NCI Forum:
NCI Best Practices for Biospecimen Resources

June 18, 2007

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The Role of Biospecimen Resources in 21st Century Medicine

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Biospecimen resources encompassing large quantities of high-quality, clinically annotated biospecimens are needed to:

- Identify targets for detection, diagnosis, treatment, and prevention
- Develop diagnostics that predict drug efficacy
- Validate new therapeutics
- Elucidate molecular mechanisms of neoplasia
- Develop a molecular-based taxonomy of cancer
- Identify biomarkers for susceptibility, screening, recurrence
- Identify biologic variations that determine drug efficacy
- Identify biologic variations leading to drug toxicity

The Role of Biospecimen Resources in 21st Century Medicine

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Biospecimen research resources are critical for the biomolecular
that will be the foundation of personalized medicine.

Key Requirements for Biospecimen Resources for Post-Genomic Cancer Research

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- Best practice-based, data-driven technical and operational standards to ensure quality and enable reproducible molecular analysis
- High-quality specimen annotation (pathology and clinical data)
- Specimen access through a timely, centralized, peer-review process
- Ethical and privacy compliance through a chain of trust
- State-of-the-art informatics systems to track specimens, associated data (clinical, pathological, and quality control), and patient consents
- Communication and outreach efforts to ensure greatest impact

NCI Biospecimen Issues

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Heterogeneity in practices among NCI-supported biospecimen resources has led to a lack of:

- **Common procedures, standards, and management principles**
- **Common definitions**
- **Common computerized access to information on specimens**
- **Common approaches to ethical, legal, and policy issues**

The Role of Biospecimen Resources in 21st Century Medicine

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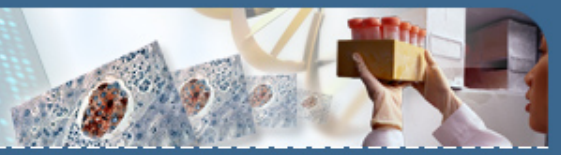
For NCI's biospecimen resources, the need for standardization and quality management is critical and long overdue.



What Is a Biospecimen Resource? *

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NCI defines a biospecimen resource as a collection of human specimens and associated data for research purposes, the physical entity where the collection is stored, and all relevant processes and policies.

*Source: NCI Best Practices for Biospecimen Resources

NCI's Biospecimen Activities

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2007

- FGGs revised based on public comments and renamed NCI Best Practices for Biospecimen Resources

2006

- First-Generation Guidelines for NCI-Supported Biorepositories (FGGs) published in Federal Register

2005

- First International Summit on Harmonization of biorepositories conducted
- caBIG™ software tools for biorepositories developed

2004

- Analysis of NCI-supported biospecimen resources conducted
- Trans-NCI Biorepository Coordinating Committee formed

2003

- Case Studies of Existing Human Tissue Repositories published
- National Biospecimen Network (NBN) Blueprint published

2002

- Internal and external review process begun
- Biospecimen resources identified as critically important to post-genomics cancer research

NCI Best Practices Development Process

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First-Generation Guidelines (FGGs) for NCI-Supported Biorepositories were reviewed by:

- NIH Office of Science Policy
- DHHS Office for Human Research Protections
- NIH Office of Intramural Research
- NIH Office of Extramural Research
- NIH Office of Technology Transfer
- NIH Office of the General Counsel

FGGs were published in the Federal Register

- Open public comment period, April-July 3, 2006
- Approximately 60 comments received on topics including:
  - biospecimen resource economics
  - informed consent requirements
  - biospecimen resources affected by the FGGs

NCI Best Practices for Biospecimen Resources were published in April 2007

- Consideration and response to public comments
- Reviewed by NIH and DHHS offices listed above
- Reviewed and approved by the NCAB

NCI Best Practices for Biospecimen Resources

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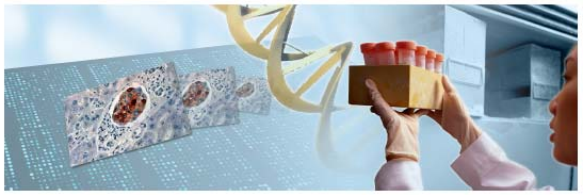

National Cancer Institute
Best Practices for
Biospecimen Resources

June 2007

Prepared by:
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

Objective:

