

Tissue Banking Issues and Concerns

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We can thank Hippocrates
for changing healing from
an occult art to a
SCIENCE.

But look at all
we have to
learn.

Yeah-let's
change it back
into an occult
art.



The US Navy Tissue Bank: 50 years on the cutting edge

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Abstract

The US Navy Tissue Bank was established in 1949 by Dr. George Hyatt, an orthopaedic surgeon at the Naval Medical Center in Bethesda, Maryland. The Navy program was the first of its kind in the world and established many of the standards that are followed today. During the 1950s, the identification of appropriate donor criteria for tissue donation, the development of procurement and processing methods, the establishment of a graph registry and documentation and the clinical evaluation of a variety of tissues were pioneered at this facility. Cryopreservation, freeze-drying, irradiation sterilization of tissue, as well as immunological principles of tissue transplantation, were developed during the 50 years of research and development by Navy scientists. Organ preservation, cadaveric bone marrow recovery and immunosuppressive protocols were also developed at the Navy Tissue Bank. The Navy was also instrumental in the establishment of the National Marrow Donor Program and the American Association of Tissue Banks in the US.

Although the Navy Tissue Bank has ceased activity after 50 years of excellence, it should be recognized as the first standard setter for the world community of tissue banks.

The University Of Michigan Human Breast Cell/Tissue Bank And Data Base

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In 1995 The University of Michigan Breast Cell/Tissue Bank and Data Base came into existence as a result of an **infrastructure grant awarded to the U of M by the Department of Defense**. This resource had been developed internally over the previous six years as a result of the Principal Investigators interest in breast cancer biology and because of the need to carry out breast cancer biology studies using freshly isolated human breast cancer cells. The need for new human breast cancer cell lines that can be cultured under defined conditions in vitro, and for which both patient information and molecular data are available, also contributed to the motivation to develop this resource.

The purpose of this resource is to provide breast cancer researchers with primary breast cells and tissues in a variety of forms that are suitable for a variety of experimental approaches. Breast cells and tissues obtained from this bank come with both demographic and clinical data on the patient sample. Furthermore, users may request cell/tissue samples from patients with specific characteristics, e.g., ER positive or P53 positive cells.



**RESEARCH INVOLVING HUMAN BIOLOGICAL
MATERIALS:ETHICAL ISSUES AND POLICY GUIDANCE**

VOLUME I & VOLUME II (COMMISSIONED PAPERS)

**Report and Recommendations of the National Bioethics Advisory
Commission Rockville, Maryland August 1999**

**ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING
HUMAN PARTICIPANTS**

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NATIONAL BIOETHICS ADVISORY COMMISSION (NBAC) ETHICAL AND POLICY ISSUES IN RESEARCH INVOLVING HUMAN PARTICIPANTS

May 18, 2001

Recommendation 3.3: A unified, comprehensive federal policy embodied in a single set of regulations and guidance should be created that would apply to all types of research involving human participants (see Recommendation 3.2).

Recommendation 3.4: Federal policy should cover research involving human participants that entails systematic collection or analysis of data with the intent to generate new knowledge. Research should be considered to involve human participants when individuals 1) are exposed to manipulations, interventions, observations, or other types of interactions with investigators or 2) are identifiable through research using **biological materials**, medical and other records, or databases. Federal policy also should identify those research activities that are not subject to federal oversight and outline a procedure for determining whether a particular study is or is not covered by the oversight system.

Policy Sites and Documents

- Information for Researchers Using Human Specimens
 - <http://www-cdp.ims.nci.gov/policy.html>
- Research on Human Specimens: Are You Conducting Research Using Human Subjects
 - <http://www-cdp.ims.nci.nih.gov/policy.html>
- Sample Consent: NCI
 - <http://www.napbc.org/napbc/consent.htm>
- OHRP
 - <http://grants.nih.gov/grants/oprr/humansubjects/guidance/reposit.htm>

MEDICAL RECORD PRIVACY

Health Insurance Portability Act of 1996

Standards for Privacy of Individually Identifiable Health Information

 Confidentiality: A tool for the protection of privacy. It mandates controls on personal data, limiting access and disclosure.

