Ethical Aspects When Using Biological Samples for Research

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Biological samples are indispensable in biology research, whether as part of basic research to better understand physiological or pathological function; in epidemiological studies; or in the development of diagnostic tests, treatments, or vaccines. A sample is a small quantity of a substance that is collected to study its characteristics, along with information about the sample. A sample without information has no scientific value. There are various types of samples: healthy or diseased tissue from humans or domestic or wild animals, elements from the environment (water, soil, air), or derivatives from these samples (proteins, nucleic acids, associated pathogens). This section will address the ethical issues related to the collection, use, storage, circulation, and sharing of samples between institutions, individuals, and countries.

Data collection and use

Sample collection: what

The type, volume, and number of samples collected should be limited to only what is necessary to achieve the objectives of the research. Samples should also be collected using the least invasive method possible: a blood sample is preferred over a tissue biopsy, for example, and blood samples should involve minimal volume and be age-appropriate. This should be clearly specified and justified in the research protocol submitted to the ethics committee before the study begins. The rules for sample collection should not change during the study without the prior approval of an ethics committee. It is not an opportunity to "collect as many samples as possible."

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For example, in a study of arboviruses in febrile patients that only requires a blood sample for diagnosis, there may be a temptation to also take throat and rectal samples, which could be used for future research. Such thinking raises ethical issues: it would be dishonest to hide the actual reason for the collection, which could result in "dehumanizing" the patient into a mere source of biological samples.

New technologies have been developed that allow research on wild animals to use droppings in place of tissue samples for some types of research (such as antibody or pathogen detection).

Would it be ethical to take a sample of cerebrospinal fluid (CSF) via lumbar puncture in patients with no neurological symptoms to study asymptomatic carriers, similarly to what is often done with blood samples, given that the lumbar puncture procedure is painful and not completely harmless?

Sample collection: how

The collection procedure should be detailed in the research protocol and should include the sampling method, associated information, collection duration and period, and the list of those who will perform the procedure. The method should be selected to minimize any discomfort for the participant, such as by using small amounts that are age-appropriate. Thus in a study of seroprevalence in the general population, it is preferable to take a blood sample by pricking the fingertip rather than using the more invasive procedure of venous puncture. When collecting samples from human subjects you must obtain their consent. This involves authorization to take the sample itself but also includes consent to participate in the research, and possibly storage of the sample for a specific use at a later date. Participants may leave the study at any time, even after sample collection, in which case their samples are destroyed. A sample may also be taken as part of medical treatment, such as the removal of a tumor that is later used in a research project.

For samples taken from animals and associated environments, the World Organisation for Animal Health (OIE) has established guidelines (OIE Terrestrial Manual, 2016) that detail sample collection (safety measures to avoid contaminating the environment, volume and type of sample appropriate for the tests to be performed, animal-appropriate sampling technique, and necropsy by a veterinarian), sample size (to be calculated based on epidemiological data and study objectives), and the information to collect along with the sample (location, description of the organism sampled, and epidemiological information).

The researcher is responsible for complying with local regulations. Authorization may be needed from the competent local authorities. The manner in which samples are collected should also be considered from an ethical perspective. The procedure should respect the target environment

and population, individual and group sensitivities, and the safety of those collecting the samples.

In a research project to characterize a type of local flora, authorizations must be obtained (from private land owners, directors of national parks, etc.) for the collection of a particular type of plant in a defined location. The researcher must take care to neither degrade nor deplete the flora during collection, and verify that the plant in question is not subject to national or international protective measures. Once on site, if the team discovers another plant of interest that is not included in the study protocol, a new protocol should be drawn up and new authorizations obtained.

How do we manage a local population's perceptions of scientists, dressed in lab coats, masks, and gloves, arriving in the countryside to take potentially pathogenic samples from wild animals?

Limitations in the use of research samples

Samples may only be used within the strict framework specified in the research protocol and included in the consent form signed by participants. Before samples can be used for any other purpose, individual consent must be obtained once again from each participant after the ethics committee has approved the new research protocol. This is also true for samples taken as part of a medical treatment, before they can be used for a scientific purpose other than the one for which they were originally collected.

When a sample is taken as part of a medical treatment, one might think that any experiments conducted on the sample that do not affect the patient have no ethical implications. However, the research that led to the development of the first immortal cell line shows us that this is not the case.

In 1951, Henrietta Lacks died from the complications of highly aggressive cervical cancer. Without her consent, her treating physician gave a sample of her tumor to an oncologist, Dr. Gey, who developed the first line of immortal cells, HeLa. Scientists later took blood samples from Henrietta's children under the guise of oncology follow-up, which they used to conduct research on HeLa cells. The scientists produced thousands of kilograms of cells for research laboratories. They are the most widely used human cells in the world. Sales of these cells have created millions of dollars of profit, but the Lacks family did not receive any share of the financial windfall and continued to live in poverty. When her children were finally informed, more than twenty years later, they publically denounced the researchers' behavior towards them and lamented the fact that their mother did not even have a decent gravesite for her service to science.[1]

1. SKLOOT, R. (2010), *The immortal life of Henrietta Lacks*, New York: Crown Publishers.

When a sample is received for pathology analysis on behalf of a patient, can it subsequently be used in a research program?

