UC Health IN SCIENCE LIVES HOPE.

Biospecimen Collection and Handling for Clinical Research

Friday, October 1st, 2021

Learning Objectives:

1) Explain the basic principles of Biobanking

2) Identify how Biobanking applies to clinical research and its importance

3) Describe a human biospecimen

4) Describe the proper acquisition, handling, and storage of biospecimens

Target Audience:

Clinical Research Professionals (CRPs) at UC/H and Cincinnati Children's Hospital Medical Center (CCHMC): including Principal Investigators (PIs), Research Nurses (RNs), Critical Care Unit Nurses (RNs), Pharmacy Technicians and Regulatory Specialists.

Off-Label Disclosure Statement:

Faculty members are required to inform the audience when they are discussing off-label, unapproved uses of devices and drugs. Physicians should consult full prescribing information before using any product mentioned during this educational activity.

Learner Assurance Statement

The University of Cincinnati is committed to resolving all conflicts of interest issues that could arise as a result of prospective faculty members' significant relationships with drug or device manufacturer(s). The University of Cincinnati is committed to retaining only those speakers with financial interests that can be reconciled with the goals and educational integrity of the CME activity.

Accreditation Statement for Directly Sponsored Activity

The University of Cincinnati is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The University of Cincinnati designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Participants should claim only the credit commensurate with the extent of their participation in the activity.

CRPs, NPs, PAs, and RNs can count activities certified for *AMA PRA Category 1 credit*™ for professional credit reporting purposes. Other healthcare professionals should inquire with their certifying or licensing boards.

Disclaimer Statement

The opinions expressed during the live activity are those of the faculty and do not necessarily represent the views of the University of Cincinnati. The information is presented for the purpose of advancing the attendees' professional development.

Speaker Disclosure:

In accordance with the ACCME Standards for Commercial Support of CME, the speakers for this course have been asked to disclose to participants the existence of any financial interest and/or relationship(s) (e.g., paid speaker, employee, paid consultant on a board and/or committee for a commercial company) that would potentially affect the objectivity of his/her presentation or whose products or services may be mentioned during their presentation. The following disclosures were made:

Planning Committee Members:

- Maria Stivers, MS, CIP; Course Director – No Relevant Relationships
- Zachary Johnson, BS – No Relevant Relationships
- Nathaniel L. Harris, BS, Course Coordinator – No Relevant Relationships
- Brandon Armstrong, CME Program Coordinator – No Relevant Relationships

Speakers:

Kelsey Dillehay Mckillip, PhD

Assistant Professor

Director, University of Cincinnati Biorepository

No Relevant Relationships

OCR Announcements:

UC Health

October 2021 Study of the Month

Memory Problems?

Memory and Metabolism Study

What
The purpose of this nutritional research study is to evaluate the effectiveness of berry fruits in preventing cognitive decline and improving insulin resistance.