 Privacy: The specific right of an individual to control the collection, use, and disclosure of personal information.

De-identification

- Standard: de-identification of protected health information. Health information that does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual is not individually identifiable health information.
- Proof
 - A person with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable: Applying such principles and methods, determines that the risk is very small that the information could be used, alone or in combination with other reasonably available information by an anticipated recipient to identify an individual who is a subject of the information; and documents the methods and results of the analysis that justify such determination

De-Identification Requirements

- **Names;**
- **All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, zip code (20,000 people rule)**
- **All elements of dates (except year) directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89**
- **Telephone & Fax numbers;**
- **Electronic mail addresses;**
- **Social security numbers;**
- **Medical record numbers;**
- **Health plan beneficiary numbers;**
- **Account numbers;**
- **Certificate/license numbers;**
- **Vehicle identifiers, serial #, license plate numbers;**
- **Device identifiers & serial #**
- **Web Universal Resource Locators**
- **Internet Protocol (IP) address**
- **Biometric identifiers,(finger voice)**
- **Full face photographic images & any comparable images; and**
- **Any other unique identifying number, characteristic, or code;**

Categories of Human Biological Materials

Repository Collections

Unidentified specimens: For these specimens, identifiable personal information was not collected or, if collected, was not maintained and cannot be retrieved by the repository.

Unidentified samples: Sometimes termed “anonymous,” these samples are supplied by repositories to investigators from a collection of unidentified human biological specimens.

Categories of Human Biological Materials Research Samples

Unlinked samples: Sometimes termed “anonymized,” these samples lack identifiers or codes that can link a particular sample to an identified specimen or a particular human being.

Coded samples: Sometimes termed “linked” or “identifiable,” these samples are supplied by repositories to investigators from identified specimens with a code rather than with personally identifying information, such as a name or Social Security number.

National Bioethics Advisory Commission (NBAC)

Categories of Human Biological Materials

Research Samples

Identified specimens: These specimens are linked to personal information in such a way that the person from whom the material was obtained could be identified by name, patient number, or clear pedigree location (i.e., his or her relationship to a family member whose identity is known).

Identified samples: These samples are supplied by repositories from identified specimens with a personal identifier (such as a name or patient number) that would allow the researcher to link the biological information derived from the research directly to the individual from whom the material was obtained.

National Bioethics Advisory Commission (NBAC)

Genetic Testing-Genetic Screening

A Definition

Definition of Genetic Test:

“The analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes. Examples of these genetic studies include: predicting risk of disease, identifying carriers, establishing prenatal and clinical diagnosis or prognosis, monitoring, and screening both prenatality and in newborns.”

(From the Task Force on Genetic Testing, NIH-DOE Working Group on Ethical, Legal, and Societal Implication of Human Genome Research, Sept 1997)

Genetic Testing-Genetic Screening

A Definition

- **Genetic Testing:** “The use of specific assays to determine the genetic status of individuals already suspected to be at high risk for a particular inherited condition. The actual laboratory examination of samples.” 5OTA 1990
- **Genetic Screening:** Usually uses the same assays employed for genetic testing but is distinguished from genetic testing by its target population. 5OTA 1990
- **Screening:** The systematic search of populations for persons with latent, early, or asymptomatic disease. 1NAS 1975

Human Tissue Repositories

- **Human tissue repository:**
 - Any collection of specimens that are identifiable and either are or have the potential to be distributed to others may be considered a repository.
 - Collections containing specimens that are not identifiable (linked to donor) in anyway are also repositories but samples obtained from them may be eligible for exemption #4 in 45 CFR 46.101(b)

Tissue Banking Sources

- Specimens obtained from routine clinical procedures and retained for future research activities.
- Specimens obtained for a specific research protocol and retained for future studies
- Specimens collected in the past for various reasons, not specifically for research purpose, and retained. (Retrospective specimen collections)

Tissue Banking

Routine Procedure vs. Specific Research Protocol Information to Donor

“Excess” Tissue

- When consent is obtained:
 - Inform the subjects that adequate tissue removed from their body will be sent to pathology for testing/diagnosis as established by hospital regulations.
 - Information will be provided that surgically removed tissue is indeed excess.

