

BIOPRESERVATION AND BIOBANKING
Volume 00, Number 00, 2020
© Mary Ann Liebert, Inc.
DOI: 10.1089/bio.2019.0132

Best Practices for Human Biobank Ethics Review in China

Shijian Liu,¹ Weiye Charles Wang,² Hongxia Zhang,³ Jianyun Tong,⁴ Xiaoyi Zhang,³ Pei Chen,³ and Chingli Hu³

The ethical practices for human biobanks in China are intended to safeguard the interests of all the participants, to standardize the construction, management, and resource sharing of human biobanks, to promote the development of medical research, and to improve public health and well-being. The practices contain several chapters: General Principles; Ethics Review; Informed Consent; Privacy Protection; Benefits of Sharing; and Conflict of Interest.

Keywords: best practice, biobank, ethics, review

Section A: General

A1: Purpose

THIS DOCUMENT HAS BEEN DEVELOPED with the purpose of protecting human life and health, respecting and protecting the rights of participants, and regulating the ethics review of medical research involving human specimens.

A2: Definition of biobank

The human biobank includes the collection, storage, delivery, and use of disease-related and health-related specimens and related information or data.

A3: Basis and principles

The ethics review of a biobank shall comply with the relevant national laws, regulations, and guidelines, mainly based on the Regulations on the Administration of Human Genetic Resources of the People's Republic of China (2019)¹ and Regulations for Ethics Review of Biomedical Research Involving Humans (2016)² adhering to the principles of informed consent, benefit, and justice. At the same time, reference is made to the International Ethical Guidelines for Health-Related Research Involving Humans (2016),³ Ethical Regulations of Human Genetic Resources (2019),⁴ the Shanghai Standard for Ethical Review of Humans (2015),⁵ Human Biological Material: Ethical Issues and Policy Guidance (1999),⁶ International Declaration on Human Genetic Data (2003),⁷ ISBER Best Practices for Repositories (2018),⁸ Introduction to Bioethics (2017),⁹ and Guideline for Sample/Data Sharing Review (2017).¹⁰

A4: Applicable subjects

This document is applicable to those biobanks and related ethics committees of medical and health institutions, universities, research institutions, and enterprises.

A5: Scope of human biobank

The scope of a biobank ranges from among the national, provincial, regional, institutional, and laboratory levels.

A6: Regulatory and enforcement agencies

The national or provincial Ministry of Science and Technology agencies are responsible for administrative approval for the collection and preservation of human genetic resources, and the administrative departments for local Health Commissions are responsible for the supervision and management of the ethics review of biomedical research involving humans in their administrative regions. Biobanks and ethics committees can refer to this document.

Section B: Ethics Review

B1: Review materials for specimen collection submitted by applicants to the ethics committee

Research projects involving human specimens must be reviewed and approved by the ethics committee of an affiliation or a third-party ethics committee before initiation of project.

B1.1: Application form for ethical review: includes instructions for filling out, commitment letter, approval

¹Department of Biobank, Clinical Research Center, Shanghai Children's Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

²MOE-Shanghai Key Lab of Children's Environmental Health Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

³Shanghai Ethics Committee For Clinical Research, Shanghai, China

⁴Shanghai Kangzheng Law Firm, Shanghai, China.

authority and time, basic information about the project, information about the applicant and donors, project overview, research process, donor population, privacy protection, benefits or risk, and so on.

B1.2: Research plan: the funded project includes the research project task proposal or application proposal; the project that is not funded needs to briefly explain the specimen collection purpose, process, subject, sample size estimation, and statistical analysis method of the research, with special attention to the information of the sample type and collection amount of samples.

B1.3: Information about the project leader: includes the resume and research experience of the leader.

B1.4: In addition to the above documents, the following documents should be submitted to the ethics committee for review when applying for the establishment of a human biobank:

B1.4.1: The standardized operation procedures (SOP) of the biobank.

B1.4.2: Material transfer agreement (MTA).

B1.4.3: Other related materials for ethics committees.

B2: Key points of ethical review for collecting and preserving specimens

B2.1: The affiliation of the ethics review applicant should be clear, such as the research project leader of the organization where the biobank is located, the director of the biobank, or the project leader of the cooperating institution.

B2.1.1: Sample collection for the funded project should include an ethical application according to research project requirements; key points of review include the following: research purpose, sample collection type, time limit of the collection, sample collection quantity and justification of the amount, and so on. A reasonable sample collection quantity shall be formulated according to research purpose, sample type, the donor age, and so on, to avoid excessive collection so as to protect the rights of the donor.

