

Sheet 14: NIH REQUIREMENTS FOR THE RESEARCH USE OF STORED HUMAN SPECIMENS AND DATA

I. INTRODUCTION

Research often involves the use of stored human specimens or data. Such use obliges research investigators and Institutional Review Boards (IRBs) to consider the rights and welfare of the individuals who provide them, especially when samples retain identifiers or codes. Individuals (sources) who provided specimens or from whom information was obtained in the past are no less deserving of protection than are prospective research subjects. The research use of existing specimens or data without the ability or intent to identify the source may pose little risk to the donors. However, when these sources can be identified, conflicts may arise between their rights and the scientific benefit that can be obtained from studying their stored samples.

This information sheet provides actions that must take place before IRP researchers may use stored specimens or data for research purposes. It is the policy of the NIH's Intramural Research Program (IRP) that prospective and continuing NIH IRB review and approval is required for the research use of stored human samples or data when IRP researchers or members of the research team can identify the sources.

The following definitions, policy and implementation discussion are consistent with the report of the National Bioethics Advisory Commission (NBAC) in August 1999, entitled "Research Involving Human Biological Materials: Ethical Issues and Policy Guidance." (Volume I. Report and Recommendations of the National Bioethics Advisory Commission, Rockville, Maryland, August 1999.), and the requirements of the Office of Human Research Protections (OHRP), DHHS.

II. DEFINITIONS

1) Human Subject means a living individual about whom an investigator (whether professional or student) conducting research obtains (a) data through intervention or interaction with the individual, or (b) identifiable private information (45 CFR 46.102(f)). At the NIH, the following research activities are not considered research involving human subjects: the collection and study of (1) samples from deceased individuals; (2) samples taken for diagnostic purposes only; (3) specimens or data that are available from commercial or public repositories or registries; (4) established cell lines that are publicly available to qualified scientific investigators, and (5) self-sustaining, cell-free derivative preparations including viral isolates or cloned DNA.

2) Human specimens/samples include blood and other body fluids, tissues, DNA and other direct derivatives from human tissues.

3) Human data include responses to questionnaires or surveys, medical histories, records and diagnoses.

4) Source means the individual who provided the sample or from whom data were collected.

5) Identified means samples or data that are still attached to a readily available subject identifier such as a name, social security number, address, telephone number, medical record number, etc.

6) Coded means that collected samples or data are unidentified for research purposes by use of a random or arbitrary alphanumeric code but the samples may still be linked to their sources through use of a key to the code available to an investigator or collaborator.

7) Unlinked means human data or samples that were initially collected with identifiers but, before research use, have been irreversibly stripped of all identifiers by use of an arbitrary or random alphanumeric code and the key to the code is destroyed, thus making it impossible for anyone to link the samples to the sources. This does not preclude linkage with existing clinical, pathological, and demographic information before subject identifiers are removed.

8) Unidentified means that the samples or data were collected without identifiers of any kind. Samples or data may retain demographic or diagnostic information and still be considered unidentified if such information cannot be used to reveal the identity of the source.

9) Exempt research means research that is exempt from the regulatory requirement for prospective IRB review and approval. This includes "research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects" {45 CFR 46.101(b)(4)}.

III. POLICY

1) The research use of stored identified or coded specimens or data, when IRP researchers can identify the sources, must receive prospective and continuing NIH IRB review and approval. This includes research protocols where the remaining research activities are limited to data analyses, and 2) the subsequent

research use of specimens or data previously collected under now-terminated protocols.

2) The research use of stored coded samples when IRP researchers cannot identify subjects, such as the receipt of coded samples from non-NIH collaborators may or may not require NIH IRB review and approval. Before receiving such samples, IRP researchers must contact OHSR for guidance.

3) The research use of stored, unlinked or unidentified samples may be exempt from the need for prospective IRB review and approval. Exemption requests must be submitted in writing to OHSR. Only OHSR is authorized to determine whether a research activity is exempt.