Human Tissue Repositories

- All identifiable tissue collected for research purposes (immediate and storage) should require IRB review at site of collection.
 - Written informed consent from donor
 - Information about repository
 - How tissue will be used/shared

Human Tissue Repositories

- A tissue repository that distributes materials requires an IRB (OHRP approved assurance) that sets conditions under which tissue distributed.
 - Privacy
 - Conditions of original collection consent
 - Intended purpose of use based on information from researcher requesting tissue

Human Tissue Repositories

- The IRB at the repository institution may either:
 - Require establishment of a committee to review each individual request for tissue to assure that IRB conditions for sharing are met and conform to purpose(s) stated in original collection consent.
 - Perform this function itself.

Human Tissue Repositories

- Researcher that is recipient of tissue sample must follow conditions specified by the repository IRB.
 - This may include review and approval by the IRB at the receiving institution.

- **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**.

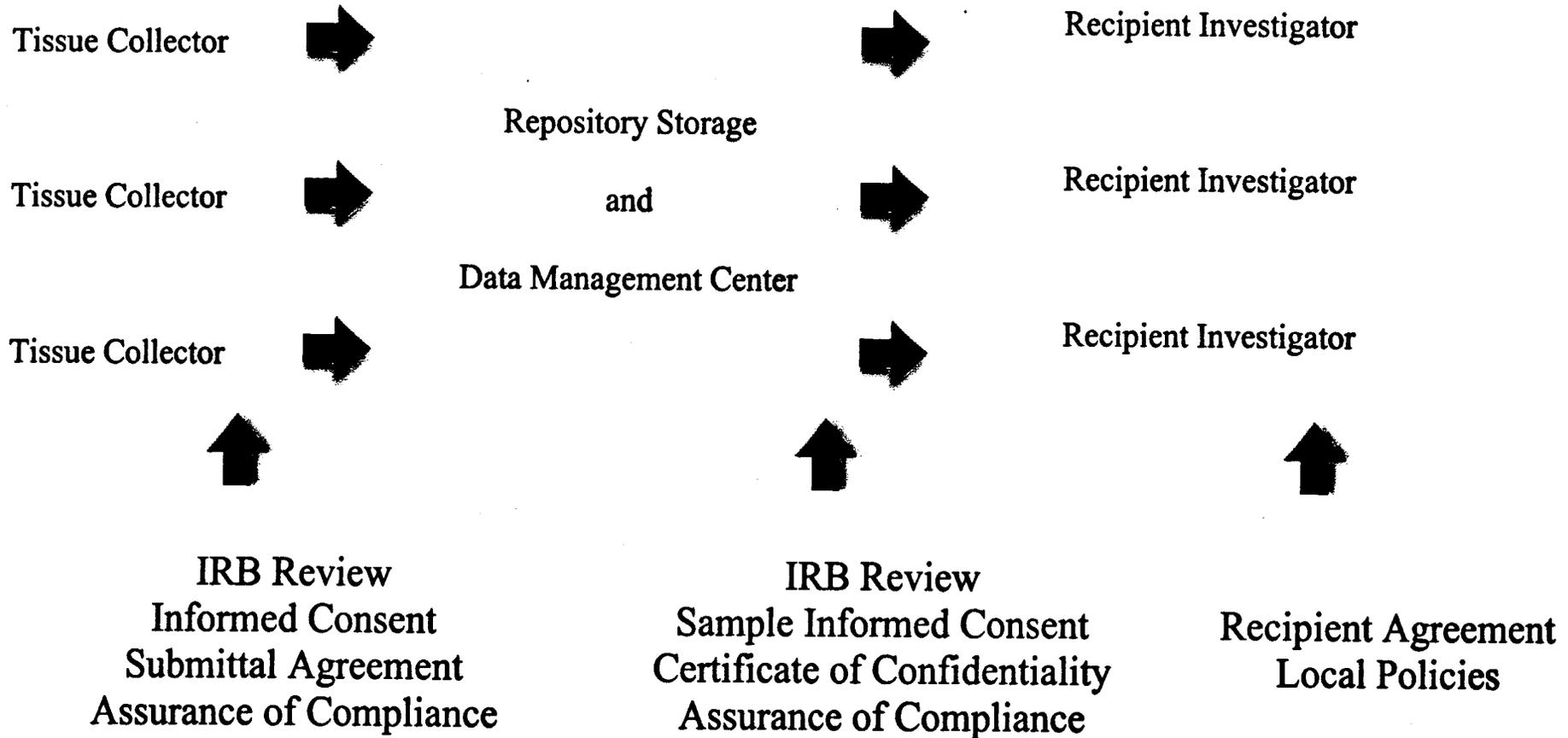


Chart 1: NBAC's Proposed Process for Research Using Human Biological Materials

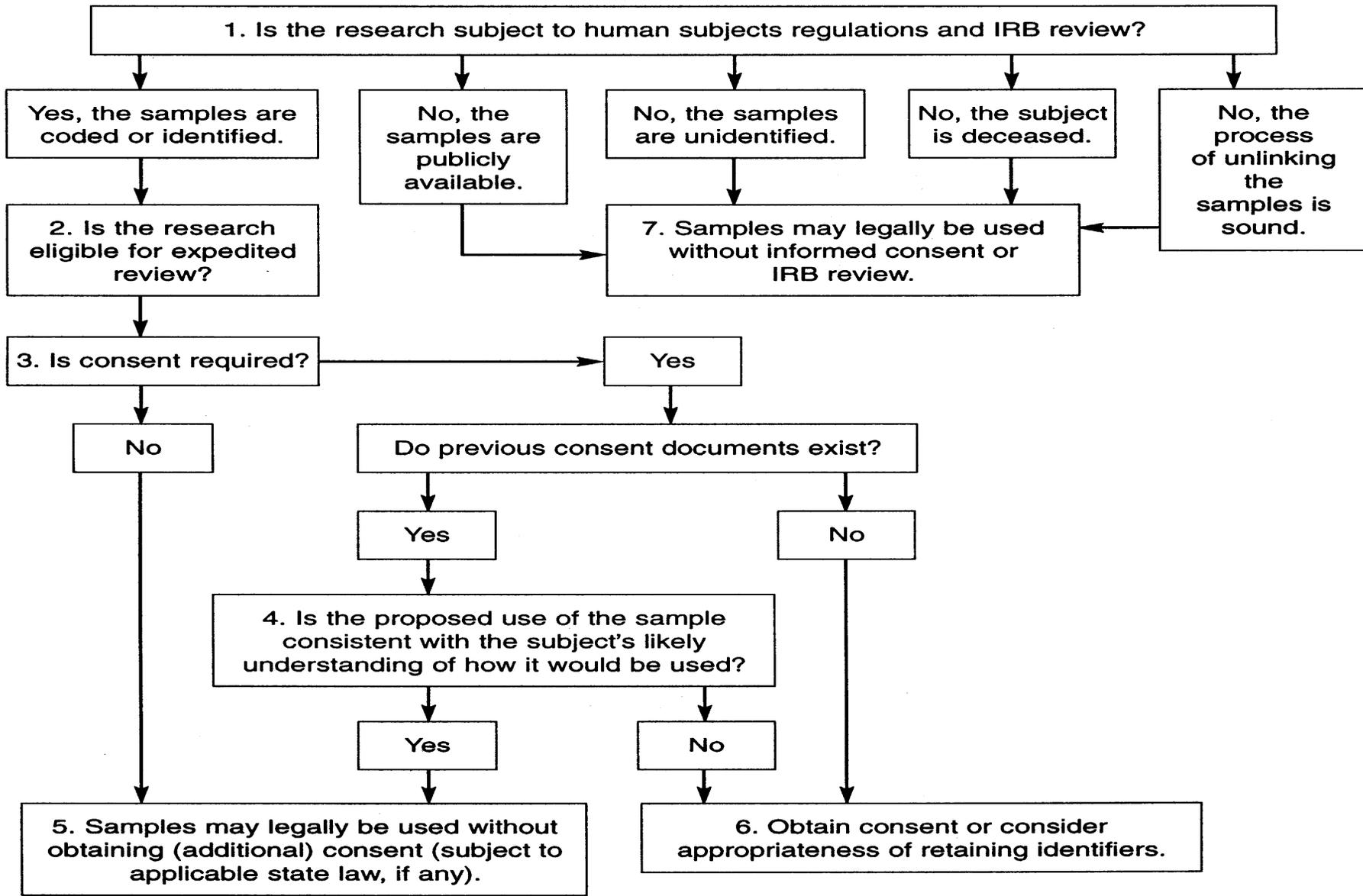


Chart 3: IRB Review for Research with Human Biological Materials

Guidelines for applying the exemption stated at 45 CFR 46.101(b)(4) and criteria for expedited review at §46.110.