B2.1.2: For sample collection projects initiated by researchers of collaborating institutions or third-party institutions, it is also necessary to refer to the relevant requirements of sample collection initiated by the above research projects according to the research purpose. It is necessary to note that the requirements of sample collection should be clear, the collection time limit should be clear, and the sample collection amount should be determined according to the research purpose and the age of the donor, so as to avoid excessive collection amount and damage to rights of the donor.

B2.1.3: For the sample collection initiated by the biobank or the researchers that are not funded and have not established a clear purpose, the ethical review is encouraged when the samples are put into storage. Collection can be carried out with a general consent according to the general specifications of the sample collection or the detection and testing requirements of the current specimens. It is recommended to consult a third-party professional testing organization to clarify the specific requirements for collecting samples and related information through the biobank, so as to avoid collecting unqualified samples.

B2.1.4: The following conditions should be met for the ethical application of a newly established biobank of an institution or enterprise:

B2.1.4.1: The institution has legal standing.

B2.1.4.2: The purpose of collection is legal and clear.

B2.1.4.3: The collection plan is reasonable.

B2.1.4.4: Has passed an ethical review.

B2.1.4.5: Has a corresponding specimen management department and management system.

B2.1.4.6: Has places, facilities, equipment, and personnel suitable for the sample collection and biopreservation.

B2.2: The qualifications, experience, and ability of the researcher must meet the following requirements. The researcher must be a member of the institution or meet the jurisdiction and responsibility relationship of the regional ethics committee. For applications that do not meet the requirements, the application may be rejected or suggested to the corresponding institution. The researcher has relevant research experience or background and ability; for researchers below intermediate level or applicants without corresponding research experience, it is necessary to strictly review or consult with experts in the relevant fields and avoid excessive research risks.

B2.3: The research plan is reasonable and sample size is evidence based: the scientific nature of the research program is an important basis for ethical review. For researcher-initiated projects that are not sponsored by funding, it is recommended that qualified institutions review the projects recommended by two academic experts in related fields or by the scientific academic committee. For the sample collection initiated by the biobank, it is necessary to provide an academic evaluation based on the discipline of the research focus or the key research field of the institute.

B2.4: The risk and benefit ratio of the donor is reasonable.

B2.5: The standardization and comprehensiveness of the informed consent form of the biobank (purpose, sample size and type, privacy protection, procedures of sample withdrawals and destruction, benefits, risks, feedback and disclosure of research results, intellectual property rights, contact information, etc.), and standardization of the informed consent procedure.

B2.6: The informed consent form must cover the privacy protection and data security of the donor, the feedback and disclosure of research results, procedures of sample withdrawals and destruction, and so on. Projects involving international cooperation (including partners that are foreign institutions or a foreigner among the participants) need to apply and become registered on the website of the Human Genetic Resources Management Agency of the Ministry of Science and Technology of China.

B2.7: It is recommended to sign a specific sample collection informed consent form. If it is combined with other clinical documents or surgical consent forms, the contents of the notification must be included in the sample collection and approved by the institutional ethics committee. The signing process must reflect the informed consent of the donor. At the same time, if other relevant information is collected by means of questionnaires and so on, it must be stated in the informed consent form.

B2.8: Scientifically and rationally set the inclusion and exclusion criteria of the donors, including the gender, age, disease diagnosis, or screening conditions of the healthy donors. Exclusion criteria require specific exclusion conditions.

B2.9: The effectiveness of measures to protect the rights and interests of sample providers, expenses and compensation of sample providers in the process of participation, compensation methods and countermeasures for damages, insurance policies, and so on.

B2.10: Conflicts of interest and measures of avoiding conflicts.

B2.11: The possibility of public opinion risk caused by improper implementation of a research program and the corresponding countermeasures.

B3: Key points of ethical review

B3.1: The consistency with the approved content of the ethical review and the frequency of sample removal from the biobank shall be taken into consideration when the samples are out of the biobank.

B3.1.1: The review of sample removal can be waived when the sample collection of the research project has been reviewed and approved by the ethics committee. If the sample users and collectors are inconsistent, they need to apply for review again.

B3.1.2: When applying for sample removal with an unclear research purpose during sample collection, the sample users need to apply to the ethics committee for review. If the sample users are the sample collectors in the same institute, rapid review is recommended. If the sample users are non-collectors or another organization's personnel, a review meeting is needed. The specific review mode should be determined by the ethics committee.

B3.1.3: When the same research project is applying for multiple sample removal and has been approved by the ethics committee, it is not necessary to apply for the ethical review every time, but it is necessary to backup the review files of previous ethical review approval.

B3.2: When the sample is delivered out of the biobank, the sample management institute needs to sign an MTA with the sample user, especially when the sample user and the collector are not the same person or the personnel are from outside the organization. The agreement includes whether the sample collection entity will charge a processing fee, how to reference the sample source when publishing in the literature or applying for a patent, research results feedback and information disclosure methods, interest distribution and how to share achievements, how to avoid conflicts of interest, and so on. This part is detailed in Section E, Interest Sharing, and Section F, Interest Conflict.

