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Study of the involvement of research ethics committees in the constitution and use of biobanks in France

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ABSTRACT

Concerns are emerging about the protection of persons taking part in genetic research involving biobanks. We used several items of a questionnaire sent to the 48 French research ethics committees (RECs) to investigate the means by which they evaluate the constitution and use of biobanks and the elements on which conclusions were based.

Most RECs felt they should evaluate the constitution of biobanks in protocols, but not all did so in practice. Harmonization of the competence of RECs for evaluating biobanks is required, particularly concerning information, consent, the duration of sample conservation and the communication of research results. Our results and others demonstrate the need to develop rules and guidelines based on common ethical approaches, particularly in the European environment.

INTRODUCTION

The collection of human biological material and phenotypic data is essential for genetic research. The French Code of Public Health (CPH) defines a collection, in the context of genetic research, as a cluster of “biological samples for use in genetic research, obtained from a group of identified patients selected according to the clinical or biological characteristics of one or more members of a group, as well as any and all derivatives of these samples” (art L.1131-4). It may consist of solid tissues, blood, saliva, or any other tissue or fluid containing nucleated cells. The biological material is associated with files (often computer files) that may contain identified, identifiable, directly anonymous data or data rendered anonymous (anonymized). We will use the term “biobank” to cover all activities relating to the storage of human biological materials.

In theory, RECs must approve all biomedical research studies, including those involving the collection of human materials, which may cause harm to the individual in his psychological and social dimensions. This view was laid down in the 1975 Declaration of Helsinki. In France, the "Huriet Law" of December 20, 1988 [1], now part of the CPH, sets out the legal requirements concerning the protection of individuals involved in biomedical research. It has led to the constitution of RECs, also known as CCPPRBs (for Consultative Committees Protecting Persons in Biomedical Research) in France. Today, there are 48 RECs in France. The recommendations formulated by the committees are transmitted to the Ministry of Health, which can independently review an opinion if judged necessary. The role of the committees, as defined by law (article L-1123 CPH.), is to evaluate the validity of research in terms of the protection of participants in general, and concerning particularly informed consent of participants,

methods of obtaining consent, indemnification of the participants, general relevance of the project and whether the means available and the qualifications of the investigators involved are sufficient.

Ethical and legal issues raised by the constitution of biological collections include organizational and medical aspects of storage duration and sample reuse. Some studies have explored practices concerning the constitution and use of collections [2-4]. In pharmacogenetic studies, clarification of the procedures concerning confidentiality, information sharing and guarantees concerning DNA storage and usage are required [5]. In 1994 [6], it was suggested that “...the constitution of the collection...requires the opinion of the REC” and, in 1998 [7], that “...an agreement will take into account measures involved in the collection, storage and abusive use (such as use in the context of employment, insurance ...) of samples and any information concerning them”.

In this study, we investigated the views of French RECs concerning their current and ideal involvement in the constitution and use of biobanks and concerning the ethical rules necessary to protect people involved in this kind of activity.

METHODS

We used a questionnaire with open and closed questions. This questionnaire was validated by a multidisciplinary team working in the Laboratory of Ethics and Public Health at the Necker Faculty of Medicine, Paris, France. It was approved by the national REC conference chairman and six former REC members. The questionnaire and a letter explaining the aims of the study, the definition of biobank to be used, and a list of

French recommendations and laws was sent to the president of each of the 48 French RECs. The questionnaire was completed by the president of each committee after discussion and validation by REC members generating a consensus. Replies to closed questions were analyzed using Excel software. The research team analyzed directly the content of responses to open questions. Four items from the questionnaire and the results are presented in table 1.

RESULTS

Twenty-eight of the 48 RECs (around 60%) completed the questionnaire, suggesting that many of the RECs, distributed throughout France, are concerned about the problems addressed and wish to be involved in the evaluation of practices. No difference in terms of size or structure was observed between the RECs that responded and those that did not. Lack of time may have been responsible for the lack of response in some cases.