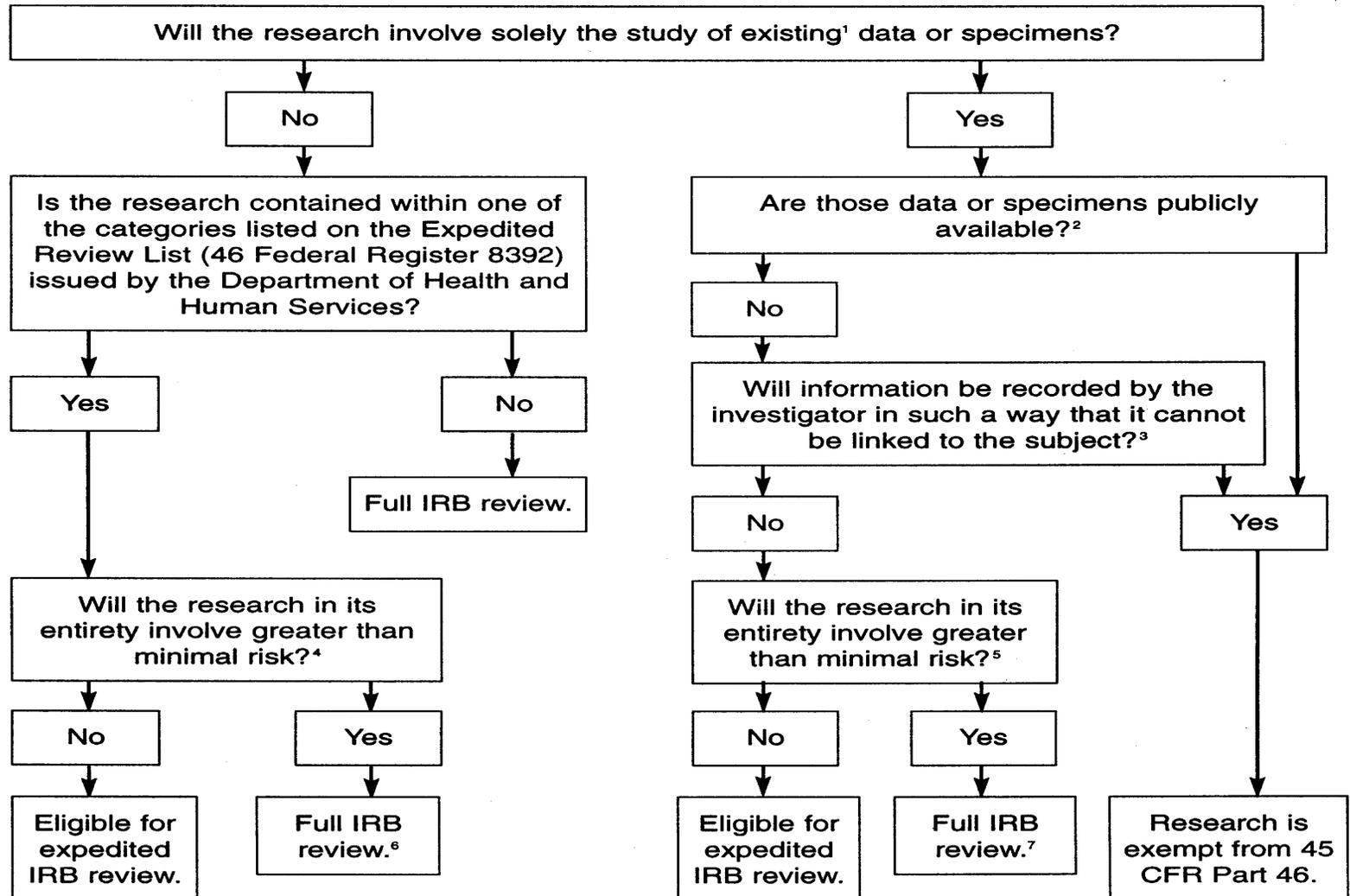