B3.3: The specific measures for the privacy and data security of the donor, the anonymous processing of the identifiable information such as the name, gender, contact information and ID card of the samples in the biobank.

B3.4: Encourage the sharing of specimens and full scientific use of the specimens. Multicenter research can establish a collaborative sample collection and review mechanism to ensure that all project research institutions follow the principles of consistency and timeliness. The ethics committee of the leading institution of the project or the regional ethics committee is responsible for the project review and provides the results of the project review to the ethics committee of the participating institution for reference. The ethics committee of the participating institution should review the participating research projects in a timely manner and rapid review is recommended, encouraging the multicenter project to be carried out and cooperation with the scientific research. If the review results are inconsistent, the project participants should provide timely feedback to the leading institution or regional ethics committee.

B3.5: If overseas institutions or individuals are involved in cooperating with domestic medical and health institutions to carry out biomedical research projects involving human beings, including biological samples or data involving hu-

man beings, when applying to the ethics committee of domestic institutions for ethical review of research projects, it is mandatory to apply to the website of Human Genetic Resources Management of the Ministry of Science and Technology of China. In the case of exporting of samples, it is necessary to apply for the exit certificate of human genetic resources materials issued by the Ministry of Science and Technology of China. The final report of the cooperative research should be submitted to the Office of Human Genetic Resources of the Ministry of Science and Technology within 6 months after the cooperative project is completed.

B4: Mode and applicable conditions of ethical review

The methods of ethical review usually include full board review and expedited review. The applicable conditions of approach to ethical review involving biobanks are as follows:

B4.1: Full board review: a large amount of biological samples being collected or preserved (more than 200 cases of common diseases or more than 20 cases of rare diseases); ethnic minority samples; samples involving children, pregnant women, and special populations with limited behavior capacity; samples of multicenter research; projects of cooperation with foreign personnel or institutions; international cooperation or projects with overseas participants, including data sharing; other sample collection projects with potential conflict of interest or high risk in the opinion of the ethics committee.

B4.2: Expedited review: the risk of collection and preservation of biological samples is relatively low, such as collecting and testing the residual samples without individual information; ethical review projects of participating institutions in multicenter research projects have been approved by the leading institution or regional ethics committee with minor modifications after full board review; research projects with research risk not greater than the minimum risk. Expedited review is approved by the chairman or vice chairman of the ethics committee or designated ethics committee.

B4.3: In particular, if the research involves testing the residual samples for the verification of testing reagents or equipment, and does not involve the privacy of patients; or if the previously collected samples have greater scientific value and the donor cannot be contacted, the risk of the study is not higher than the minimum risk, and the informed consent can be submitted for exemption from review when submitting the application to the ethics committee.

B5: Ethical review results of sample application

The ethics committee makes a review decision on the research project, including approval, approval after revision, retrieval after revision, disagreement, suspension or termination of the study, and explains the reasons.

B5.1: An approval of the ethical review is issued for the project with the lowest risk or the project reviewed again with minor modifications.

B5.2: If the project has obvious deficiencies after the ethics committee's review, the applicant should make a revision of the research plan or informed consent form and resubmit it for review.

B5.3: For projects with greater ethical risks, if more than half of the ethics committee members disapprove, the

project should be suspended or terminated, and sample collection should not be carried out.

B6: Tracking review of the project

For research projects that have been approved for implementation, the ethics committee shall designate committee members to conduct follow-up examinations. The tracking review includes the following contents:

B6.1: Is the sample collected or preserved in accordance with the approved research plan by the ethics committee?

B6.2: Is the informed consent form standardized during the sample collection process? In case of any nonstandard situation that needs to be rectified in a timely manner, the project leader can be informed to suspend or terminate the sample collection project if the project still fails to meet the ethical requirements after rectification.

B6.3: Judging whether it is necessary to suspend or terminate sample collection in advance based on the sample collection amount.

B6.4: Other contents that need to be reviewed.

The number of members who follow up the review shall not be less than two, and the review results should be reported to the ethics committee in a timely manner.

Section C: Informed Consent

C1: Method of informed consent

Informed consent should be obtained from participants before collecting their specimens and related information for research.

When written informed consent cannot be obtained from the participants, consent should be obtained orally, and researchers should provide to the research ethics committee documentation of consent and related evidentiary material.

Written informed consent should be obtained from participant's legal guardian or other duly authorized representative when research involves individuals incapable of giving informed consent or institutionalized persons such as children, pregnant women, or patients with intellectual disability, or who are unconscious.

C2: Content of informed consent form

C2.1: The informed consent form may be created either for a particular use or for unspecified future use. The template of the informed consent from an institution or professional association is recommended.

