

Ethical Management Guidelines for the Shanghai Disease-Based Biobank Network

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The Ethical Management Guidelines for the Shanghai Disease-Based Biobank Network are intended to safeguard the interests of all the participants, to standardize the construction, management, and resource sharing of the Shanghai Disease-based Biobank Network, to promote the development of medical research, and to improve public health and well-being. The guidelines contain seven chapters: General Principles; Informed Consent; Use of Bio-samples from Persons without the Capacity to Consent; Privacy and Confidentiality; Applications of Use of Biological Samples and Data; Intellectual Property and Resource Sharing; and Conflict of Interest.

Introduction

A BIOBANK IS AN INTEGRATED RESOURCE of biological samples of high quality and related data including donors' health-related data and all biological, demographic, and epidemiologic information. This infrastructure plays an irreplaceable role in performing research for prediction, diagnosis, and treatment of diseases. In recent years, with the promotion of translational medicine, there is a need to have large-scale collections of samples and data. Accordingly, the requirement for international sharing is a high priority. New tools need to be developed to accelerate the process of forecasting, prevention, and diagnosis of diseases, as well as to develop more effective, less toxic effects using new drugs and molecular targets for personalized treatment.

With a population of 30 million, Shanghai is one of the largest cities in China. Shanghai has the advantage of strong medical and scientific research institutes with qualified professional personnel, and a wealth of biomedical material, clinical data, and health-related information. Therefore, it has the potential for establishing a large biobank for resource-sharing.

Supported by the Shanghai Municipal Commission of Science and Technology, The Shanghai Disease-Based Biobank Project (Project NO.12DZ2294903) started in 2012. The project is led by the Shanghai Shen-Kang Hospital Development Center, involving 20 tertiary level hospitals and research institutes, which are affiliated with Shanghai Fudan University, Shanghai Jiao Tong University, and Shanghai Traditional Medical University, respectively.

However, there is a broad distribution of the biological samples, clinical and other health-related data, a lack of unified operational procedures and management systems, a

shortage of specific legal regulations and ethics guidelines, and a deficiency of willingness and inspiration for sharing of resources among the participating hospitals and research institutes. It is therefore important for the Shanghai Clinical Research Center (SCRC) to serve as the third party management and operations institute, in order to take responsibility for supervision and quality control of the biological samples. In line with this approach, a set of ethical management guidelines for the Shanghai Disease Based Biobank Network was developed. In addition, a unified platform was established to facilitate exchange of sample and data information, and to promote sample shared services and operations for the Backup Repository for the Shanghai Biobank.

The clinical data and relevant information from all the participating hospitals will be integrated, followed, shared, and updated through this Medical Unified Project. The biosample information will be integrated by the medical unified web system through cloud computing technology, as well as the ethics issues related to the biobank management. Consequently, the Ethical Management Guidelines were developed by the SCRC Independent Ethics Committee (hereafter referred to as The Central Committee). To meet this requirement, a 3-year project, led by Professor Qing-Li Hu, including an extensive literature review, a local situation analysis, and academic opinions exchange, was conducted by the Central Committee. The final document is presented here as the study outcome.

The ethics guidelines related to the collection of biological samples, genetic and health related data, the issues of consent, withdrawal of consent, the issues of storage, processing, and access, and the issues of international cooperation and benefits sharing were developed with reference to the international guidelines, particularly the International

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Declaration on Human Genetic Data (UNESCO 2003),¹ The National Bioethics Advisory Commission Research Involving Human Biological Material (USA 1999),² and the German National Ethics Council, Biobanks for Research: Opinion, 2004.³

The principle of “informed consent” has been adopted as a central standard in this guideline. However, the collection of biological samples and data for long-term storage in biobanks may require rethinking the traditional concept of informed consent.⁴ Using previously donated biological samples in future research may be impossible due to the lack of proper consent.⁵ In addition, given the speed of scientific development in the area of genetics, and the vast spectrum of potential research directions that may arise and can legitimately be pursued by such databanks, there is really no way to predict possible future uses of donated samples.⁶

In sum, if we want to allow research based on biobanks to progress, we need to recognize that adherence to the classical model of informed consent is problematic. As the UK Human Genetics Commission recently concluded: “the difficulties involved in tracing and securing re-consent for different forms of medical research may make obtaining fresh consent impractical and would seriously limit the usefulness of large-scale population databases.”⁷ It was for this reason that we proposed an alternative approach for China: One-time broad consent with an opt-out provision.

The Chinese Version of these guidelines was published in a domestic core journal: *The Medicine and Philosophy* (2014, Vol. 35, No. 3A).⁸ For further improvement of the guidelines, we have drafted this English version, and we are looking forward to receiving any suggestions or critical opinions to make it more helpful for biobankers in the field.

