

From the biobank to the research biorepository: ethical and legal recommendations

*An initiative of the Independent Ethics Committee
Fondazione IRCCS
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FROM THE BIOBANK TO THE RESEARCH BIOREPOSITORY: ETHICAL AND LEGAL RECOMMENDATIONS

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Note

The Italian version of this paper proposes the word "bio-teca" (i.e., biological repository), which was felt as more appropriate for those "biobanks" which comply with some criteria laid down in the document. The metaphor of the bank, however effective, recalls a lucrative scope, which does not apply at all to the type of entities that this document foresees and reduces a new field of biomedicine that will thoroughly reshape the idea of health to the perspective of individual profit. On the contrary, the word "teca" (from the Greek noun "theke") gives an idea of sacredness, which corresponds to the content of a biobank, which is precious, as precious is its function of advancing research for public interest.

PREMISE

In 2009, Time magazine devoted a special issue to 10 ideas that are changing the world: among them there were biobanks for research purposes. The ability to store human tissue (mostly blood samples, but also isolated cells and solid parts) separated from the body, to gain molecular, and particularly genetic, information, to cross match with clinical information, even on large numbers of individuals with similar conditions, represents a great opportunity for medical science. In particular, this is true for the study of cancer, the only pathological tissue that has a genome (and therefore a molecular make-up) which is different from that of the carrier and is capable of rapid evolution.

The potential of these tools is given by the enormous amount of information contained in the samples, which, along with the continuing evolution of technologies, renders their use for research or therapy unpredictable.

It follows that, at the time of sampling, we are inherently unable to specifically inform the donor about all assessments that might be carried out in the future on his/her tissue. However, it is possible to fully and specifically inform the donor about the methods and aims regarding the use of personal data that will be obtained from the sample.

Biobanks are designed to maximize this research potential, with foreseeable advantages for the community, in terms of knowledge, treatment and technologies. There are also foreseeable gains for the industry, which may be able to transform such knowledge into products, whether diagnostic or therapeutic, to bring to the market.

Many ethical and legal issues are thus open, particularly affecting relationships with donors, researchers and sponsors. Today the main problems have to do with:

- **the meaning and implications of the concept of donation;**
- **the extent of informed consent;**
- **withdrawal of consent and its consequences;**
- **protection of personal data (privacy);**
- **guarantees for individuals and the community.**

In 2008, the Independent Ethics Committee of Istituto Nazionale dei Tumori, Milan, Italy, focused on the issue of uses of human tissue samples for research purposes, and embarked in consultations thereon with other ethics committees and different stakeholders: researchers, bioethicists, lawyers, patient representatives, industry representatives, and experts on regulatory issues, including some from the Italian Drug Agency and the Authority for Protection of Personal Data.

The goal of this initiative was to develop a set of recommendations on critical aspects pertaining to the use of biological samples for research purposes. There was a first meeting, held at Istituto Nazionale Tumori in November 2008, ending up in the first draft of a consensus document. On this basis, a second meeting was organized in June 2009, and consultation ended in November 2009 with a public workshop. At the end of this process, a writing committee was set up with the task of summarizing the ethical and legal recommendations into a final document, which is presented herein for diffusion and possible subscription by all interested parties.

ETHICAL AND LEGAL CRITICAL ISSUES

Donation for research purposes: Is donation a metaphoric concept or should it be taken seriously?

This is not the place to discuss how much the concept of "ownership" applies to the body and its parts. For the aims of this document, it is enough to state that with his/her disposition the donor allows the use of samples for research purposes and transfers some powers of control over them in their material nature. However, the donor retains a social interest as regards the correct use of samples for research and an individual interest as regards the information content of samples, especially for two aspects:

- **protection of personal data;**
- **availability of information useful for him/herself or family members.**

Consent to the processing of personal data: How specific should the consent be? Can it be broad or open?

All parties agree that the need to get back to donors to seek their approval every time a new, previously unforeseen biological assessment on samples is done would prevent functioning and continuity of biobanks.

Indeed, according to the Italian Authority for the Protection of Personal Data: "The storage and further use of biological samples and genetic data collected for research projects and statistical studies, different from those for which the informed consent was originally acquired, are permitted but *limited to the pursuit of scientific and statistical purposes directly related to the original aims.*"

However, the interest of the donor to protect his/her data does not apply to the "scientific and statistical purposes" of further studies, but rather to the procedures and limitations of data handling, namely:

- **possibilities and modalities of identification of data (anonymous, identifiable, tagged with aliases);**
- **flow of information (to whom, how);**
- **processing (comparisons, linkages);**
- **retention and subsequent availability of data.**

As far as all this is concerned, there is no doubt that the consent to the processing of data must be specific, and any use of the biobank that goes beyond what was specified in the original consent should imply a new consent.

On the contrary, specificity in regard to the scientific purposes of further researches improperly assimilates the "consent to data processing", which protects confidentiality, and the "consent of an

individual to participation in a clinical research”, which protects directly the safety and dignity of the person. In the case of biological samples, safety and dignity of the person are at stake only indirectly, when an abuse takes place.