IV. IMPLEMENTATION

Implementing the NIH requirements for research activities with stored human specimens involves addressing the following issues:

1) Is the proposed research activity “human subjects research”?

Researchers engaged in activities which are not considered research involving human subjects (see Definition 1., above) do not need IRB or OHSR review and approval; however, these activities may be subject to other requirements such as rules governing technology transfer.

For any other research use of human samples, specimens or data, only an NIH IRB or OHSR may make the determination of whether the research involves human subjects. The final responsibility rests with the OHSR.

2) How does an IRP investigator obtain approval to use stored anonymized specimens?

The research use of existing unidentified or unlinked samples or data is generally exempt from the requirement for prospective IRB review and approval. Exemptions are issued only by OHSR and may be sought by completing Form #1, "Request for Review of Research Activity Involving Human Subjects" available from that office or on the OHSR homepage <http://ohsr.od.nih.gov/info/info.html>. NIH investigators should not make determinations about exemptions without consulting OHSR.

Research involving stored identified or coded samples or data, when IRP investigators can identify the sources, must receive prospective and continuing NIH IRB approval.

3) What points must an NIH IRB consider in reviewing a request for the research use of stored identified or coded specimens or data when an IRP researcher can identify the source?

The investigator must submit a written request (i.e., a memorandum or protocol) to the IRB which includes the following:

- a. The nature of the proposed research including a complete description of the samples or data;
- b. A justification for retention of the identities or codes of the sources of samples or data, and, in the case of codes, a description of the ease or difficulty with which linkage can be made between the code and the source, and a description of who can make the linkage.
- c. A description of the extent to which confidentiality of research data will be maintained;
- d. The informed consent document to be utilized, or a request for waiver of informed consent. When research involves stored samples or data previously collected under now-terminated protocols, an important question is whether a consent signed in the collection protocol is sufficient for the proposed research activity. The IRB will pay special attention to requests for waiver of informed consent. In order to waive informed consent, Federal regulations currently require that an IRB must find and document in its minutes that all of the following four conditions have been met:
 - the research involves no more than minimal risk;
 - the waiver will not adversely affect the rights and welfare of the subjects;
 - the research could not practicably be carried out without the waiver; and
 - whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- e. In those cases where a waiver of informed consent is sought, a statement that a source will not be contacted by anyone connected with the research without prior approval by the IRB.
- f. A description of how the samples, specimens and/or data will be stored; how they will be tracked; what will happen to the samples/specimens/data at the completion of the protocol; what circumstances would prompt the PI to report to the IRB loss or destruction of samples.

The IRB will review the research in keeping with the requirements of the NIH Human Research Protection Program (HRPP) and as set forth in the NIH IRP Standard Operating Procedures.

4) What happens after an NIH IRB approves the research?

Continuing IRB review and approval of the research must take place at least annually.

Research protocols that require full IRB review for their initial reviews generally require it for their continuing reviews. The expedited review process may be used when: (1) the protocol is permanently closed to enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; or (2) where no subjects have been enrolled and no additional risks have been identified; or (3) where the remaining research activities are limited to data analyses.

5) What review is necessary for research collaborations involving sending or receiving stored specimens or data?

For discussion of IRP guidelines on research collaborations, please review the information found in The Gray Booklet at <http://ohsr.od.nih.gov/guidelines/guidelines.html>. Prospective and continuing NIH IRB review and approval is required for research collaborations in which IRP researchers send coded samples (for which they maintain the key) to non-NIH investigator(s). The protocol must identify the names of the collaborating researchers and their affiliated institutions. Before sending the samples, IRP investigators should contact an IC technology development coordinator for guidance on an appropriate NIH transfer agreement. IRP researchers whose collaborations involve the receipt of samples collected and sent by non-NIH researchers from non-NIH subjects should contact OHSR for guidance.

If you have questions, contact your NIH IRB Chair or OHSR. OHSR is located in Building 10, Room 2C146, (p) 301-402-3444 and (fax) 301-402-3443. The web site is <ohsr.od.nih.gov>.