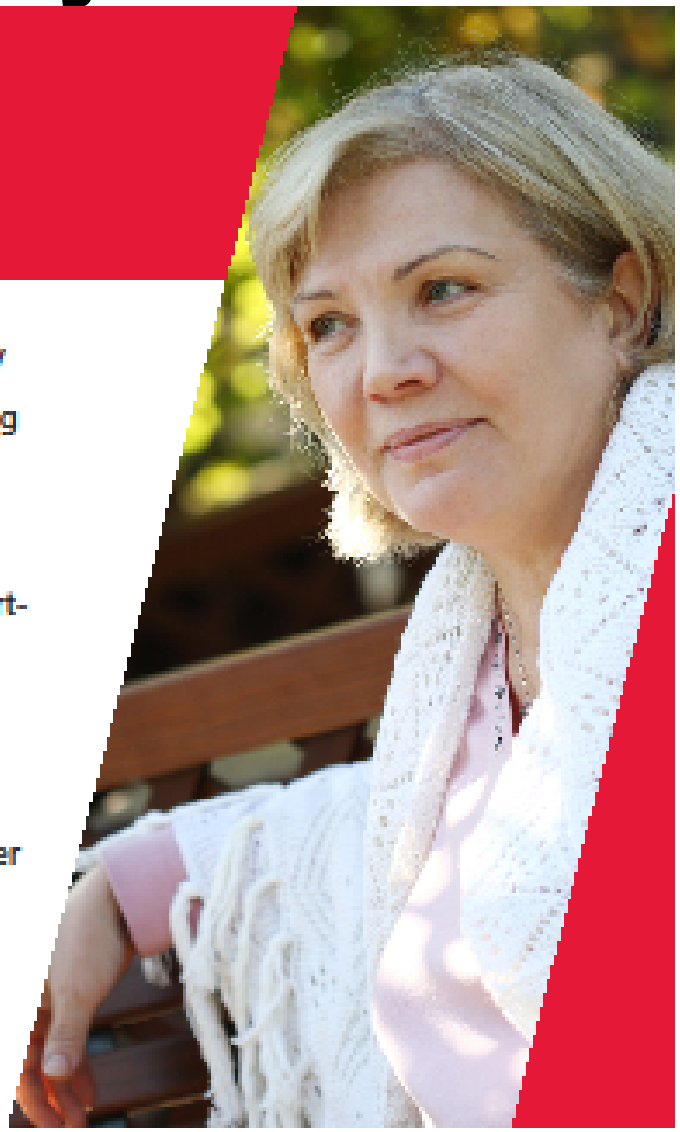
Who
Overweight men and women 50 to 65 years old without diabetes who are aware of mild memory decline such as forgetfulness or short-term memory difficulty.

Pay
Compensation may be available for time and travel for each completed study visit.

Details
For more information, contact Marcelle Shidler at shidlemd@ucmail.uc.edu or call (513) 558-2455.

UC Health.

41-15 IRB# 2015-1256



OCR Announcements:

S.O.P. Update:

Electrical Safety Testing of Research Equipment

Any device or equipment which must be plugged into an electrical outlet and requires electricity in order to function, that is intended to be used for Research purposes, needs to be registered and approved for use by Clinical Engineering.

Please refer to the following recently updated UC Health SOP:

UCH-OCR-OPS-SOP-009-03: Electrical Safety Testing of Research Equipment

Updates to this S.O.P. include the contact information for Clinical Engineering.

All OCR SOPs are accessible from the UC Health intranet home page utilizing the Compliance 360 policy search function or reach out to the Office of Clinical Research with any questions or concerns.

OCR Announcements:

Thursday, October 21st, 2021, 12:00noon - 1:00pm
Virtual Presentation

The Consent Process for Central IRBs

Please join us and for an overview of reliance on commercial IRBs, including currently executed agreements, number of studies, requirements for reliance determinations, completing the External IRB cover page, processes for changes to informed consent language, and approval release for studies housed at Advarra IRB and the WCG Group IRB.

Kareemah Mills, CIP
Assistant Director
Human Research Protection Program
UC Office of Research Integrity

UC Health

Today's Presentation:

Biospecimen Collection and Handling for Clinical Research

Kelsey Dillehay Mckillip, PhD

Assistant Professor

Director, University of Cincinnati Biorepository

Department of Pathology & Laboratory Medicine

University of Cincinnati College of Medicine

Biospecimen Collection and Handling for Clinical Research

Kelsey Dillehay McKillip, PhD
Director, University of Cincinnati Biorepository

Medical Science Building Room 1252
Tel: (513) 558-7111
Email: uccitb@uc.edu

Website: http://cancer.uc.edu/Research/CoreFacilities/TumorBanking.aspx

UNIVERSITY OF Cincinnati

Learning objectives

1. Understand the importance of biospecimens in clinical research and clinical trials

2. Understand the ethical, legal, and social implications of using human biospecimens in research

3. Describe the proper acquisition, handling, and storage of biospecimens for clinical research

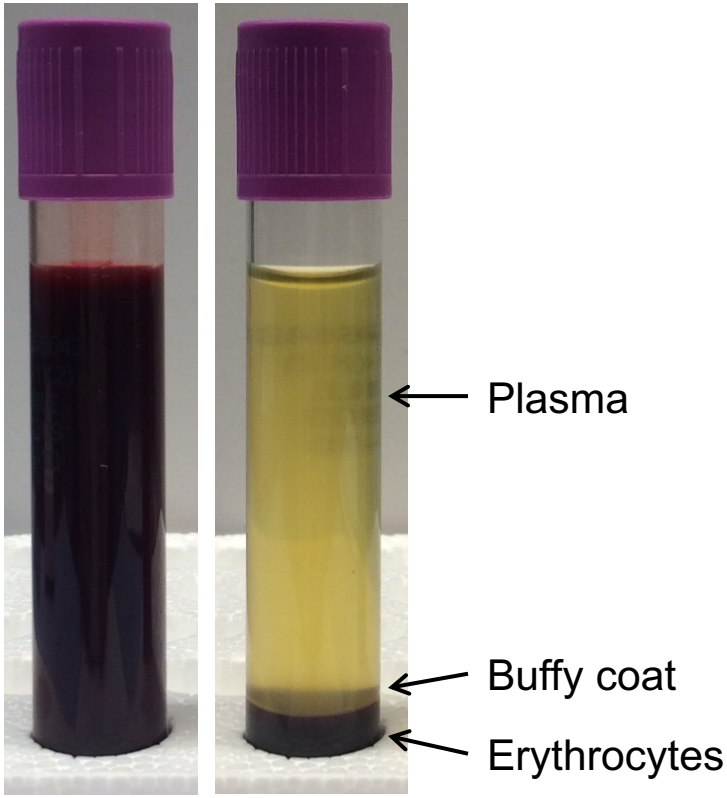
4. Explain the basic principles of biobanking

- Human biospecimens are critical for the advancement of scientific research and medicine
  - Research leading to better understanding of the biology of human disease
  - The discovery of new diagnostics and treatments that are tailored to individual patients ("personalized medicine")
  - Improved clinical outcomes for patients

UNIVERSITY OF Cincinnati

Biospecimen:

"A sample of material, such as urine, blood, tissue, cells, DNA, RNA, or protein, from humans, animals, or plants. Biospecimens may be used for a laboratory test or stored in a biorepository to be used for research."



Biospecimens in Clinical Research

- Biospecimens provide a biological snapshot of the physiological profile of a research participant

- Biospecimens are used to answer research questions:
  - Is a new medication safe?
  - Is a new medication effective?
  - Can a biomarker help diagnosis disease or predict the effectiveness of a new medication?

Many of the human biospecimens collected for clinical research are stored in biobanks

"It is your choice whether or not to let researchers share your data and biospecimens for research in the future. If you say "yes," you can change your mind later, but your data and biospecimens might still be used if they have already been shared. If you say "no," you can still fully participate in this study. Please initial next to your choice:

_____YES, *use my data and biospecimens in other research studies*

_____NO, do NOT use *my data and biospecimens in other research studies"*

Biorepository / Biobank:

"Any entity that collects, processes, stores, and/or dispenses, biospecimens, their derivatives and relevant data."