Storage and sharing

Why store samples?

Biological samples are precious both by their very nature and for their scientific value, and may harbor far more information than that gleaned from their initial use. It became clear early in medical studies that human-derived samples and pathogenic agents needed to be conserved in order to understand diseases and improve treatments.[2] Specimens from wild animals are usually stored by recognized institutions such as natural history museums. Samples containing microorganisms are generally stored at medical institutions.

While it is not considered ethical to use biological samples for anything other than the original purpose, it can also be argued that it is equally unethical to dispose of samples at the end of experimentation. Take the example of a study of the seroprevalence of dengue viruses circulating in a general population, during which serum samples are taken from individuals of all ages. Once the study is completed, the samples are thrown away. If another research team is subsequently interested in studying the public health significance of hepatitis C virus infection and wants to conduct a seroprevalence study in the same population, they would need to subject this population to another needle stick to collect more blood samples, when the previous ones could have been used had they been conserved.

Biological sample collections are evidence of a biological situation at a given place and time. New technologies may be able to extract new information from them at a later date. Advances in molecular biology, for example, have resulted in some species being reassigned to a different taxonomic classification.

A researcher's decision to store or dispose of samples at the end of a study should be included in the research protocol and information for participants.

What is a biobank?

The term "biobank" has several definitions, depending on its contents and purpose. A group of experts from the European Commission defined the

2. Lajaunie, C., & Morand, S. (2015). Barcoding, biobanking, e-banking: From ecological to ethical and legal aspects. Insights from the PathoDivSEA Project. In S. Morand, J-P. Dujardin, R. Lefait-Rollin, & C. Apiwathnasorn. (Eds.), *Socio-ecological dimensions of infectious diseases in Southeast Asia*. Singapore: Springer, 217–27.

term as "the biological samples themselves, plus the related databases, allowing a certain level of accessibility, availability, and exchange for scientific studies."[3]

A biobank is a way for the scientific community to share samples and related information, and thus has an obligation to provide high-quality storage of materials and related information. The quality of the collection may differ from one biobank to another, depending on their resources. Anne Cambon-Thomsen[4] makes the following distinctions: (i) simple sample storage (several samples in a laboratory); (ii) an organized collection for the specific purposes of research, diagnosis, or donation; and (iii) a sample bank operating independently with storage as its primary activity.

Many researchers are unaware that the samples stored in their laboratory constitute a biobank. There is no international standard as of this writing for biobank operations, although there are ethical standards in human health to guide researchers (statements from UNESCO, Council for International Organizations of Medical Science (CIOMS) Guidelines). For samples to be useable, a certain amount of information must be stored with them: type (blood, liver biopsy, etc.), species, collection site, and date. Other additional data are often quite useful as well, such as the nucleic acid sequence, results of analyses, environmental information, photos of the collection site, photos of the specimen the sample was taken from, GPS coordinates, and so forth. Medical and personal information is usually stored for human samples, which are rendered anonymous to ensure confidentiality. However, researchers must be able to contact every donor personally for any future request for consent, and the source of every sample must be known in case the donor decides to withdraw from the study. Therefore identification data must be stored in such a way as to maintain strict confidentiality vis-à-vis those who use the samples.

An example of the process: I have returned from collecting mosquito samples. How should I organize the storage of these samples in my laboratory?

Who owns the samples?

Biological samples collected as part of scientific research belong to the research body itself and not to its researchers. When samples are transferred from one institute to another, these bodies sign an agreement defining the rights of both the source and the receiving institute regarding the use of the samples and any derivatives therefrom. The transfer of

3. Lajaunie C., et al., *Op. cit*.
4. Cambon-Thomsen, A. (2001). Les problèmes pratiques et éthiques que pose le stockage des échantillons biologiques. In: Dossier : Médecine prédictive : mythe et réalité, *Actualité et dossiers en santé publique, 34,* 55–61.

samples from one country to another is more complex; the regulations of each must be followed, including any rules about leaving the territory. The Nagoya Protocol addresses access to genetic resources and the fair and equitable sharing of benefits arising from them, including when such resources leave a country.

The issue of ownership is even more complex for human samples, because it relates to the question of who owns the human body and its parts. Consent must be obtained from an individual before any of his or her body parts can be used, but this person cannot derive any financial gain from such use.[5]

Every year flu vaccines are developed in countries in the global North using strains circulating in the southern hemisphere. Going forward, sharing of these benefits between the pharmaceutical companies and the countries where the viral strains originate should be considered within the context of the Nagoya Protocol.

Conclusion

It is important to work with local actors when collecting any types of samples, bearing in mind the basic principle that use of the samples should primarily benefit the source population. Fieldwork does not end with sample collection. Consideration should always be given as early as possible to the local impact, in accordance with the Nagoya Protocol. Some of the non-monetary benefits suggested in the Protocol include contribution to scientific research programs and local development; international collaboration between researchers; and contributions to education and training. Such benefits should be envisioned and clearly formulated from the start of the research project.

5. Council of Europe. (1997). Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine. Convention on Human Rights and Biomedicine.

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