If this is true, the debate on the need for a broad or open consent (or other variants thereof) could be settled by keeping the two areas distinct: the protection of personal data on one side and the protection of safety and dignity on the other.

Withdrawal of consent to the processing of personal data: What does the withdrawal implies? How can we reconcile the citizen's right to withdrawal with stability of biobanks?

For the reasons stated above, the withdrawal of patient's consent to the processing of data cannot include an obligation to destroy samples in their material consistency, but only the obligation to render them no longer identifiable.

The main European document on the collections of biological materials for scientific purposes, Recommendation 4 (2006) of the European Council, assimilates the destruction of samples and their anonymity, reserving to Member States the power to decide between the two modalities of protection of confidentiality. Indeed, making the two options equivalent would have serious consequences. In order to avoid the instability of biobanks in time, the donation should not be subject to withdrawal in regard to the preservation of samples as such. In the case of withdrawal of consent to data processing, the sample could be made anonymous, respecting the provisions of the Italian Authority: "If the person withdraws consent to treatment of data for research purposes, the biological sample is also destroyed, provided it was collected for such purposes, *unless the sample, originally or after being manipulated, can no longer be associated to an identified or identifiable person.*"

Mention should be made of the objection that genetic data are inherently self-identifiable, so that it would be impossible to make a biological sample anonymous: proof of that is the use of genetic data for criminal identifications. Yet, the possibility to trace back the identity of the person from whom samples were taken is concrete only if it is possible to match data extracted from samples with the genetic data of the alleged donor (to say that this is a sample of Tom, I need to compare it with another sample of Tom). However, in the case of samples made anonymous as per donor's willingness, this would result in a double violation of provisions on protection of personal data. Furthermore, any damage would result only from discriminatory uses of the information, which can effectively be prohibited by law (see Genetic Information Nondiscrimination Act in the U.S.).

Guarantees for individuals and the community: How can we make biobanks "third" parties, guaranteeing citizen donors and the society?

In return for transferring to the biobank some control over the sample, the citizen donor may have some benefits (such as the free conservation of his/her samples for personal use, or the retrieval of information useful for him/herself or family members), and, above all, some guarantees.

Guarantees can protect both individual interests (confidentiality of data) and interests of the community (availability of the results of research and technologies derived).

The guarantees should affect:

- **the function of the biobank** and its procedures (functions of public interest, independence, transparency, confidentiality and professional secrecy, explicit agreements of transfer, standards of conservation);
- **decision-making processes and players involved** (Institutional Review Board, Ethics Committee, Boards of Trustees including representatives of associations of patients and citizens);
- **information and communication to all stakeholders** (citizens and their associations, health institutions, public and private research institutes, industry, political institutes);
- **the rights of donors** (personal information, use of the samples, consent withdrawal).

To ensure these guarantees, the biobank should be conceived as a body that:

- **exercises a public function** (which does not exclude that it can be private, but implies compliance with rules and standards established to ensure the public interest);
- **is independent of** donors, researchers (and their sponsors) and institutions of research and health care (this does not exclude that it is located within a research institution, but its independence must be recognized, as is the case for institutional Ethics Committees);
- **is a tool for collecting, sharing, spreading knowledge and for technology transfer** (which implies procedures to encourage that knowledge gained from studies on samples get back to it and explicit policies regarding eventual patents developed using the samples).

ETHICAL-LEGAL RECOMMENDATIONS FOR THE OPERATION OF RESEARCH BIOREPOSITORIES

1. For the purposes of this document, the term "Research biorepository" ("Bioteca") means an institution that collects, preserves, and transfers to third parties, human biological samples, for purposes of scientific research. Biological samples can be made up of cells, tissues and biological fluids, including all molecular fractions (proteins, RNA, DNA, etc.) derived from them. Such materials can come both from healthy volunteers and patients. Given the social and civil dimensions of the activities of the Research biorepositories, it is recommended that all donors are viewed primarily as citizens.
2. With their activities, Research biorepositories exert a public function for improving health care in the interest of the general public. Thus, it is recommended that the constitution and the activity of Research biorepositories is regulated at a national and an international level, in order to set operative standards and shared quality criteria.
3. The Research biorepositories, even if located in hospitals or public or private research institutes, must be able to act as warranters, in a position of "neutrality" towards citizen donors

as well as researchers and their institutions, including the hosting institution, and their sponsors. It is therefore recommended to foresee regulations that ensure the independence of Research biorepositories in terms of responsibilities, procedures and financing, with a Chair and a dedicated staff. A good model for the legal structure of the Research biorepositories is that of the Charitable Trusts, by which a citizen donor transfers his/her own powers to a trustee, who has a legal duty to use them in the interest of a beneficiary, in this case the community.