Types of Biobanks

TABLE 2. COMP

Type of biorepository	*Biobank, typical*	*Epidemiological, popu based, or environm*	*Clinical trial*	*Combination model*
1) Usual types of specimens	Solid tissues and biofluids; Specimens may vary with goals of the biobank; Frequently only FFPE tissue and biofluids are available	Usually only biofluids – b components and someti	Solid tissues and biofluids depending on requirements of the clinical study.	Specimens requested by investigators; Biobanked specimens collected, processed and stored based on biorepository goals.
2) Specimen collection	Collected in a medical facility for future research; Usually disease-based.	Usually collected from inc without disease, but car specimens from individu increased risk for a dise Collected for future res Longitudinal samples s available.	Collected in a medical facility in association with therapeutic interventions for disease.	Collected for future research or at request of investigators; Many specimens are rapidly distributed, but some are banked.
3) Processing, storage and distribution	Processed via a SOP; Stored until distributed to an investigator.	Processed by a SOP; Stor periods until an endpoin (e.g., development of a study of an environmen Distribution usually is r research on specific issu not associated with an e (e.g., development of a frequently are not initia available for distributio	Processed by a SOP; Stored until distributed to an investigator; Use may be restricted due to the informed consent.	Processed based on a SOP (bank) or according to investigator request; Distributed to a requesting investigator or stored in bank until requested; Strong emphasis on distribution.
4) Data	Extensive data may be available upon request including outcome.	Extensive data available f based upon interview o participants; Usually pa are healthy; Outcome (e development of a diseas variable.		Data models vary based on goals of biobanking component; Demographic data available and other data via health record; Outcome of prospective component not available when specimens first requested.
5) Advantages	Specimens and data including outcome usually are immediately available.	Longitudinal specimens m available; Extensive dat individual can be provi		Prospective specimens collected and processed based on investigator needs; Banked specimens and outcomes may be immediately available; Prospective specimens will not have long-term storage artifacts.
6) Disadvantages	Many specimens are not utilized; Specimens may not meet needs of the investigator; Potential artifacts and molecular degradation based on long-term storage.	Many specimens are not u Specimens subject to ar molecular degradation term storage.		Specimen and outcome data not immediately available on prospective specimens; Potential artifacts and degradation of banked specimens on long-term storage; Banked specimens may not be utilized.

Grizzle et al., Biopreserv Biobank, 2015

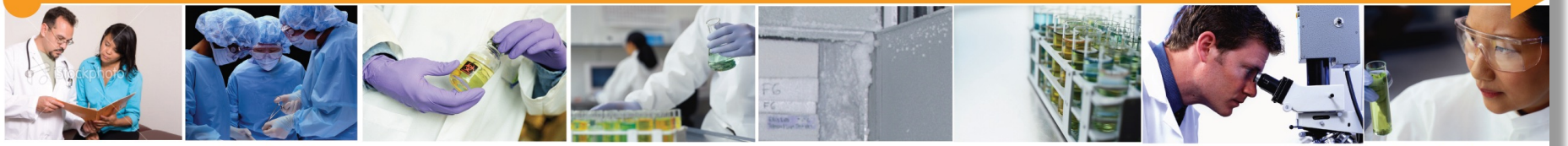
Notable National Biorepositories

- The National Pathology Repository
  - The largest and most comprehensive collection of pathology material in the world
    - > 2.8 million cases since 1917
    - > 50 million microscopic slides
    - > 30 million tissue blocks
- Framingham Heart Study
  - Longitudinal, population based, multi-generational study that began in 1948
  - The first prospective study of cardiovascular disease
    - Original cohort: 5,209 participants
    - Second and third generation cohorts
- Million Veteran Program (MVP)
  - Since launching in 2011, over 825,000 Veteran partners have joined
- All of Us Program
  - 1 million or more participants donating longitudinal samples and data

Local Biorepositories

- Fernald Community Cohort
  - Specimens and data collected from Fernald Medical Monitoring Program (FMMP) participants (1990 – 2008)
- UC Biorepository
  - Specimens and data collected from individuals diagnosed with cancer (2002 – present)
- Cincinnati COVID-19 Repository
  - Specimens and data collected from individuals diagnosed with COVID-19 (2020 – present)
- Discover Together Biobank (CCHMC)
  - Pediatric biobank