C2.2: If clinical institution informed consent form is included together with the clinical and laboratory notification, admission notice, surgery consent form, and so on, it must be approved by the ethics committee. Key elements of the informed consent need to be included in the integrated document, containing, but not limited to, the individual's willingness to enroll in the research and informed consent process:

C2.2.1: The purpose of the research, its methods and procedures, and research period.

C2.2.2: Potential benefits to the participants and related individuals and society.

C2.2.3: Potential discomfort, possible hazards to the participants, and special protection.

C2.2.4: Donors informed of research outcomes, return of research results, confidentiality, and a description of specific measures of personal information, especially the anonymization of the specimens when they are delivered.

C2.2.5: The manner of informing about biobank research results should be included.

C2.2.6: The rights of donors, including voluntary participation and withdrawal at any time, being informed and consent or refusal, confidentiality, compensation, free treatment and compensation for damage, and resigning of the informed consent form.

C2.2.7: The contact information: name of the researcher and research institution.

C2.2.8: Precautions for participants before, during, and after studies.

C3: Process of signing informed consent

The informed consent form should contain necessary and complete information.

The informed consent form should be signed only when the participant expresses his or her willingness freely and independently.

The language and expressions of informed consent should be easily understood by the participants. The process of informed consent should be recorded when obtaining informed consent from participants with limited capacity for civil conduct, such as children and persons with intellectual disabilities, in which case it should be signed by a guardian or legal agent.

C4: Renewing consent

Researchers should contact the participants again to obtain the informed consent under the following conditions if there is no general informed consent:

C4.1: The research protocol, scope, and contents changed.

C4.2: Using identified samples from previous diagnosis and treatment.

C4.3: Using identified samples from biobank and relevant clinical medical records.

C4.4: Obtaining informed consent for continued storage and use of their samples and data or providing the option to withdraw consent for future use when children and adolescents (younger than 18 years) reach the age of majority at 18.

C4.5: Other major changes in the research process.

C5: Waivers of informed consent

An ethics committee may approve a waiver of informed consent to research if:

Using identified specimens or data in research when it is impossible to contact the participant as well as there is great scientific and social value of the sample and related data involving no commercial interests.

Section D: Privacy Protection

D1: Ethical requirements

The biobank must protect the privacy of the donor when collecting, storing, and using specimens and the related data or information to avoid harm, stigma, or suffering to the donor and the ethnic group. Biobank could only use the

collected information, specimens, and related data of the donor within the scope approved by the ethics review committee; if the research is outside the approved scope, the researcher must resubmit to the ethics committee for approval.

D2: Informed consent to privacy protection

This procedure echoes the content of informed consent.

The biospecimen collector (biobanker, researcher, medical staff, laboratory personnel) should inform the donor about privacy protection measurements and the limitations for biospecimens and related data or information in the informed consent process before collecting biospecimens.

The informed consent can only be signed after the donor agrees to donate.

D3: Privacy protection measurements

The biobank must store specimens, data, and other relevant information in a safe manner.

Biospecimens can be stored as follows:

D3.1: Biospecimens stored without identity: Specimens are initially collected without identification and the donor cannot be contacted by the collector.

D3.2: Biospecimens that cannot be linked or anonymized: Biospecimens were originally identifiable, but all identifiers have been removed and their donor cannot be contacted.

D3.3: Traceable or coded storage: Researcher cannot identify the biospecimens while conducting the research, and the identity information is represented by an unrelated code, but can be linked to the donor by the code.

D3.4: The biospecimen storage with identification: Researcher can obtain the identifier of the biospecimens, such as name, address, and telephone number.

The biobank should establish a privacy protection system and different levels of access to the biobank.

Biospecimens stored by a traceable or coding method, the research leader or supervisor controls the key that associates the code or password with the donor's identity, and the decoding procedure must be stipulated.

The biobank should sign a confidentiality agreement with the employees and provide training to employees on privacy protection.

Biobank staff access to the personal identity, medical, genetic, social, and personal medical history of the donor is limited in the scope of their duties.

Any unauthorized individual or third party cannot access the biobank.

The privacy protection strategy of the biobank must be reviewed and approved by the ethics review committee.

D4: Privacy protection operational procedures

The biobank shall establish "Privacy Protection Practice Procedures," annotating the effective date and issue it. The biobank should provide the researchers with coded or anonymized data only and strictly restrict the access of other third parties to the data.

The biobank's "Privacy Protection Practice Procedure" should cover the following:

D4.1: Confidentiality commitment: The biobank should release a letter of commitment for the confidentiality of the personal identity information, biospecimen data, and related

information of the donor, and clarify the scope and time limit. The confidentiality commitment should indicate the date, version, contact information, and affix the official seal of the responsible entity of the biobank.

