



University of Puerto Rico
MEDICAL SCIENCES CAMPUS
San Juan, Puerto Rico

Institutional Review Board

RESEARCH USING HUMAN BIOLOGICAL MATERIALS

Policies and Procedure

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I. Introduction

This document will address the use of human biological materials for research purposes, and will serve as an informational source for investigators who desire to know what their obligations are with respect to meeting institutional requirements and protecting the rights and welfare of potential research subjects. The following areas of concern to investigators will be addressed: 1) The applicability of federal regulations concerning the protection of human research subjects; 2) The necessity of obtaining informed consent from subjects representing the source of the material; 3) The review of proposed research by the University of Puerto Rico Medical Sciences Campus Institutional Review Board.

Human Biological Material refers to any human material, from sub-cellular constituents through tissue blocks to intact organs. In particular, the term covers genetic material, the substrate of much modern research.

II. The Scope of Federal Regulations

The Federal Policy for the Protection of Human Subjects was promulgated in August 1991, and is commonly referred to as the Common Rule. The University of Puerto Rico Medical Sciences Campus has negotiated a Multiple Project Assurance (M-1291) with the Office for Protection from Research Risks, declaring as intent to comply with the provisions expressed in the Common Rule. This MPA covers all the affiliated institutions. The MPA declares that all research, whether or not federal funds are involved, is subject to its provisions.

While the Rule was drafted prior to the era of widespread research on genetic material, its provisions are applicable to research on human biological material in many instances. Research is defined as "... a systematic investigation designed to develop or contribute to generalizable knowledge". A human subject is defined as a "... living individual about whom an investigator conducting research obtains: (a) data through intervention or interaction with the individual, or (b) identifiable private information." Identifiable is defined as "... the identify of the subject is or may readily be ascertained by the investigator or ... associated with the information." Thus, research involving material that is linked, directly or indirectly by a code, to

personal information concerning the source of the material constitutes research that is subject to federal regulations. Even though it is not the focus of this document, please note that research involving access to a patient's medical record, in whole or in part, is subject to the Federal regulations in exactly the same manner. Access to a person's medical record is also subject to separate state and federal statutory provisions.

Because the notions of *linkage* and *identifiability* are central to review and consent issues, the following definitions are germane:

An *unidentified sample* is supplied to the researcher from a repository that has a collection of unidentified human specimens. Research using such material is typically exempt from the requirement for IRB review.

An *unlinked sample* is one that lacks an identifier or code that may link the sample to an individual. An investigator must differentiate between an unlinked sample that is provided to him / her by a third party from a sample under the investigator's control from samples is not generally not subject to IRB review and consent requirements, the later situation is not exempt from IRB approval as the proposed research may be eligible for expedite review as described in a following section.

A *coded sample* is one that is associated with a code that will permit as agent of the repository to link it with the subject. Even though the investigator may not be able to directly link the sample with a subject, research using such samples is subject to IRB review.

An *identified sample* is one that is associated with a personal identifier such that the researcher may directly link it with a subject. Research involving this sample is subject to IRB review and approval.

Thus, after reviewing the nature of the proposed research protocol relative to these definitions, the investigator will know whether the protocol is subject to IRB review and approval.

III. Institutional Review Board Policies and Procedures

In contradistinction to therapeutic research, risks to subjects representing the source of biological material provided to investigators are primarily psychosocial in nature – particularly in the context of genetic research. The risks involve one or more of the following: a) a general loss or diminution in privacy and confidentiality; b) potential discrimination related to the acquisition or maintenance of health insurance and employment; c) the potential for social stigmatization, related to both individual and group identity status; and d) the potential for –family conflict when knowledge concerning genetic determinants and traits are suddenly acquired by the subject or his / her next-of-kin.

In order to minimize these potential harms and facilitate the review of applications for genetic research, the Committee has adopted the following policies and procedures:

When research involving human biological material is conducted in the context of therapeutic research protocols, informed consent for the former should be obtained separately from consent for the clinical aspects of the study. The subject should be provided the option of choosing whether or not to participate in the ancillary study involving genetic research, and participation in therapeutic research should not be made contingent on such participation. The subject should be informed that his refusal to permit the use of his tissue or blood such research would not affect the quality of the clinical care he/ she receives. When pertinent, this should be addressed in a separate subsection of the consent document provided to the patient.

