

APPENDIX I

**OFFICE FOR PROTECTION FROM RESEARCH
RISKS**

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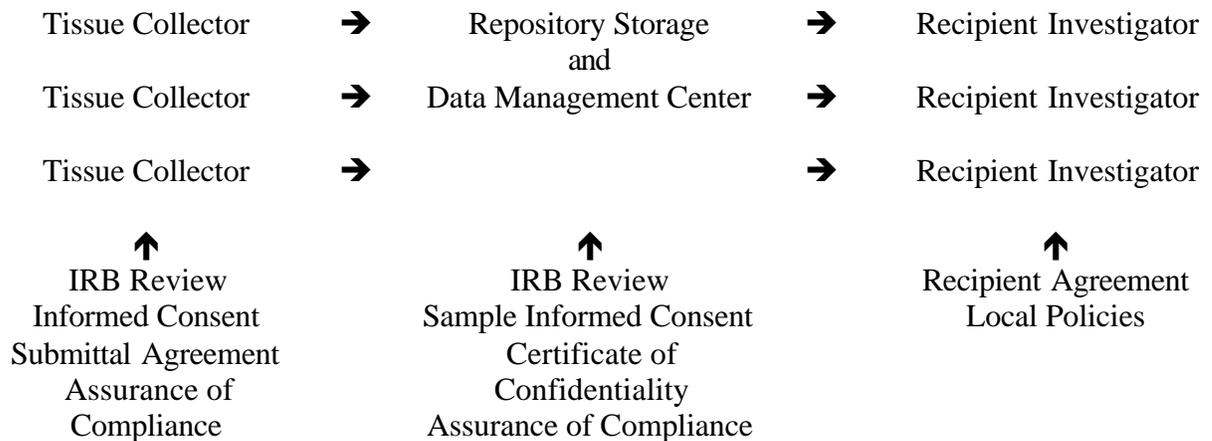
**ISSUES TO CONSIDER IN THE RESEARCH USE
OF STORED DATA OR TISSUES**

OFFICE FOR PROTECTION FROM RESEARCH RISKS

Issues to Consider in the Research Use of Stored Data or Tissues

November 7, 1997

- **Human Tissue Repositories** collect, store, and distribute human tissue materials for research purposes. Repository activities involve three components: (i) the **collectors** of tissue samples; (ii) the **repository** storage and data management center; and (iii) the **recipient** investigators.
- If supported by the Department of Health and Human Services (HHS), each component must satisfy certain **regulatory requirements**.



- Operation of the Repository and its data management center should be subject to **oversight by an Institutional Review Board (IRB)**. The IRB should review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. The IRB should also review and approve a sample collection protocol and informed consent document for distribution to tissue collectors and their local IRBs. A **Certificate of Confidentiality** should be obtained to protect confidentiality of repository specimens and data.

For Additional Information:

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August 19, 1996

TO: Professional Staff
Division of Human Subject Protections

FROM: Melody H. Lin, Ph.D.
Acting Director
Division of Human Subject Protections

SUBJECT: Operation of Human Cell Repositories
Under HHS Regulations at 45 CFR 46

OPRR offers the following guidance concerning operation of human cell repositories under Department of Health and Human Services (HHS) regulations for the protection of human subjects ([45 CFR 46](#)). The guidance assumes that repository activities include nonexempt human subjects research as defined under HHS regulations.

- (1) The operation of any HHS-supported human cell repository and its data management center should be subject to oversight by an Institutional Review Board (IRB) convened under an applicable OPRR-approved Assurance of Compliance. This IRB should set the conditions under which data and specimens may be accepted and shared. OPRR strongly recommends that one such condition stipulate that recipient-investigators not be provided access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained.
- (2) Collection of data and specimens should be subject to oversight by local IRBs convened under applicable OPRR
- (3) Written informed consent should be obtained from each donor-subject in accordance with HHS regulations at [45 CFR 46.116](#). Included among the basic elements of informed consent should be a clear description of (i) the operation of the cell repository; (ii) the specific types of research to be conducted; (iii) the conditions under which data and specimens will be released to recipient-investigators; and (iv) procedures for protecting the privacy of subjects and maintaining the confidentiality of data.-approved Assurances
- (4) Informed consent information describing the nature and purposes of the research should be as specific as possible.
- (5) Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing (e.g., regarding possible paternity determinations).

- (6) Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights.
- (7) OPRR recommends that the cell repository develop a sample collection protocol and informed consent document for distribution to collector-investigators and their local IRBs.
- (8) A written submittal agreement for collector-investigators should require written informed consent of the donor-subjects utilizing an informed consent document approved by the local IRB. It should also contain an acknowledgment that collector-investigators are prohibited from providing recipient-investigators with access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained.
- (9) A written usage agreement for recipient-investigators should include the following:

“Recipient acknowledges that the conditions for use of this research material are governed by the cell repository Institutional Review Board (IRB) in accordance with Department of Health and Human Services regulations at [45 CFR 46](#). Recipient agrees to comply fully with all such conditions and to report promptly to the cell repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects.

This research material may only be utilized in accordance with the conditions stipulated by the cell repository IRB. Any additional use of this material requires prior review and approval by the cell repository IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OPRR-approved Assurance.”

- (10) OPRR recommends that a Certificate of Confidentiality be obtained to protect confidentiality of human cell repository specimens and data.