- **Unify policies and procedures for NCI-supported biospecimen resources**
- **Provide a baseline for operating standards on which to build as the state of the science evolves**

The NCI Best Practices Overview

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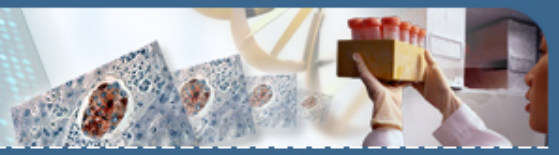
The NCI Best Practices include recommendations for:

- **Common technical, operational and safety best practices for research biospecimen resources**
- **Quality assurance and quality control programs**
- **Implementation of enabling informatics systems**
- **Establishing reporting mechanisms**
- **Providing administration and management structure**
- **Addressing ethical, legal, and policy issues**
- **Definitions of key terms**

NCI Best Practices for Biospecimen Resources

Technical and Operational Guidelines

http://biospecimens.cancer.gov



Specimen Collection, Processing, Storage, Retrieval, and Dissemination

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- Handle specimens as appropriate for specimen type and study design.
- Develop SOPs for all protocols and a training program for all appropriate personnel.
- Minimize collection/processing time as appropriate.
- Develop a comprehensive quality management system.
- Annotate specimens with key collection, processing, and storage data.
- Monitor specimen inventory with a tracking system.
- Store specimens in a stabilized state without unnecessary thawing/refreezing.
- Dispose of specimens according to clear rules.
- Review and document storage equipment performance on regular basis.
- Follow specimen-appropriate biosafety, packaging, and shipping procedures.

Collecting/Managing Clinical Data/QA/QC

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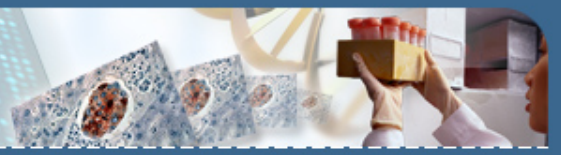
Collecting and Managing Clinical Data

- Collect and store relevant clinical and epidemiologic data associated with a specimen, including longitudinal data, if applicable.
- Use an informatics system that tracks all aspects of collection, processing, and distribution.
- Comply with applicable privacy rules and human subjects regulations.

Quality Assurance/ Quality Control

- Have a quality management system that describes QA and QC procedures.
- Maintain QA/QC training records for personnel.
- Adhere to and periodically review SOPs.
- Have security systems in place, including alarms and backup power.
- Include a computerized inventory tracking system in the data management plan.
- Develop a facility disaster plan.
- Maintain all equipment properly according to SOPs.



Biosafety/Biospecimen Resource Informatics

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Biosafety

- Assume that all specimens are potentially infectious – provide appropriate vaccines.
- Adhere to governmental and accrediting agency requirements.
- Identify and address biosafety risks.
- Record exposure incidents and provide personnel with appropriate treatment.
- Establish indemnification agreements with users of biospecimens.
- Develop policies and procedures as appropriate for chemical, electrical, fire, occupational, and radiological safety.

Biospecimen Resource Informatics: Data Management, Inventory Control, and Tracking

- Assign a unique identifier (number and/or barcode) to each specimen.
- Update the database each time the specimen is moved or modified.
- Use informatics systems that support the linking of specimens with associated data and protect the health information of patients.
- Adhere to or initiate review of NCI Center for Bioinformatics guidelines and tools; caBIG™ “silver-level” compatibility is recommended.

NCI Best Practices for Biospecimen Resources

Ethical, Legal, and Policy Guidelines

http://biospecimens.cancer.gov

Informed Consent

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- Consider allowing research participants to specify the types of research for which their specimens may be used.
- Develop policies for handling specimens for which consent has been withdrawn.
- Develop policies for obtaining consent for studies involving children.
- Consider special U.S. Food & Drug Administration regulations.
- Establish and document transparent policies to govern the retention of records and specimens.

Access to Biospecimens and Data

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- Develop clear policies for specimen and data access.
- Develop clear guidelines for sample distribution and clinical data sharing (Protocol-specific requirements to be met before other access is considered).
- Ensure that investigators have timely, equitable, and appropriate access, without undue administrative burden.
- Charge for samples only to recover costs.
- If a resource needs to close, announce the availability of specimens for transfer.
- Restrict access to subjects' identities and medical, genetic, social, and personal histories via data access system with defined privilege levels.

