

## Ethical considerations in the use of biological specimens collected in emergency departments

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### Background

Biomedical research is intimately related to medical care and an essential activity for the advancement of medicine.

The experience accumulated in this field indicates that hospitals need to have an appropriate framework in which to attempt to resolve the many questions that constantly arise in clinical practice, including (but no less important) medical practice in emergency services.

We need to be able to shorten the time interval between the production of new knowledge (efficacy) and its research application to the real conditions of implementation (effectiveness and efficiency) in daily clinical practice. This is an interactive chain that goes from basic research to clinical research and on to daily medical care, and forms the basis of so-called translational research.

Biomedical research must be considered as a habitual activity and an essential part of good medical practice. The integration of research and clinical practice ensures higher quality of health services and better implementation of medical advances in the prevention and treatment of diseases, and more ethical and efficient patient care.

Quality research is not possible without excellent medical practice, performed with the highest ethical and technical safeguards.

Clinical research is aimed at patients or human diseases. Naturally, it requires the collaboration of patients and their families. It is increasingly clear that biomedical research builds on the progress made in the field of cell and molecular biology, knowledge of genetic mechanisms

and new techniques developed by basic scientists. Of particular importance in this context is the acquisition of biological samples for research.

Biomedical research includes so-called clinical research or research performed with patients. There are several categories or stages involved in the process of clinical biomedical research.

The first is translational research, which includes the process of transferring knowledge and technology (diagnostic or therapeutic) from the laboratory to the bedside and vice versa, in small groups of patients. It involves the application of basic knowledge (molecular biology and genetics) to the process of attending patients<sup>1,2</sup>.

Clinical trials are the second category of clinical research, characterized by the regular inclusion of large numbers of patients, carried out with single or multicentre studies. Initial testing of new drugs or treatments is done with phase I or phase II studies, which establish new knowledge about the particular disease being investigated in small cohorts. Phase III studies, of great length and complexity in most cases, involve large cohorts. The pharmaceutical industry is interested in the development of these trials provided they meet the criteria for time period and budget. The rapid recruitment of valid patients for the final analysis and quality of data are the essential factors that healthcare institutions should offer the industry in this case. Pharmacogenomics is another example of translational research converging with clinical trials, where computerised data processing is essential.

Finally, there is epidemiological research or research on health service results, based on the study of populations, which attempts to ascertain the effect of different diagnostic or thera-

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peutic strategies, or variations in clinical practice, on the final results, both health and economic, so that the medical care offered is increasingly based on scientific evidence. There are numerous examples of the potential benefits of such biomedical translational research, in clinical trials and in the evaluation of health services.

Quality clinical research is only possible with attention of equal quality. At the same time, clinical research improves physician quality, and should be an essential activity in the practice of modern medicine. Hospitals, as research centres, should develop specific clinical research projects in all three aspects, especially translational research.

It is important to properly inform and create a climate of opinion and debate in which biomedical research is appreciated by our citizens. One of the essential conditions for such research to be understood and supported by society is that it always performed with the highest possible standards of quality and safety.

### **Biological samples, biobanks and biomedical research**

For some time, many researchers, clinical or research laboratories have stored biological samples, for attending purposes (surplus from diagnostic processes, reserves for diagnostic review, validation of new diagnostic techniques) or surplus samples obtained from a previous research project. The ethical and legal requirements of modern society oblige us to establish standardized procedures for the management of biological samples and associated data, so that they meet a series of requirements in the process of informed consent from the donor, and ensure technical quality of the process and confidentiality of the associated data.

The management of associated data, procurement, processing and storage of biological samples and their distribution to researchers, must meet the ethical and legal norms and standards of quality set out by the Law on Biomedical Research<sup>3</sup>.

Biobanks are establishments which store organized collections of biological samples and associated information for the purpose of keeping them available for the scientific community to develop biomedical research projects, including population and specific disease or disorder studies. They are useful to explore the role of environmental, social, dietary and lifestyle factors on

disease and risk, identify the genes involved and foment pharmacogenomics.

A biobank must have full institutional support. The host institution is responsible for custody and must provide it with the structure, human and technical resources, organization and internal written rules that determine its operation, define its responsibilities, policy on quality and its healthcare or scientific objectives.

Biobank activity is governed by an ethics and clinical research committee, to ensure compliance with the ethical principles of biomedical research projects using samples of human origin. Biobanks must also have a scientific committee to supervise the management and scientific objectives and develop performance standards.