The specimen is biologically viable



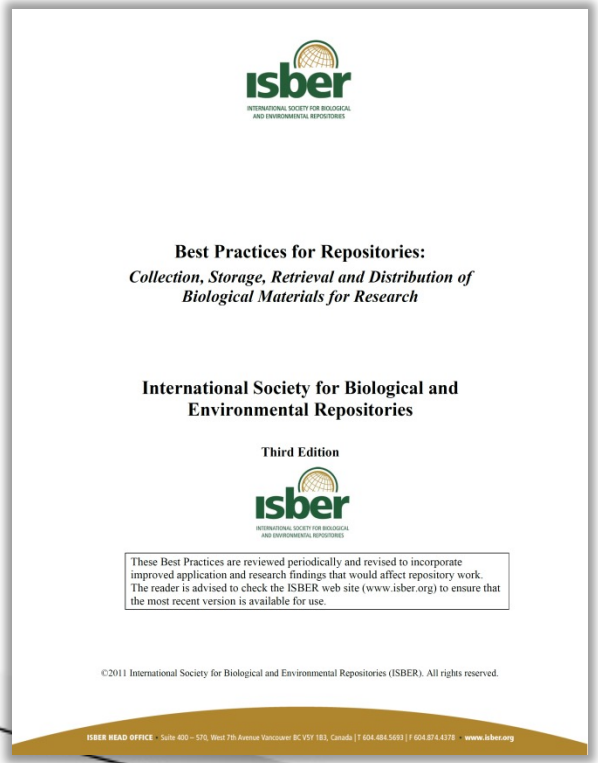
Patient | Medical/ Surgical Procedures | Acquisition | Handling/ Processing | Storage | Distribution | Scientific Analysis | Restocking Unused Sample

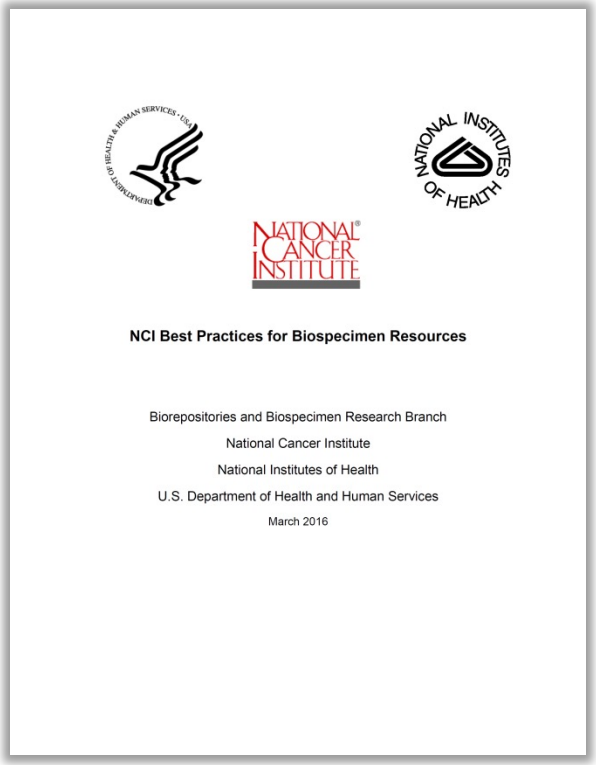
Pre-acquisition **Post-acquisition**

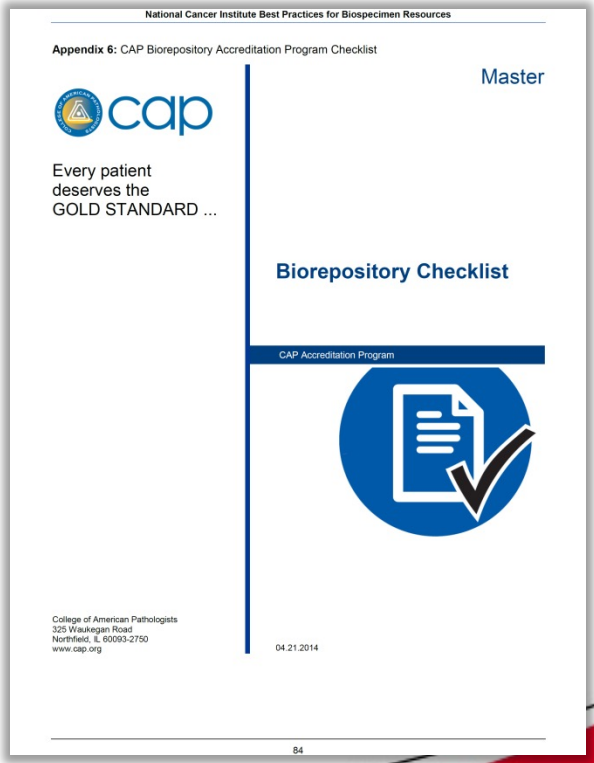
NCI, Office of Biorepositories and Biospecimen Research (OBBR)