Following is the English Version of the Ethical Management Guidelines for the Shanghai Disease-Based Biobank Network:

General Principles

1. The Shanghai Clinical Research Center (SCRC) is supported by the Shanghai Municipal Development and Reform Commission; Science and Technology Commission of Shanghai Municipality; Shanghai Municipal Health and Family Planning Commission; Shanghai Shen Kang Hospital Development Center and Shanghai Xuhui District Government. SCRC was appointed as the third party management, and set up the Central Ethics Committee of Shanghai Disease-Based Biobank (hereinafter referred to as “Central Ethics Committee”), responsible for coordinating ethical issues among Participating Institutes.
2. This guidance document is being distributed for the standardization and unification of the construction, management, and operation of the Shanghai Disease-Based Biobank Network (hereinafter referred to as “Biobank”), guarantee the legal interests of the participants, promote the development of medicine, and improve the welfare of human beings.
3. In accordance with the “Regulations on Ethical Review of Biomedical Research Involving Human Subjects” by the National Health and Family Planning Commission (NHFPC);⁹ “Guiding Principles for Ethics Review on Drug Clinical Trial” by the China Food and Drug Administration (CFDA);¹⁰ “Declaration of Helsinki” by the World Medical Association;¹¹ “Declaration on Genetic

Data” by the United Nations Educational, Scientific and Cultural Organization (UNESCO);¹² and the “Guidelines for Human Biobanks and Genetic Research Databases” by the Organization for Economic Cooperation and Development (OECD),¹³ the Central Ethics Committee follows the principles of beneficence, autonomy, non-maleficence and justice, and conducts reviews independently, objectively, justly, and transparently.

4. The construction of the Biobank must follow the principle of transparency (i.e., relevant policies must be made public). This is in order to ensure the quality of specimens, protect the privacy of participants and the confidentiality of the data, as well as proper use of the data, and ensure that the collection, storage, distribution, and use of biological materials is in accordance with ethical procedures.
5. All participating institutes should follow the ethics requirements, offering explicit fairness and sufficient and appropriate information, including the risks and consequences, prior to asking consent of the donors. The consent must be obtained beforehand, and be voluntary, informed, and explicit. It should also inform the donors of the right to withdraw consent at any time without any consequences of harm and discrimination.
6. When the donors choose to withdraw the consent, their specimens and data should be immediately removed from the Biobank. All participating institutes should develop relevant procedures to follow up on the disposition of the specimens and relevant data after the donors withdraw their consent. Where specimens are provided to a third party, those samples should be disposed of according to the Biobank management unless:
 - (1) Agreement to continue to use the specimens and data was explicitly stipulated in the written consent of the donors.
 - (2) Specimens and data were anonymized.
 - (3) Approval of the ethics committee was provided.
7. If the donor is deceased or becomes incompetent to make such decisions, the Biobank should store and use the specimens/data in accordance with the original consent, unless expressly stipulated otherwise.
8. Donors can trace back the conditions of storage, disposal, and use of the specimens, but cannot request read, copy, add, or correct the relevant data/information unless it concerns their identified information (age, gender, address etc.).
9. If necessary, or if different opinions among two or more participating institutes arise on ethics issues involved in collecting, disposing, storing or using biological specimens or data, they should request the opinion of the Central Ethics Committee.

Informed Consent

10. All participating institutes should assure that the use of specimens is in full compliance with the informed consent, regardless of the options the donors have chosen.
11. All participating institutes should develop a document explicitly describing the process of informed consent, including when and how to obtain informed consent. The Central Ethics Committee of the Shanghai Disease-Based Biobank recommends that specimens collected from now on adopt the principle of a “Broad Consent.”

12. The collection, use, and disposal of specimens in biomedical research should respect individual preferences, religion, cultural background, and various customs.
13. Procedures involving biological specimens collected from participants involved in therapeutic processes for research, including when to obtain the informed consent (e.g., before or after the medical procedure) should consider many other issues, and not involve coercive implementation.
14. Informed consent should highlight that the donors have the right to withdraw consent at any time without consequences of harm and discrimination. (For details, please refer to Articles 5 and 6.)
15. In the case of an accident, the donor is deceased or loses capacity for such actions, use of the specimens must be consistent with the original consent, and in line with the donor's wishes of continued deposit of the specimen in the biobank. (or completely or partially withdraw from the research.)

Use of Biological Specimens of Persons with Limited or No Capacity

16. According to the general principles of the Civil Law, persons with limited capacity for civil conduct include minors aged 10 to 18, and psychotics who are unable to fully account for their own conduct. Persons with no capacity for civil conduct include minors under the age of 10 and psychotics who are unable to account for their own conduct. Under such situations, only a study which benefits the persons with limited or no capacity (including minors) and involving minimal risk, is allowed from both the ethical and legal perspectives.
17. If the Biobank collects identified specimens and/or data from minors, a new consent may be required from the participant once he or she reaches the legal adult age.
18. When the participant with limited capacity, or with no capacity, becomes a person with full capacity for civil conduct, a new informed consent should also be considered.