OFFICE FOR PROTECTION FROM RESEARCH RISKS

Guidance on Protections for Human Subjects in the
National Institute of General Medical Sciences
Human Genetic Mutant Cell Repository
May 21, 1997

The Office for Protection from Research Risks (OPRR) provides the following guidance in response to requests from Institutional Review Boards, the National Institute of General Medical Sciences (NIGMS), and the research community.

- (1) **Local IRB Review.** Collection of data and specimens for inclusion in the NIGMS Human Genetic Mutant Cell Repository should be subject to oversight by local Institutional Review Boards (IRBs) convened by the collecting institutions under OPRR-approved Assurances.¹ The local IRB is familiar with the particular circumstances of its research setting and is in the best position to weigh critical considerations like local professional and community standards, institutional policies and resources, and the needs of differing patient or subject populations.
- (2) **Informed Consent.** Written informed consent should be obtained from each donor-subject in accordance with Department of Health and Human Services (HHS) regulations at [45 CFR 46.116](#).

Included among the basic elements of informed consent should be a clear description of (i) the operation of the cell repository; (ii) the specific types of research to be conducted; (iii) conditions under which data and specimens will be released to recipient-investigators; and (iv) procedures for protecting the privacy of subjects and maintaining the confidentiality of data. Informed consent information describing the nature and purposes of the research should be as specific as possible. Where human genetic research is anticipated, informed consent information should include information about the consequences of DNA typing (e.g., regarding possible paternity determinations). Informed consent documents may not include any exculpatory language through which subjects are made to waive or appear to waive any legal rights.

The Cell Repository should provide tissue collectors with an NIGMS-approved sample informed consent document containing these elements and with a sample protocol for tissue collection. IRBs may request copies of these sample documents to assist in their review of local informed consent documents and protocols.

- (3) **Oversight of Repository Activities.** Operation of the NIGMS Human Genetic Mutant Cell Repository and its data management center should be subject to oversight by an Institutional Review Board (IRB) convened by the Coriell Institute of Medical Research under an OPRR-approved Assurance of Compliance. The IRB should review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect

the privacy of subjects and maintain the confidentiality of data. The IRB should also review and approve a sample collection protocol and informed consent document for distribution to tissue collectors and their local IRBs. A Certificate of Confidentiality should be obtained to protect confidentiality of repository specimens and data.

- (4) **Submittal Agreement.** A written submittal agreement for tissue collectors should require written informed consent of the donor-subjects utilizing an informed consent document approved by the local IRB. It should also contain an acknowledgment that collectors are prohibited from providing recipient-investigators with access to the identities of donor-subjects or to information through which the identities of donor-subjects may readily be ascertained.
- (5) **Usage Agreement.** A written usage agreement for recipient-investigators should include the following: “Recipient acknowledges that the conditions for use of this research material are governed by the cell repository Institutional Review Board (IRB) in accordance with Department of Health and Human Services regulations at [45 CFR 46](#). Recipient agrees to comply fully with all such conditions and to report promptly to the cell repository any proposed changes in the research project and any unanticipated problems involving risks to subjects or others. Recipient remains subject to applicable State or local laws or regulations and institutional policies which provide additional protections for human subjects. This research material may only be utilized in accordance with the conditions stipulated by the cell repository IRB. Any additional use of this material requires prior review and approval by the cell repository IRB and, where appropriate, by an IRB at the recipient site, which must be convened under an applicable OPRR-approved Assurance.”

¹ Under certain circumstances, collecting institutions may elect to rely upon the Cell Repository IRB at Coriell Institute. This requires a written Cooperative Amendment, signed by the collecting institution and the Coriell Institute, and approved by OPRR. Contact OPRR for details.

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OFFICE FOR PROTECTION FROM RESEARCH RISKS

Protections for Human Subjects in the
NIGMS Human Genetic Mutant Cell Repository
Submission of Non-Identifiable Materials to the Repository
May 22, 1997

In response to requests from the National Institute of General Medical Sciences (NIGMS), the Office for Protection from Research Risks (OPRR) provides the following clarification regarding submission of “non-identifiable” materials to the Human Genetic Mutant Cell Repository.

As Chart 1 (attached) illustrates, human subjects are involved in research when the research involves (i) an intervention or interaction with a living individual that would not occur (or would occur in some other fashion) but for the research; **or** (ii) the use of identifiable private data or information in a form associable with a living individual [also see [45 CFR 46.102\(f\)](#)].

Human subjects would not be involved when material submitted to the Repository satisfies **both** of the following conditions:

(1) The material, in its entirety, was collected for purposes other than submission to the Repository (e.g., the material was collected solely for clinical purposes, or for legitimate but unrelated research purposes, with no “extra” material collected for submission to the Repository).

and

(2) The material is submitted to the Repository without any identifiable private data or information (i.e., no codes or linkers of any sort may be maintained, either by the Submitter or by the Repository, that would permit access to identifiable private data or information about the living individual from whom the material was obtained).

While OPRR requires neither an Assurance of Compliance nor a Certification of Institutional Review Board (IRB) review [[45CFR46.103\(a\)\(f\)](#)] for activities that do not involve human subjects, local institutional requirements regarding review of such activities are, nevertheless, binding. Some institutions may require IRB or administrative review of all research activities involving human materials, even where “human subjects” are not involved.

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