Best Practices

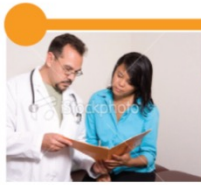
Provide guiding principles for biospecimen resources, promote biospecimen and data quality, and support adherence to ethical and legal requirements







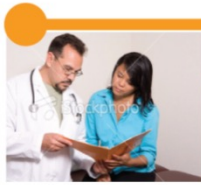
UNIVERSITY OF Cincinnati



Patient

Legal and Ethical Considerations

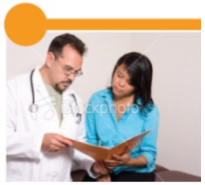
The collection, storage, distribution, and use of biological materials in research raises many legal and ethical issues and is subject to both national and international regulations



Patient

Human Subject Research Regulations

- Declaration of Helsinki (1964)
  - Ethical principles for medical research involving human subjects developed by the World Medical Association (WMA)
- Basic principles that guide human subject research (The Belmont Report)
  - Respect (informed consent and protection of vulnerable populations)
  - Beneficence (risk/benefit assessment)
  - Justice (participant selection criteria)
- US federal regulations pertaining to human subject research
  - 45 CFR 46 (Common Rule)
  - 21 CFR 50 and 56 (FDA regulations)
- Health Insurance Portability and Accountability Act (HIPAA)
- Human subject research is regulated by Institutional Review Boards (IRB)



Patient

Key Ethical and Legal Considerations

1. The research should be well designed and conducted by persons with appropriate expertise

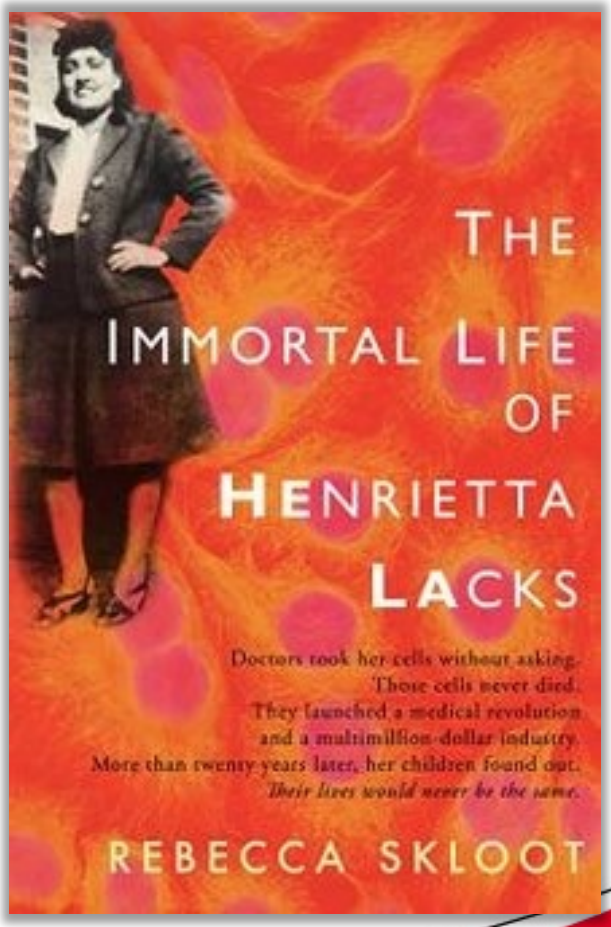
2. Freely-given informed consent is required prior to the procurement and research use of human biospecimens