D4.2: Anonymization process: The identifiable information (name, address, date of birth, ID number, etc.) collected during the enrollment process should be coded for safe storage; after the biospecimens enter the biobank, the identifiable information should be separated from the specimens, data, and other information, with only a code with no special meaning as the unique link code. All identifiable information should be centrally managed and personnel access permissions should be strictly restricted.

D4.3: Conditions for reidentification: When researchers consider reducing the health risk of donor due to research findings, they must identify the source of biospecimens again; or the redundant data need to be eliminated; or for confirming the correctness and completeness of the data and the original record; or when the donor needs to withdraw the consent of biospecimens and related data.

D4.4: Management of access to the biobank: The biobank must establish an access authorization table, and only the authorized personnel have access to the specimens and related information of the biobank.

D4.5: Transferring and use of specimens and related data or information: Before transferring specimens and related data or information, stakeholders must sign an MTA, and state the content of confidentiality on the type of specimens and related information.

D4.6: Privacy protection training: Relevant personnel of the biobank must be trained at least once a year to protect privacy, including the purpose, importance, basic measures, and risk control methods of privacy protection; qualification is one of the conditions of appointment of personnel.

D5: Processing of specimens and related data or information

Data identifying the donor such as name, ID number, and date of birth should be coded or anonymized; when such data need to be used in linking with specimens and related data or information, an audit system should be set up. And those specimens and related data or information should be returned and re-encrypted after use.

When the data and information are used for comparison, they should be encoded, encrypted, delinked, or otherwise anonymized using methods that do not recognize the identity of donor, and data and information should be restored immediately after the comparison.

Section E: Benefits of Sharing

Framework about guiding principles, elements, and activities about the benefits of sharing biological materials and associated data, derived from the sharing procedures thereafter is discussed in this section.

E1: Defining benefit sharing

Benefit sharing in this concept refers to the scope of personal and institutional legal rights and public interests involved in samples and their collection, samples and/or data sharing, and other derivatives therefrom.

E2: Normative management of benefit sharing

Benefit sharing has been a recurring theme in biobanking for years. The bottom line should make benefit sharing to be regulated based on fairness, justice, and any benefits to those who have been involved. The partners involved in benefit sharing should formulate and abide by the sharing norms in a transparent, comprehensive, and sincere manner to safeguard their respective interests and establish regulations for benefit sharing with relevant regulation and policy.

E3: Benefit from sharing activity

E3.1: In implementing sharing in a biobank, all aspects must be considered, including the interests of the donors. On top of that, the key to donors is not to be harmful to their individual rights and privacy while protecting the interests of those who participate. The biobank should not take any action before the individuals are informed and gain consent from them concerning procedures that will be used in collecting samples.

E3.2: Benefit sharing may involve multiple agencies. All parties should fully understand any benefits that might be involved, and should be clearly defined and consistently adhered to in the normative and written manner.

E4: Types of sharing activities

E4.1: Shared content includes plan design, collection of biospecimens with or without data collection; provision of resources (biospecimens and/or data); preservation of biological resources only (biospecimens and/or data); use of biospecimens for testing and analysis only; all of which are considered to be involved in generating the benefits of sharing.

E4.2: Shared content can also arise from the use of benefits by implementing various forms of technical settings. Such benefits include, but are limited to, the following scenario as well: use of research results, that is, discovery of biomarkers; establishment of special cell lines; animal models with genetic materials such as 3D cell culture, organoid technology, cell immortalization technology, cancer-derived xenograft modeling, patient-derived xenograft modeling, and conditional reprogramming cell technology.

In addition, authorship and copyright, applying for rewards, intellectual property rights, patent filing, and economic benefits should be included. All parties who are involved in such categories of benefits as described above should adhere to the formulated benefits of sharing norms among parties.

E5: Benefit sharing agreement

E5.1: Any potential benefits of sharing should have a corresponding benefit sharing agreement, contain comprehensive, complete, true, and accurate information, and should not be concealed and misleading.

E5.2: All of those who are involved in the benefits of sharing shall discuss clearly in advance and make sure to understand the benefits and sharing plan.

E5.3: Such an agreement shall fully express its wishes and reach a consensus on various opinions and be signed.

E6: Material transfer agreement

An MTA is a contract that governs the transfer of sample material between two organizations. Therefore, for any scenarios of samples being transferred, it is important to establish a transfer agreement and maintain it in accordance with the terms required for research specifications, data sharing practices, and other benefit sharing.

E6.1: The transfer agreement shall include, but is not limited to, the following: (1), a clear description of the nature of the biospecimens and the establishment of the material receiving and/or storage conditions; (2), the individual rights and/or limitation of material use that are involved; and (3), clarify the legality of the origin of the biospecimens. Overall, all activities around the biospecimens should abide by the Administrative Regulations of the People's Republic of China on Human Genetic Resources (the "Regulations").