Twenty-five of the RECs thought approval should be sought from an REC when creating a biological collection. Only three RECs disagreed, for different reasons. One expressed doubts about their ability to evaluate the constitution and/or use of biobanks and the means of following up and assessing the fate of the samples. Another argued that this task should be the responsibility of the CNIL (the French Data Protection Agency [DPA]), which protects individual rights concerning the computerization of medical data used in research. The third highlighted a problem encountered when biological material is collected in the absence of a specific research project; should

biobanks constructed in this way be considered biomedical “research” requiring the approval of a REC?

The RECs focused principally on the consent form, information to the patient, confidentiality and the communication of results to the patient (item 3, table 1). Most RECs took into account the constitution or use of a biological collection, although six said they did not.

The responses to item 5 demonstrate that RECs were primarily concerned about (i) protecting the participant (ii) informing the participant at the time of sampling, (iii) obtaining consent, and (iii) evaluating the ways in which confidentiality is handled. They were less concerned about management aspects, such as the handling of the collected data, when making decisions about biobanks.

DISCUSSION

The RECs generally agreed that their opinion should be sought for the constitution of a biobank and that they have a particular responsibility in the use of samples. The RECs not concerned about the ethical evaluation of biobanks may feel this way because the CPH has not clearly identified banking activities as being part of the tasks of an REC [4].

Historically, the role of the RECs was to evaluate clinical trials that might affect the physical integrity of the person. Changes in human research have extended their competence to protocols potentially affecting not only physical integrity but also the

identity (social and familial) of the person, bringing psychological and spiritual aspects to the forefront. If a person is considered in all these dimensions, not just as a physical being, then it is appropriate for ethics committees to assess biobanks. The concept of protecting persons, as stipulated by law, and concerning both users of the health system and research participants, may be central when developing biomedical research projects involving new biobank technology, and should not be restricted to classical therapeutic trials. This concept of protecting individuals from whom DNA samples are collected differs from that in most other clinical protocols or experiments on humans, but this does not lessen its importance.

Who should be responsible for ensuring the protection of human subjects in the management of a biobank? In France, the French Data Protection Agency [DPA] or CNIL, has been proposed. In this case, evaluation would be limited to the protection of individual rights associated with the computerization of medical data used in research. According to the former NBAC (National Bioethics Advisory Commission of the USA), it is essential that IRBs (Institutional Review Boards) evaluate research involving human biological resources [8]. The integration of biobank evaluation into the work of RECs has been proposed as part of a project to revise French law concerning biomedical research, with a view to applying a European directive [9-10].

The RECs appear to be appropriate bodies for evaluating research projects involving biobanks. They are concerned about the necessity to inform participants, to obtain consent for sample use, confidentiality, and decisions concerning the transmission of research findings to the participants. These points are coherent elements in the

recognized role and daily practice of RECs. However, questions concerning the fate of the bank and conditions of access and exchange appear to be taken into account to a lesser extent.

The RECs also have a role to play in determining whether overall and/or individual results should be transmitted to participants. They may be involved in the decision to use directly anonymous data (no link between the data and the participant) or to render identifiable data anonymous (thereby destroying the link between the sample and the individual). The use of anonymous data precludes the communication of individual results and this element must be considered when consent is sought.

Standardized consent forms for use in genetics have been proposed [11-12]. Clauses have been drafted for numerous issues: sample storage, benefits, risks, confidentiality, communication of results to the patients, genetic counseling, possibilities of transfer or commercialization, and time for reflection before giving consent. International harmonization of ethical controls on genetic research projects would be desirable, rendering consistent the rules applied to the content of information, the consent form, and the functioning of biobanks. This is becoming increasingly important with the growing number of international projects and differences in the constitution, use, reuse and transfer of biological samples. Indeed, these activities are not necessarily routinely evaluated by RECs as they are not covered by laws concerning biomedical research.

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