Privacy Protection/Custodianship

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Privacy Protection

- Protect the privacy of information and follow applicable regulations.
- Follow documented policies on employee access to data or specimens.
- Provide levels of security appropriate to the type of biospecimen resource.

Custodianship

- Include plans for custodianship of collected specimens and associated data in biospecimen resource protocols.
- Develop plans to handle/dispose of specimens and associated data:
  - At end of the budget period of the grant
  - At completion of the specific research objectives of the study
- Identify and disclose financial conflicts of interest.
- In informed consent language, disclose that specimens may help to develop products, tests, or discoveries that may have commercial value.

Intellectual Property

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- Use a material transfer agreement (MTA), such as the NIH Simple Letter of Agreement, to transfer materials.
- Specify in MTAs that research data obtained through the use of biospecimen resource specimens and/or associated data should be made available to the research community.

Next Steps

NCI Best Practices: Next Steps

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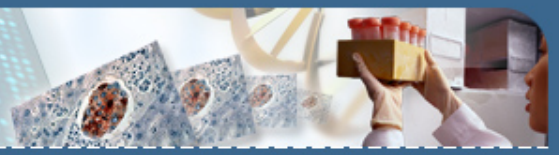
- NCI Best Practices will be made publicly available on the OBBR Web site.
- NCI Best Practices will be distributed to managers of all NCI-supported intramural and extramural biospecimen resources.
- The OBBR will launch a national education and outreach program:
  - Local meeting – NIH campus, June 18, 2007
  - Regional meetings – Fall 2007
    - Boston, MA
    - Chicago, IL
    - Houston, TX
    - Los Angeles, CA
    - Seattle, WA
- The OBBR and NCI Biorepository Coordinating Committee will create a biospecimen resource self-evaluation checklist based on the Best Practices



NCI Best Practices: Next Steps

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- Periodic revision of the Best practices will occur with input from researchers, biospecimen resource managers, advocates, policymakers, and related stakeholders as new technologies and clinical practices emerge.
- OBBR's Biospecimen Research Network will conduct research to establish the scientific basis for data-driven standards for specimen collection, processing, and storage.
  - **Develop an extramural program to study the effect of pre- and post-acquisition variables on biomolecular profiles in specimens of different types**
  - **Create a searchable Web-based tool to access biospecimen research data**
  - **Partner with College of American Pathologists to develop evidence-based specimen type-specific and analysis-type specific SOPs**

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Biospecimen Science *

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What is biospecimen science?

- The multidisciplinary field of study responsible for establishing tested and proven biospecimen resource-related procedures based on experimentation in the areas of specimen collection, processing, shipping, and storage

Why is it needed?

- Biospecimens are composed of active and reactive living cells or cell products, making them highly complex.
- The collection, handling, and storage process can profoundly alter the molecular profile and quality of biospecimens.
- Such alterations, though artificial, can be misinterpreted as disease related or disease specific.
- High degrees of sensitivity and specificity in new molecular techniques raise the bar for analyte (specimen) data and quality.

*Source: http://biospecimens.cancer.gov/sciences/symposium.asp

The Premise of Biospecimen Science

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- Quality is not a generic concept.
- Quality of human biospecimens is multifactorial and is determined by the:
  - Type of specimen: normal tissue, tumor tissue, serum, plasma
  - Physical state of the specimen
  - Amount and type of specimen characterization data
  - Amount and type of quality control exercised
  - Amount and type of clinical data
  - Permitted use of the specimen
  - Analysis platform to be used; the biomolecules targeted by the analysis
  - The goal of the research (application of the data)

Public Comments – Major Issues

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- Technical and operational guidelines perceived to be beyond the capability of smaller biospecimen resources in terms of both technical expertise and cost of compliance.
- Informatics requirements related to tools, particularly NCI's caBIG™, that have not yet been fully developed or made available for widespread adoption.
- Informed consent recommendations went beyond current regulations and were not clearly related to biospecimen collection and usage.
- Overall, the Guidelines were too prescriptive and difficult for smaller biospecimen resources to adopt.