NCI Forum:
NCI Best Practices for Biospecimen Resources

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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
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

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

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

2002
- Analysis of NCI-supported biospecimen resources conducted
- Trans-NCI Biorepository Coordinating Committee formed
- Case Studies of Existing Human Tissue Repositories published
- National Biospecimen Network (NBN) Blueprint published

2003
- First International Summit on Harmonization of biorepositories conducted
- caBIG™ software tools for biorepositories developed

2004
- First-Generation Guidelines for NCI-Supported Biorepositories (FGGs) published in Federal Register

2005
- FGGs revised based on public comments and renamed NCI Best Practices for Biospecimen Resources

2006

2007
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
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 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

- 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 a regular basis.
- Follow specimen-appropriate biosafety, packaging, and shipping procedures.
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.
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.

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.
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

- 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

**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.
• 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

- 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

• 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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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

- 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

- 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.