E6.2: The agreement shall be determined to comply with laws and regulations, as well as the confidentiality of personal privacy, with the informed consent of the individual participant and the ethical approval of the institution to which it belongs, or an independent regional ethics committee.

E6.3: It should be confirmed that recipients of the biospecimens still have the same rights and interests of the samples when collected and stored, and will not be restricted by the source of the transfer.

E6.4: The biospecimens will not hinder the end user's right to conduct a series of biobank research projects and publish research results as well.

E6.5: The data attached to the biospecimens, and the data produced from use of the biospecimens in research thereafter, should abide by the use of conditions and/or limitations, such as restrictions on commercial use.

E7: Economic interests of benefit sharing

E7.1: In terms of potential economic interests, the activities involved in the collection, storage, and utilization of biospecimens with associated data should closely follow the corresponding regulatory compliance mandates of the Administrative Regulations of the People's Republic of China on Human Genetic Resources (the "Regulations").

E7.2: According to the regulatory compliance mandates, the biological material of a human source (human genetic resources) is not tradable. However, any charges necessary to cover the cost generated by labor and/maintenance while collecting, processing, shipping, and storing samples are allowable.

E7.3: Sharing biospecimens and/or data in a collaborative manner may involve economic interests, so any agencies with such potential shall bear the responsibilities accordingly.

E7.4: Any longitudinal study, for example, a cohort study, requires long-term collaboration among multicenter actors. More and more cohort studies have been initiated in China during the past decade. Sharing in such a collaborative manner will be heavily involved in all of phases from design to completion. Economic interests of sharing would be one of the key sharing factors, including sharing resources and subsequently generating a series of shared benefits. It would be critical for the partners who are involved to understand and agree upon the benefit sharing agreement with a broad spectrum, long term, and diversity of interests.

E7.5: For long-term collaboration, a management committee may need to be established to undertake the formulation of related norms associated with the planning, implementation, management, and auditing the sharing of interests.

E7.6: All legal and ethical particulars associated with shared content ought to be taken into account to protect the interests of all the organizations.

E8: Benefits of data sharing

Data sharing is the practice of making data available for researchers who collected the samples and data originally, and also available to other investigators who have needs. Data sharing has great potential to support scientific research by increasing the efficiency of scientific analysis. The activities of data sharing could be particularly useful when biological materials are limited in availability, or integration for a larger data resource from multiple sources after harmonization. The following points define the key elements of data sharing activities.

E8.1: The fair and equitable sharing of the benefits arising out of the utilization of data is the key to data sharing. Funding agencies, institutions, and publication venues have policies regarding data sharing because transparency and openness are considered to be part of the scientific method. The ethics of data sharing should be thus governed appropriately regardless if data are shared with or without biospecimens. Data sharing can happen as a whole at one time. In such scenarios, information attached to the shared information, including data type, content of data sets, as well as other associated benefit potentials, should be stated in a comprehensive manner.

E8.2: Data sharing format could be also available by allowing those who have been approved access to a network platform, along with a designated data storage location, such as a designated server or FTP site. Such a method of data openness should specify login permissions, search methods, number of logged in users, access or download retention data, open period of time, and deadline as well. Closing and reopening access can be the way to manage the sharing process while needed.

E8.3: Open-form data sharing should establish an application procedure and an approval system, that is, the qualification to apply for the access to relevant data (access policy).

E8.4: The approval system for the access application should adapt a two-step procedure. The first step is to allow a member of the sharing community to complete an application. A designated data manager will check and complete the integrity, rationality, and compliance parts of the preliminary application according to sharing principles. This is followed by the next step of the approval procedure, by a committee designated for the sharing activity. The data content and utilization purpose of the application should be of scientific merit and feasible for availability, and guarantee consistency with the established guiding principles and data restriction policy, if any.

E9: Shared content of data

E9.1: Data can be shared with or without biological materials. Therefore, the sharing method and interests of data sharing could be also unique from sample sharing.

E9.2: Data sharing mainly refers to data collected with related activities such as collection, preservation, and utilization of biospecimens in biobanks. It is mainly, but not limited to, storing in a database, or could be stored in paper or electronic format. The diversity of data types is relatively wide, so the scope and binding management of open data sharing should be stated clearly.

E9.3: In the view of the heterogeneity of data collected by different institutions and with different contents, it is necessary to harmonize data in such a scenario before the data are shared between the institutions.

E10: Guiding principles for sharing data

E10.1: Legal and ethical consequences of data sharing from an international perspective shall comply with the preregistration policy before sharing any data, as required in the Administrative Regulations of the People's Republic of China on Human Genetic Resources (the "Regulations").