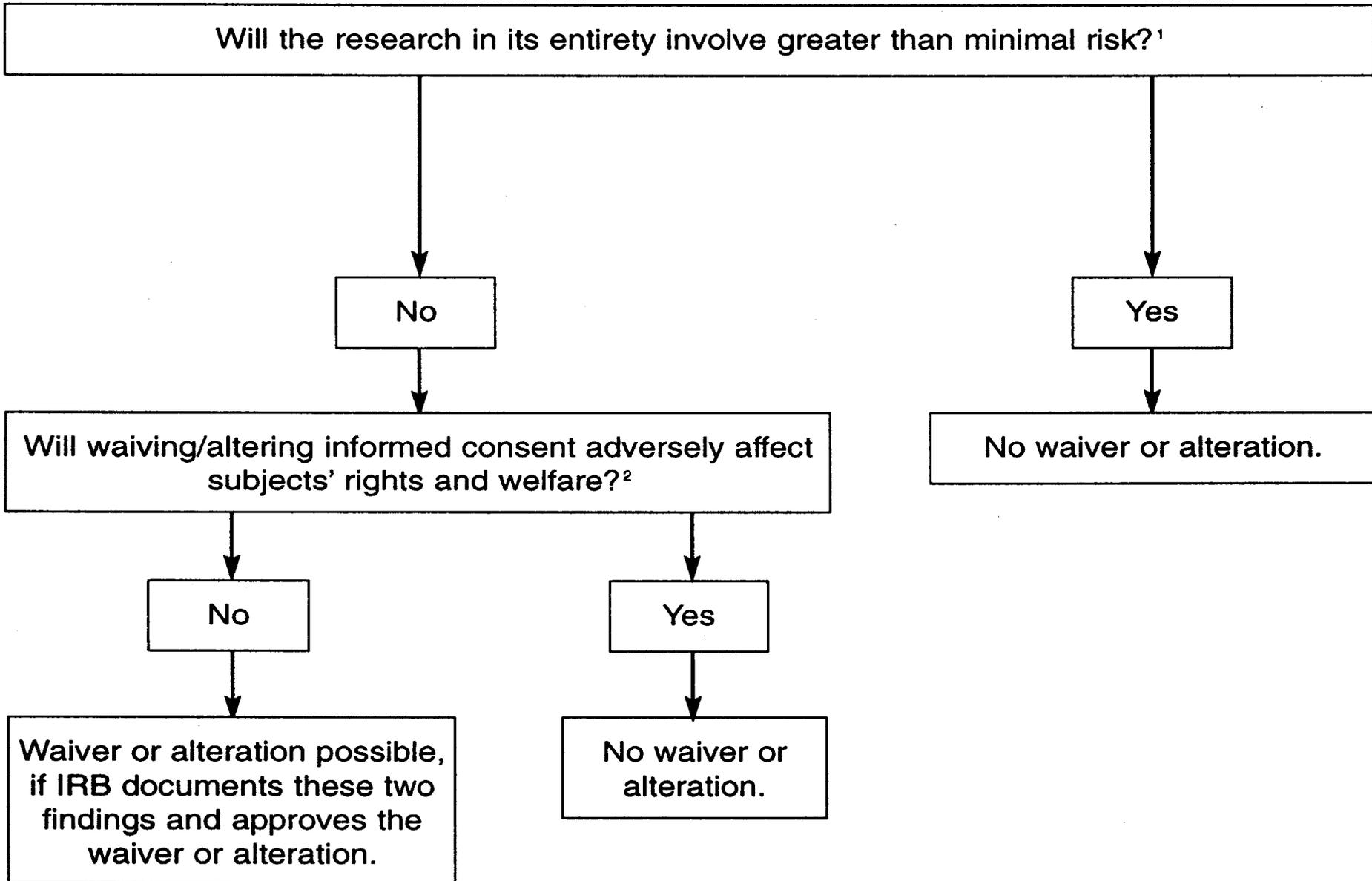