In accordance with Recommendation 5 of the National Bioethics Advisory Committee, the Committee requires that the investigator set forth:

- a) a thorough justification of the research design, including a description of procedures used to minimize risk to subjects,
- b) a full description of the process by which samples will be obtained,
- c) any plans to obtain access to medical records of the subjects, and
- d) a full description of the mechanisms that will be used to maximize the protection against inadvertent release of confidential information.

The investigator should address the relevant aspects of these issues in an appropriate manner in the Consent Document.

An application for research involving human biological material should be submitted using the *Application for Research Involving Human Biological Material* form.

The Committee will consider the application by means of an expedited or full committee review process.

IV. Expedite Review of Research Applications

Federal regulations provide for expedited review of research applications that meet certain criteria. With respects to research using biological materials, the crucial criterion concerns the concept of minimal risk. Minimal risk is generally defines as:

... the probability and magnitude of harm or discomfort anticipated in the research are not greater in and on themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

In the context of the research under consideration, the risks of primary concern relate primarily to the inappropriate release of information to the subject and third parties.

The Committee adopts Recommendation 10 of the NBAC, and will consider the research to be of minimal risk if:

- a) the study adequately protects the confidentiality of personally identifiable information, and isolates research results from the subject's general medical records
- b) the study does not involve the inappropriate release of information to third parties, including other researchers and institutions, and
- c) the study design incorporates a plan for whether, when and how to reveal findings to the source or their physicians, with disclosure to the subject permitted only when all the following apply
 - i. the findings are scientifically valid and confirmed
 - ii. the findings have significant implications for the subject's health concerns
 - iii. a course of action to ameliorate or treat these concerns is actually available, and
 - iv. the communication of genetic information is provided by a trained genetic counselor when appropriate.

In adopting these requirements, the Committee also intends to fulfill the regulatory requirement for expedite review that stipulates:

The expedited review procedure may not be used where identification of the subjects and / or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented to that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

If the investigator believes he / she has adequately addressed these issues, he / she may request an expedited review which will be performed by a designated sub-committee of the Committee, comprised of the Chairperson and two other Committee members.

V. Informed Consent Requirements

The necessity of obtaining informed consent from the subject applies to research involving human biological material. As a general rule, the identified or coded samples, the Committee recognized that it may be feasible to obtain such consent, and, in cases where documents exist, the latter are unlikely to address the possibility of such research.

However, federal regulations in 45 CFR 46.116(d) provide for waiver of this requirement when the following conditions are met:

1. the research involves no more than minimal risk to the subjects;
2. the waiver or alteration will not adversely affect the rights and welfare of the subjects
3. the research could not practically be carried out without the waiver or alteration; and
4. whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Thus, the Committee will consider requests for waiver of the requirement for informed consent. In determining whether a waiver of consent would adversely affect the rights and welfare of subjects, the Committee will consider the following:

1. whether the waiver would violate any state or federal statute regarding an entitlement to privacy or confidentiality;
2. whether the study will examine traits commonly considered to have political, cultural, or economic significance to the study subject's; and
3. whether the study's results might adversely affect the welfare of the subject's community

If the study poses more than minimal risk, and consent cannot practicably be obtained, the Committee may request the removal of identifiers.

The prospective collection and use of human biological material must be pursuant to a procedure that involves the procurement of informed consent from the sample's source. Hospitals typically mandate the use of a general consent document prior to the performance of surgical procedures during which tissue samples are obtained for diagnostic purposes. These consent documents may contain a provision such as *Any tissue removed from your body may be examined and then disposed of by the hospital personnel*, which does not address the possibility of the subsequent research use of retained tissue, such as that stored in a Department of Pathology. The Committee does not consider this general consent sufficient to negate the necessity of obtaining the subject's specific consent to use his / her tissue for the specified research purposes.

If the proposed research study involves the potential for psychosocial harm to the subject's family members, relatives or members of the subject's ethnic group, this should be disclosed as part of the consent process. The subject may consider these risks material to his / her decision to participate in the research study.

Finally if the investigator believes that the research has a reasonable likelihood of culminating in the development of a commercial product, and the investigator may benefit financially therefore, directly or indirectly, that fact should be divulged in the consent document.