E10.2: To develop the capacity to benefit from sharing research outputs and to analyze relevant data sets by others, it is important to realize the full benefits of data sharing arising out of the utilization of data, and the final research output and metadata should be shared as much as possible.

E10.3: The data type or the restricted data type should be defined clearly; it should be clear whether the shared data are the entire data set, whether the data analysis method would be in the scope of sharing, and whether the report parameters and/or methods are included or not.

E10.4: It should be also clearly stated whether the implementation of data quality control would be needed, and whether the measurement of quality is required to meet any needs of the established data standard.

E10.5: The requirements for the sharing with data format, use of controlled vocabulary, additional interpretation of data, coding method, and ensuring interoperability with other data systems should be clear.

E10.6: It should be clear whether, in addition to the data sharing, the final research outputs, other available data, such as available from other databases through links, are included.

E11: Authorship of publications as sharing benefits

Publishing research outputs arising from use of shared data is one of the primary benefits of data sharing as well.

E11.1: How to share the benefits arising from publishing research results in peer-reviewed scientific journals should be clearly defined, guided, and governed by the institutions involved in the sharing activities. Regardless of sample and/or data sharing or any additional benefits derived thereafter. The guiding principles and governance framework should be established and regulated to protect the interests of sharing.

E11.2: All of the members who are involved in the sharing activity shall abide by the publication authorship principles, by submitting an application for publication review and approval as long as any data associated with shared resources have been used. Articles should be submitted for approval before submitting to a journal as well.

E11.3: Publication review should give an evaluation about the scientific merit, and verify whether the data analysis included is in the clear scope and meets the corresponding requirements of sharing.

E11.4: It should be ensured that the authors listed in the publication comply with the relevant regulations. It should also be ascertained that the content of the publication application declares the shared interests.

E11.5: The review shall also ensure an assessment of data accuracy and the analysis results, including, but not limited to, all of the contributors who might be involved in the sharing procedure.

E11.6: A lifecycle of the data from the research output should be established and attached to the sharing principles. If nothing is published after an application for publication has been approved within a time limit, it might be considered to allow others to use the data set for publication as well.

E11.7: A research publication should include a special statement of gratitude for sharing biospecimens and/or associated data offered by other institutions in the acknowledgment section of any scientific publication and presentation.

E11.8: Publications arising from shared resources should follow the same principles and policy established for scientific publication even if they only use part of the shared resources.

E12: Intellectual property rights involved in benefit sharing

E12.1: Shared resources might generate a variety of intellectual property issues, including but not limited to authorship, patents, and knowhow.

E12.2: Use of the resources available for sharing may involve and/or generate multifaceted intellectual property rights.

E12.3: The intellectual property rights generated by shared resources shall be subject to the norms and constraints of different institutions, including but not limited to the requirements set by sharing principles and policy.

E12.4: It is encouraged to publish and/or present achievements in public forums, but all such activities should abide by the legal regulations and policies of the intellectual property rights of researchers and their institutions as well.

Section F: Conflict of Interest

F1: Definition of conflict of interest

The conflict of interest refers to the conflict between personal interests and their research responsibilities in this document, that is, economic or other interests that may affect an individual's ability to perform his or her research duties. When the interest does not necessarily affect the individual's judgment, it may lead to a significant conflict of interest when the individual's objectivity is questioned by others.

There is a potential conflict of interest when any reasonable person is uncertain about whether the benefit should be reported.

The conflict of interest from a medical institution/clinical research institution refers to the undue influence of the economic interests of the institution itself or the economic interests of its senior managers on the decisions concerning the interests of the institution.

F2: Conflict of interest management policy

The ethics committee is responsible for correctly identifying research-related conflicts of interest and taking management and preventive measures.

F3: Applicable objective and scope of conflict of interest policy

F3.1: Conflicts of interest among the medical institutions, universities, ethics committees, and biobanks:

F3.1.1: The institution refers to the research findings' owner and the patent holder of the biobank involved in the research, and the medical research approval applicant.

F3.1.2: The legal representative of the institution has an economic interest relationship with the owner or manager of the biobank.

F3.1.3: The legal representative of the institution and the person in charge of the GCP office are also among the members of the ethics committee.

F3.2: Conflicts of interest between members of the ethics committee and researchers:

F3.2.1: There is a relationship between them in which they buy, sell, or lease any property or immovable property.

F3.2.2: There is an employment and service relationship or sponsorship relationship, such as when a consultant or expert of the company accepts gifts, instruments or equipment, consulting fees or expert consulting fees from the sponsor.

F3.2.3: Members/independent consultants, spouses, children and spouses of researchers, close relatives, partners, and sponsors of research projects have economic interests and hold positions in the institution.