Privacy and Confidentiality

19. In recent years, with the development of genomics technology, proteomics technology, and human genome sequencing, biobanks can track data relying on electronic databases and on the Internet. It is therefore more critical and urgent to determine how to handle the risks of privacy.
20. Attention should be paid to infringement on privacy, which may lead to discrimination and/or stigmatization of related persons and relevant groups.
21. All participating institutes involved in the storage, use, and disclosure of information concerning their biological materials and relevant data should follow well-documented procedures to protect the privacy and confidentiality of the donors. Such procedures may include: encoding, encrypting, anonymizing, or removing all identifying information.
22. Identified data such as: names, ID card numbers, date of birth, and so on should be encrypted and managed independently. Well-documented procedures must be re-

- quired to allow the matching of data with biological specimens, and restoring the encrypted form immediately after access is granted.
23. If a comparison study of different data and information is carried out, it should restore the encoding, encrypting, anonymization, or otherwise remove all identifying information immediately after the comparative study.
24. Staff members responsible for the collection, storage, use, and disposal of specimens shall not take advantage of their position to easily access and disclose any private data or information about the donor.
25. Based on the Information Security Regulation of the Centre Biobank, all participating institutes should establish Information Security Regulations and make them public.
26. Protection of the data by further encoding, encrypting, or by setting different levels of access permissions to specimens and/or data can be achieved, and the repository should sign a confidentiality agreement with staff members.
27. Different levels of access permissions must be explicitly stipulated in the operational regulations, and when appropriate, receive the approval of the ethics committee.
28. Access permissions to specimens and/or data, including the donor's identifiers, diagnoses, family history, and treatment history must be restricted to authorized repository staff members.
29. Minimize the number of staff members allowed to access specimens and/or data, as well as provide timely supervision of access activities and ensure follow up of the standard procedure.

Utilization of Biospecimens and Data

30. To better serve research groups, repositories should establish guidelines and regulations for distributing specimens and sharing clinical data in compliance with ethical principles.
31. Researchers are required to obtain approval from the biobank's administrator for the use of specimens and/or data. The biobank's administrator should review the qualifications, experience, research methods, and the rationale of the applicant's proposed program. Documentation of such approval should be obtained prior the utilization of specimens and/or data.
32. If a researcher discloses information about specimens and or data to a third party, the Repository will immediately terminate the further right to their use, and the researchers will be subject to corresponding legal liabilities.
33. These regulations are suitable for all specimens and data. For specimens collected in the future, we recommend adopting the principle of "Broad Consent" (refer to Article 11). For specimens collected earlier, we recommend adopting the principle of "Opt-Out," presuming that donors give their consent for continued use their specimens and data, unless they had declared their objection. However, the specimens and data can only be used after the approval of the ethics committee.
34. As the third party in charge of management, the Shanghai Clinical Research Center has the responsibility to mediate disputes regarding issues related to access of specimens and/or data.

Intellectual Property Rights and Resource Sharing

35. All participating institutes must not transfer either partially or entirely all Biospecimens in the Biobank to others without the permission of the Ethics Committee. When the specimens, related data and information are provided to others, the process should be impartial as well as fair, and a Material Transfer Agreement should be signed.
36. The agreement for transferring samples should be specific according to the nature of the organizations:
 - (1) Internal use in hospital, academic use and use by nonprofit organizations;
 - (2) Commercial organizations
37. The data, specimens, and their derivatives in the Biobank in principle should not be exported overseas. If the exportation is necessary (e.g., for a rare disease), it should comply with the Human Genetic Resources Administrative Management Regulation¹⁴ and be approved by competent authorities.
38. According to Chinese Patent Law,¹⁵ staff members working for the Biobank are not the inventors with regard to samples stored in Biobank. The inventor should be determined by Patent Law.
39. The Biobank has no inherent rights with regard to the future terminal user's intellectual property. If the Biobank only provides samples, investigators may acknowledge the Biobank in any published articles. However if the Biobank has actively participated in the research, intellectual property rights would be dealt with based on applicable regulatory requirements.
40. If the intellectual property rights originated from research with the biospecimens where a patent is obtained, the situation should be dealt with based on applicable regulatory requirements. According to Subparagraph 4 of Article 69 of the Patent Law, research using relevant patents solely for the purposes of scientific research and experimentation will not be deemed as an infringement of a patent right.

Conflicts of Interests

41. During the process of review by the ethics committee, all known or possible financial and nonfinancial interests related to an institution or biobank must be reported, and conflicts of interest avoided.
42. Conflicts of both financial and nonfinancial interests must be avoided. Financial interest conflicts include for example, the investigator holding stock of the sponsor. Nonfinancial interest conflicts include, for example, if the investigator also supervises the biobank. The ethics committee needs to pay attention to compliance with review procedures. Those with a conflict of interest should not participate in an ethics review.
43. Conflicts of both financial and nonfinancial interests should be identified and managed practically (i.e., on a case-by-case basis).

With the development of biomedical research and the gradual improvement of ethical and regulatory policies, all participating institutes can put forward modifications and opinions for further consideration, in order to ensure the sustainable development of these guidelines. The guidelines

interpretation officially resides with the Shanghai Major Disease Clinical Biological Samples Library Central Independent Ethics Committee.

Author Disclosure Statement

No competing financial interests exist.

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