4. Biological samples may be acquired by Research biorepositories only with the consent of donors, who thus transfer for free their powers on the biological samples to the biorepository, also defining the limits within which they can be used. To ensure compliance with the wishes of donors, it is recommended that the Research biorepository uses the samples in the public interest and in accordance to the purposes set out in the consent. In no way samples can be considered, or become, owned by private for-profit entities.
5. Although the transfer of samples to a Research biorepository represents an absolutely free act, it is necessary to give citizens who donate their tissues the possibility to access the information these harbour, if available. It is therefore recommended that the Research biorepository foresees to store samples for a sufficiently long period and ensures that donors, as long as technically feasible, have access to their own samples for personal investigations. Moreover, it is recommended that the Research biorepository allows interested donors to have access to the results of assessments done on their samples, in the case that such information may be useful for predictions regarding diagnosis, treatment and prevention of diseases, following agreed procedures and standards of quality of the communication process (counseling).
- 6.. Continuous developments in biomedical sciences do not allow to give prior notice to donors of all possible assessments that may be performed in the future on donated samples. However, this does not lead to any limitation to the rights of parties involved, in that donors will not be involved directly in such assessments, nor will their health or dignity be at stake. Nevertheless, privacy of citizens involved must be protected, and they have the right to be informed in detail about how their data are handled.

It is therefore recommended that the consent to the processing of personal data extracted from samples at least include information on:

- the degree to which samples can be identified (being marked by a code, a pseudonym, a double code, or being anonymous);
- arrangements for return to the citizen donor (on notice, on request, toward other recipients) of personal information useful for diagnosis, treatment or prevention of diseases.

It is also recommended that — under secrecy constraints, definition of procedures and through appropriate technological tools — only the staff of the Research biorepository can link the identity of donors to the stored samples and update the clinical data related to samples.

7. The consent to the processing of personal data should be revocable, whereas the donation of the specimen to the Research biorepository should be irreversible. It is therefore recommended that, in case of consent withdrawal, the Research biorepository does not need to destroy the sample but only to make it anonymous. It is important to inform the citizen donor that fully anonymous samples are of little or no use for research, since it is impossible to correlate them to clinical data.
8. As far as biological samples taken during diagnostic or therapeutic interventions during normal clinical activity and liable to be destroyed ("left over") are concerned, in the absence of any reasonable opportunity to ask the patient to consent to donation for research purposes and to the processing of personal data, aside from the case of an explicit refusal by the patient him/herself, it should be permitted to keep them in the Research biorepository and to use them for research purposes, provided it is impossible to trace patient's identity. It is therefore recommended that such samples are stored only after they have been made completely anonymous, and that also the clinical data related to the samples are such that they do not allow retracing the identity.
9. The Chair's office of the Research biorepository should be responsible for the use of biological samples. It is recommended that it is supported by a scientific committee (Institutional Review Board), which evaluates the scientific value of projects, and a Board of Trustees, including representatives of patient associations and citizens.
10. Researchers from the same institution where the Research biorepository is set up, or other researchers, who want to use the biological samples stored therein, should apply by submitting a research protocol to the Chair of the Research biorepository, which can authorize the research after evaluating its scientific consistency and appropriateness, with the assistance of the Scientific committee, the Ethics Committee and the Board of Trustees. It is recommended that biological samples and related clinical data are given to applicant researchers or research institutions only in coded form and under an explicit transfer agreement (Material Transfer Agreement). Denials to release the biological samples should be motivated by the Chair of the Research biorepository.
11. The Research biorepository should have rules that explicitly and clearly define all procedures. It is recommended that these rules lay down the minimum requirements which applicant researchers and research institutions must comply with in order to obtain samples, and criteria to use for prioritization in the event of multiple requests.
12. The use of biological samples and related data for each specific research project should be subject to authorization by an independent Ethics Committee, which may be that of the institution where the Research biorepository is located, on the basis of a submitted research protocol. The Independent Ethics Committee has to verify that the use of samples complies with the objectives agreed upon by the citizen donor in his/her consent. It is also recommended that citizen donors may be informed of proposed and approved projects, within the limitations imposed by the protection of intellectual and industrial property, and that the criteria followed by the independent Ethics Committee are made public.

13. Samples cannot be sold for money, but the Research biorepository may ask for a reasonable fee to cover its operating costs and sample storage. It is recommended that the Research biorepository's rules also govern economic transactions with research organizations and their sponsors. Moreover, the Research biorepository can also foresee specific policies for the development of patents from research carried out on samples and require researchers to adhere to such policies. In this regard, criteria shared at national and international level should be adopted, in order to avoid that patent policies give rise to inappropriate competitions among different Research biorepositories. In the absence of common guidelines, patent policies adopted by Research biorepositories should be worked out with the aim of protecting the public interest to enjoy new technologies for health at reasonable costs.
14. To act as an instrument of accumulation, sharing and transmission of knowledge and technology transfer, the Research biorepository must rely on feedback from researchers who use the samples, in order to make such information available to the entire scientific community. It is therefore recommended that in the agreement of transfer of samples to researchers it is requested to communicate to the Research biorepository the type of tests and assessments carried out on samples, in order to enable the biorepository to record such information. It is also recommended to provide incentives and priority of access to researchers and research institutions that pledge to fully communicate to the Research biorepository the results of tests and assessments.
15. The Research biorepository should effectively disclose its rules, activities and results to the scientific community, and the general public. It is recommended that the organization of Research biorepositories explicitly foresees information and communication activities, with allocation of proper resources, also to promote a culture of solidarity and consent to donations.

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