F3.2.4: The member/independent consultant serves as researcher in the projects that are reviewed/consulted by them

F3.2.5: The members/independent consultants, the spouses of the researchers, the children and their spouses, close relatives, and partners act as researchers in the project under their review/consultation.

F4: Conflict of interest declaration and avoidance system

A member/independent consultant of the ethics committee should sign a conflict of interest statement when accepting appointment.

A member/independent consultant should declare the conflict of interest voluntarily in advance if there is conflict of interest within the research project under reviewing or consulting and the process must be recorded.

Applicants, independent consultants, and members with conflicts of interest in research projects should leave the ethics review meeting when voting.

F5: Disciplinary measures and legal consequences

If a conflict of interest with the research project is not declared, the ethics committee will take the following disciplinary measures, according to the circumstances:

Public criticism will be given.

Members will be disqualified.

Independent consultants will no longer be invited to consult on projects.

The researchers would be restricted to undertake new research projects; those who have adverse consequences will be recommended to be disqualified.

If a member of the ethics committee who has a conflict of interest with the research project votes, the result of the vote is invalid.

Acknowledgments

Special thanks to Mingxian Shen, Rong Wu, Jianzhong Ying from Shanghai Ethics Committee for Clinical Research, CongRong Wang from Shanghai East Hospital, Menghong Sun from Fudan University Shanghai Cancer Center, Xiaonan Kang from Renji Hospital, and Junmei Zhou from Shanghai Children's Hospital, who provided constructive comments and valuable suggestions. In addition, special thanks to Shanghai Engineering Research Center of Biobank who contacted these experts.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

This study was partly supported by National Science Foundation of China [81872637], Shanghai Municipal Commission of Health and Family Planning [201840324], Program of National Science and Technology Commission for Association of Diabetes and Nutrition in Adolescent [2016YFC1305203, 2016YFC1305204], Medical and Engineering Cooperation Project of Shanghai Jiao Tong University [YG2017ZD15], The Project of Shanghai Children's Health Service Capacity Construction [GDEK201708], National Human Genetic Resources Sharing Service Platform [2005DKA21300], Science and Technology Development Program of Pudong Shanghai New District [PKJ2017-Y01] and Shanghai Professional and Technical Services Platform [18DZ2294100]. Shanghai Science and Technology Commission of Shanghai Municipality (17411965300, 17XD1402800,19441904400). Shanghai Clinical Research Center funded this project.

References

1. Ministry of Science and Technology of the People's Republic of China. Regulations on the Administration of Human Genetic Resources of the People's Republic of China.

- Available from www.gov.cn/zhengce/content/2019-06/10/content_5398829.htm (accessed March 30, 2020).
2. Health and Committee of the People's Republic of China. Regulations for Ethics Review of Biomedical Research Involving Human. Available from www.gov.cn/gongbao/content/2017/content_5227817.htm (accessed March 30, 2020).
3. Council for International Organizations of Medical Sciences (CIOMS) in Collaboration with the World Health Organization (WHO). *International Ethical Guidelines for Health-Related Research Involving Humans*. Geneva: WHO Press; 2016.
4. Fudan University, National Engineering Center for Biochip at Shanghai. Ethical Standard for Human Genetic Resources Centers. Available from <http://std.samr.gov.cn/gb/search/gbDetailed?id=5DDA8B9DA4C518DEE05397BE0A0A95A7> (accessed March 30, 2020).
5. Shanghai Standard for Ethical Review of Humans. Available from <http://yxky.fudan.edu.cn/4f/d3/c6382a85971/page.htm> (accessed March 30, 2020).
6. National Bioethics Advisory Commission Research Involving. *Human Biological Material: Ethical Issues and Policy Guidance*. Rockville: US Government Printing Office; 1999. Available from <https://bioethicsarchive.georgetown.edu/nbac/hbm.pdf> (accessed March 30, 2020).
7. United Nations Educational, Scientific and Cultural Organization. International Declaration on Human Genetic Data; 2003. Available from www.unesco.org/new/en/social-and-humansciences/themes/bioethics/human-genetic-data/ (accessed March 30, 2020).
8. International Society for Biological and Environmental Repositories. ISBER Best Practices for Repositories; 2018. Available from www.isber.org/page/BPR (accessed March 30, 2020).
9. Zai X, Qiu R. *Introduction to Bioethics*. Beijing, China: Tsinghua University Press; 2017.
10. National Gene Bank. Guideline for Sample/Data Sharing Review. Available from <http://sz.people.com.cn/n2/2017/0425/c202846-30086772.html> (accessed March 30, 2020).

Address correspondence to:

Qingli Hu, MD

Shanghai Clinical Research Center

380 Fenglin Road

Shanghai 200032

China

E-mail: huchingli32@163.com