Chart 4: NBAC's Proposed Informed Consent Requirements for Research with Human Biological Materials¹



Tissue Banking

CONSENT GUIDELINES

When informed consent to the research use of human biological materials is required, it should be obtained separately from informed consent to clinical procedures.

The person who obtains informed consent in clinical settings should make clear to potential subjects that their refusal to consent to the research use of biological materials will in no way affect the quality of their clinical care.

Tissue Banking

Purpose of study

Storage:

- Inform subjects how long sample will be stored.
- Inform subjects where the sample will be stored.
- Inform subjects how the samples will be safeguarded.
- Inform subjects who would be the point of contact if retrieval of sample becomes necessary.

Tissue Banking

Specimen Use: Primary Storage or Specific Research

- If institutional policy, disclose plans for future re-contact the subjects.
- Describe plans for deciding priorities for future research projects involving this tissue.
- Describe a plan outlining who will control the decision regarding the use of these samples by other researchers.

Tissue Banking

Specimen Use: Original purpose-Specific Research Protocol

- Inform subjects if subsequent investigators may be given access to samples.
- If subsequent investigators will be given access to the samples, inform the subject whether the samples will be provided with or without identifiers.
- Give subjects the option of consenting now to a future second use.

Tissue Banking

Subject access to results

- Inform the subjects what information, if any, regarding the results of the study that they will receive (will this be individualized results or general summary results?).
- If results will not be provided to the patient, state this and explain why.

Tissue Banking/ Genetic Research

Subject access to genetic information

- If results are to be disclosed,
 - Indicate at what point in the research that the findings will be disclosed;
 - Describe who will be responsible for disseminating the information;
 - Describe what supports are available after the subject is provided this information (genetic counseling, etc.?)
- Describe plans to handle incidental findings (paternity, disease or conditions other than the one under study).

Consent Language

Secondary Use

I am consenting to allow the following:

- Use of my biological materials for this study only
- Use of my biological materials for this study and other studies based on this study or for the same disease.
- Use of my biological materials for any research purposes.

- I wish to be contacted for each new study.
- I do not wish to be contacted for any study after providing this consent.

Tissue Banking

Risks

- Inform the subject of any applicable potential social risks that could be associated with learning the results of the research or a breach of confidentiality.
- Inform the subject of any applicable potential psychological risks that could be associated with learning the results of the research or a breach in confidentiality.
- Inform the subject of any applicable potential physical risks that could be associated with a breach in confidentiality.

Tissue Banking

Family members

- If family members are involved in the research protocol, describe how each subject will be protected against disclosure of medical or other personal information about themselves to other family members?
- If family members are involved in the research protocol, describe how individual subjects will be given the option not to receive information about themselves.

Tissue Banking

Confidentiality issues

- Inform the subjects whether patient identifiers will be maintained with the samples.
- If identifiers will be maintained, describe what identifiers will be maintained and detail a plan to keep research results and clinical identity separate.

Tissue Banking

Confidentiality issues

- Describe plans for physical security of data and sample.
- Inform the subject about the limits of confidentiality (who will have access to the research results and under what circumstances). This should include the plan regarding access to the data by the subject's family, third party payers, employers and the subject's physician.

Tissue Banking

Withdrawal from research

- Inform the subject that they have the right to withdrawal and have the sample destroyed at any time.
- Inform the subject that they have the right to have identifiers removed without destroying the sample.
- Provide instructions regarding how to withdraw from the study or how to have identifiers removed.

Tissue Banking in the AMEDD Summary

- Be aware of latest guidelines for consent & tissue disposition
- Have fail-safe consent system in place
- Have accurate tissue procurement and storage system
- Follow confidentiality guidelines