish the intended research project, and compliant with the MTA of the respective biobank.
Obligations of the user(s), in particular to secure the donor's rights and privacy, should be laid down in a (written) contract; this includes also publication of research results, in particular publication of individual genetic information. In addition, it must be made sure that upon withdrawal, the donor's non-anonymized biosamples will be disposed of on demand of the respective donor. Material that has not been utilized should be returned to the respective biobank or is to be destroyed in mutual accordance.

f. Conditions for re-contact
The user/handling guidelines of a biobank should clearly determine if and under which conditions/circumstances re-contact of individual donors is permitted. For researchers, however, pseudonymization must never be unravelled.
The user/handling guidelines of a biobank as well as the information sheet for potential donors should, in particular, determine under which conditions and by which procedure incidental findings will be fed back to the donor(s), e.g., if the outbreak of a possibly life-threatening disease can be prevented or a previously eventually not diagnosed health disorder can be treated. In doing so, the donor's right of not to know must generally be respected.
The biobank should regularly evaluate the efficiency of the implemented feedback procedure(s) (e.g., appropriateness of the number and frequency of feedbacks given per year).

g. Compensation for the biobank (fees-for-service)
The biobank may charge an appropriate compensation for providing human biological materials and/or related data.

f. Quality management & control and transparency
The legal owner and/or the head of a biobank must ensure compliance with all procedures and processes; compliance must be documented according to current standards/guidelines. Biobank staff must be trained for their specific tasks and must be bound by professional discretion.
Larger (e.g., interdisciplinary and/or faculty-wide operating or cross project) biobanks should regularly inform the public on their activities, e.g. by releasing information on a homepage and/or a web-portal.