The Importance of Tissue Banking and Tissue Research

Mark E. Sobel, M.D., Ph.D.
Executive Officer,
American Society for Investigative Pathology
mesobel@asip.org

The Era of Molecular Medicine

Molecular techniques, information generated from the Human Genome Project, and advances in information technology are transforming the:

- **public's fears and expectations**
- **practice of medicine**

"Eye on the Prize" Improve the public's health

- **Conduct biomedical research to increase knowledge and understanding of biological processes.**
- **Respect subjects' rights and personal autonomy; minimize harm.**

Use of Human Biological Materials in Research

Human subject protections are applicable not only to clinical trials but also to the use of human biological materials in research studies, including basic science projects.

Human Biological Materials HBMs

- **Tissue samples**
- **Blood, sputum, urine, bone marrow, etc.**
- **Freshly obtained and archived materials**

Repositories

- **Tissue banks**
- **Stored blood/urine samples**
- **Freezers containing HBMs under individual control of principal investigators**
- **Histologic slide files**

Requirements of Repositories

- Security of samples
- IRB oversight
- Record keeping for informed consent
- Confidentiality
- Anonymization of samples
- Increased workload !!

HBMs in Research

- Historical use of archived specimens
  - Tobacco smoke and lung cancer
  - Diethylstilbesterol
- Re-use of specimens
  - Pathologists and the histological slide file
- Increased demand for tissues
  - Tissue microarrays
  - Gene expression arrays

Challenges

- Educating researchers
- Use of previously archived HBMs that were obtained without consent
- Re-use of HBMs
- Utility of anonymized samples
- Utility of autopsy specimens
- Assessment of risk by IRBs
- Demands on Tissue Repositories

Educating Researchers

- Clinical research
- Translational research
- Basic science research
- What is a Repository?

Anonymized Samples

- Basic science studies
- Translational/clinical research
  - Studies not optimal
  - Inability to perform long-term follow-up or prognostic studies
  - Clinically useful information cannot be conveyed (rare)

Classifying HBMs: Assessment of Risk

- Unidentifiable
  - Anonymous
  - Anonymized
- Identifiable
  - Coded (Linked)
  - Identified

Use of HBMs in Genetic Research: Assessment of Risk

- **Germline**
  - **Inheritability**
  - **Implications for immediate and extended family**
  - **Implications for ethnic group**
  - **Use of "normal" tissues**
- **Somatic cell**
  - **Acquired mutations**
  - **Use of diseased tissues**
  - **No implications for family**

Classifying HBMs: Assessment of Risk

- **Basic Science Studies**
  - **Source for substrates**
  - **Biochemical studies**
- **Translational Research**
- **Clinical Research**

Identifiable HBMs- The Common Rule

- **Any HBM that can be identified by any one person, anywhere, is an identifiable sample**
- **If a sample is coded, and any investigator keeps a key to the code, the sample is identifiable**
- **Exception: If the recipient of the HBMs signs an agreement that there is no intent to identify the samples, the sample may be considered unidentifiable.**

Waivers of Informed Consent-Common Rule

An IRB may grant a waiver of informed consent under the Common Rule (not the FDA) if four criteria are met:

- Minimal risk
- Respect for autonomy and the rights of the individual
- Impracticable
- Notification

Specimens from Deceased Individuals

- **Common Rule- exempt**
- **Local regulations**
- **HIPAA-**
  - **Information associated with HBMs**
  - **Exemption for research with proof**
- **If anonymized, how does the Tissue Repository know the individual is deceased?**

HIPAA: Final Rule- April 14, 2003

- http://www.hhs.gov/ocr/hipaa
- In general, final modifications of the HIPAA regulations that went into effect April, 2003 are "friendlier" to research with HBMs than the original version:
  - Authorizations for research-use simplified
  - Waivers of consent
  - Limited Data Sets and "de-identification"
  - Application to deceased individuals
- New guidance from OCR expected shortly

HIPAA and HBMs

- Although HBMs are considered part of the medical record, they are not covered by HIPAA.
- Annotations concerning HBMs are covered by HIPAA so that data accompanying the sharing of HBMs may have to be recorded in the medical record.

HIPAA: Authorizations

- Authorizations may be part of the consent for a treatment-associated study
- Blanket consent is not acceptable
- Consent may be granted for an undefined period of time:
  - No specific date except "end of study"
  - Beyond the end of the study
- Consent may be revoked but data obtained up to that time may still be included in the study.

HIPAA: Waivers of Consent

- Minimal risk to the privacy of individuals:
  - Plan to protect the identifiers from improper use or disclosure
  - Plan to destroy identifiers as soon as possible
  - Written assurance not to reuse or disclose
- Impracticable to conduct research without waiver
- Impracticable to conduct research without access to protected health information

HIPAA: Limited Data Sets

- Create and disseminate a limited data set that does not include directly identifiable information
- Data use agreement between the "covered entity" and the recipient:
  - Limited use of the data set
  - Ensure security of data
  - Do not identify the information or contact any individual
- A code may be assigned to allow re-identification

HIPAA: Definition of Unidentifiable

- Since a code may be used for re-identification of data in Limited Data Sets, the definition of unidentifiable is broader under HIPAA than under the current OHRP interpretation of the Common Rule

Limited Data Sets: De-identification

- A covered entity may de-identify protected health information so that such information may be used and disclosed freely, without being subject to the Privacy Rules' protections.
- A person with appropriate knowledge may render the information not individually identifiable and certify to a very small risk
- Privacy Rule's safe harbor method: 18 enumerated identifiers must be removed

Limited Data Sets: Safe Harbor Method

- Direct identifiers:
  - Name, street address, social security number
  - Medical chart, surgical pathology, prescription numbers
- Other identifiers:
  - Birth date, admission and discharge dates, five-digit zip code (first 3 digits usually OK)
- Permitted demographic information:
  - Age, gender, ethnicity

HIPAA- Deceased Persons

- The Privacy Rule covers deceased persons' protected health information (PHI) in perpetuity.
- However there is an exception for research

HIPAA- Deceased Persons-Research Exception

- Disclosure of a decedent's PHI without authorization if:
  - Disclosure is solely for research
  - Documented death of the individual
  - Disclosure is necessary for the research to proceed
- Therefore, under HIPAA for research purposes, no review necessary by an IRB or Privacy Board for deceased persons

Principles for the 21st Century

- **Ethical Principles:**
  - **Respect for persons (personal autonomy):**
    - **Informed consent**
  - **Respect for privacy and confidentiality**
  - **Beneficence**
  - **Justice**
- **Impact of Biomedical Research**