### **Informed consent for the collection of biological samples**

To ensure the rights of citizens, the acquisition and transfer of biological samples and associated health data must always be accompanied by donor consent, expressed in a free, voluntary, explicit, specific and written manner. Prior to obtaining biological samples and/or associated data to store in a biobank or collection, or at any time before initiating an investigation which considers using surplus samples from the attending process, the donor must be informed in a complete, clear, understandable and explicit manner by authorized personnel on the following aspects:

- Purpose of sample acquisition: why it is to be stored.
- Method of sample acquisition, explaining potential risks and inconvenience arising from the procedure of acquisition.
- Identification method: how the samples are identified (identified or identifiable versus anonymous samples).
- Conservation: where, how and how long the samples are kept.
- Voluntary nature of participation: consent of the donor should be free and after being properly informed.
- Right of revocation: the donor retains the right to withdraw the samples and information at any time and, if exercised, the samples will be destroyed or made anonymous.
- Confidentiality: Data are always confidential. Access to personal information is restricted to authorized personnel. The donor must be informed about the method of secure storage of

the data obtained from the sample analysis.

- Sample donation is free, with no financial compensation. The donor or family members may not receive any economic benefit from donating the sample, nor may they obtain any part of commercial benefits that might result from the research results.

- Transfer of data and samples: transfer must always be after donor consent and the data or samples can never be sold to a third party.

- Desire to be informed, or not, of the research findings: not applicable to research using anonymous data or data that does not allow reasonable identification of the donor.

When the donor has understood all these points and his/her questions have been answered, consent may be solicited. If consent is given, this will be recorded on a consent form and archived in the patient's medical record file.

## Types of data associated with biological samples

The data associated with biological samples refer to epidemiological, genealogical and demographic information (age, sex, place of birth, place of residence, physical activity and dietary habits, toxic habits (alcohol, tobacco, etc.) and work activity, to which are added clinical and biological data related to disease if samples are from patients.

The information associated with biological samples is collected and stored in electronic form. These data are likely to be analysed statistically for those scientific research purposes for which consent has been obtained.

The creation of files with personal data (any information about an identified or identifiable person) must be accompanied by a formal notification for registration in the "Registro General de Protección de Datos" (RGPD) related to the Spanish Agency of Data Protection (AEDP). The purpose of this record is that any person can know about the existence of personal databases, its purposes, and the identity and address, which facilitates the exercise of rights of access, rectification, cancellation and opposition established by law.

Notification to the RGPD merely states the existence of the database, indicating responsibility, purpose, location, level of security measures required and expected use of the data, as well as transfers to other countries, regardless of whether they are members of the European Union members or form part of the European Economic Area.

There are three basic types of data:

1.- Anonymous data: collected without a link to identify the source, so that its origin is impossible to identify.

2.- Anonymised or irreversibly dissociated data: this is information which does not identify an individual directly, and which cannot reasonably be used to determine identity.

3.- Encrypted data: this is encrypted or irreversibly dissociated information that cannot reasonably be used to identify an individual. The link still exists but access is highly restricted (to the biobank director or established delegate only).

## Who can use biological samples?

The decision on distribution of the samples to researchers should not rest only on the biobank director. This decision requires the consensus of two official bodies unrelated to the biobank. Any project involving the use of samples requires approval by an established external scientific committee (ESC) and a Clinical Research Ethics Committee (CREC).

The role of the ESC is to ensure the project's scientific quality and feasibility. This requirement may be waived or shortened in the case of a project previously approved by a public evaluation agency (eg ANEP). On the other hand, all research projects must undergo evaluation and approval by the CREC, which aims to safeguard the welfare and rights of subjects participating in medical research, which includes research on people, based on health data (medical record) or biological samples.

The guarantee of respect for research subjects provided by the CEIC is necessarily bound to the guarantee provided by the project researchers and promoters, who are ultimately responsible for ensuring that the research is conducted in accordance with ethical principles and the regulations established by law.

## Conclusion

The use of biological samples is a new challenge in the field of bioethics, because of the implications that research may have for genomics. The transfer of this material between national and international institutions, the non-profit use or eventual commercial use of the advances (diagnostic tests, treatments, etc.) derived from

such research are issues we should continue to analyze together as researchers, institutions and ultimately citizens, to democratically establish a modern, ethical and legal framework which is valid and transparent, allowing scientific advance and respect for the fundamental rights of individuals. The newly enacted Law on Biomedical Research represents a new legal framework along these lines, to be developed in the immediate future.

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