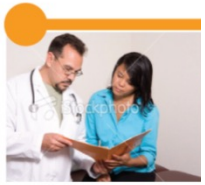
3. Participants should have the right to withdraw consent and have their unused specimens and data destroyed

4. Every effort should be taken to minimize the risks to study participants
   - The physical and psychological risks associated with biospecimen collection should be minimized
   - Protecting the privacy and confidentiality of research participants

The story of Henrietta Lacks

- A story of respect for autonomy
- Her cancer cells were used to establish the HeLa cell line without her knowledge or consent
  - The first immortalized cell line
  - The most important cell line in medical research history
    - Development of the polio vaccine
    - AIDS research
    - Cancer research
    - Genome was sequenced and published in 2013
  - Still widely used today
- In the media:
  - The Immortal Life of Henrietta Lacks, 2010 (book)
  - Law and Order, “Immortal”, 2010
  - The Immortal Life of Henrietta Lacks, 2017 (movie)
- The lay public are now more aware of the use of biospecimens in research and their rights as research participants than ever before

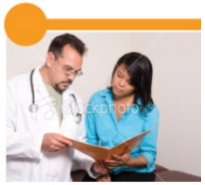




Patient

Informed Consent

- The goal of informed consent is to enable individuals to decide for themselves whether to participate in research
  - Individuals should understand the purpose, procedures, risks, benefits, and alternatives, and make a voluntary decision to participate in the research study
- Published data suggests that people support research using their biospecimens
  - People typically want to be asked whether their specimens can be used for research
  - Beyond initial consent, many do not want significant control over how their specimens are used
  - Many people are accepting of broad consent for future unspecified research use
- Use of biospecimens for research purposes should remain within the scope of the consent obtained
- Types of informed consent:
  - Specific consent: details of the proposed use of the biospecimen(s) are specifically outlined
  - Broad consent: permits broad research use of biospecimen(s)
  - Multi-layer consents: allow participants to decide how their biospecimen(s) will be used



Patient

Privacy Protections

- Procedures to protect the privacy and confidentiality of the research participants include:
  - Completely anonymizing biospecimens and data such that they cannot be linked either directly or indirectly to the donor
  - Assigning a unique code and/or removing all individually identifying information from the specimens and data (de-identification, coding, etc.)
  - Storing biospecimen and data securely
  - Restricting access to biospecimen and data

Medical/ Surgical Procedures

Acquisition

Collection Procedures

1. Biospecimens collected as part of standard of care
   - Remnant ("leftover") biospecimen
     - Collected during a routine medical procedure (e.g., surgical resection)
     - "Minimal risk"
     - Blood, urine, isolates, etc. – typically released after mandatory hold (1 week)
     - Tissue - must be examined by qualified pathology personnel to ensure that remnant tissue can be provided without compromising diagnostic integrity of the specimen

2. Biospecimen collection specifically for research purposes
   - Examples include a blood draw or a tissue biopsy procedure
     - May qualify as "greater than minimal risk"

Medical/ Surgical Procedures

Acquisition

Biospecimen Collection

Key considerations:

1. Analytical objectives of the study
   - Ensures that biospecimen collection and subsequent processing procedures are fit for purpose
2. Biospecimen availability (i.e., feasibility)
3. Collection kits / tubes / containers
   - Use of stabilizing reagents
4. Professional support / oversight for biospecimen collection procedures
   - Pathologist, phlebotomist, etc.


Medical/ Surgical Procedures

Acquisition

Biospecimen Collection

Key considerations continued:

5. Transportation between collection and processing / storage sites

6. Proper handling is essential to ensuring the integrity and quality of the biospecimen
   - Standard operating procedures (SOPs)
   - Proper labeling
   - Chain of custody

Medical/ Surgical Procedures

Acquisition

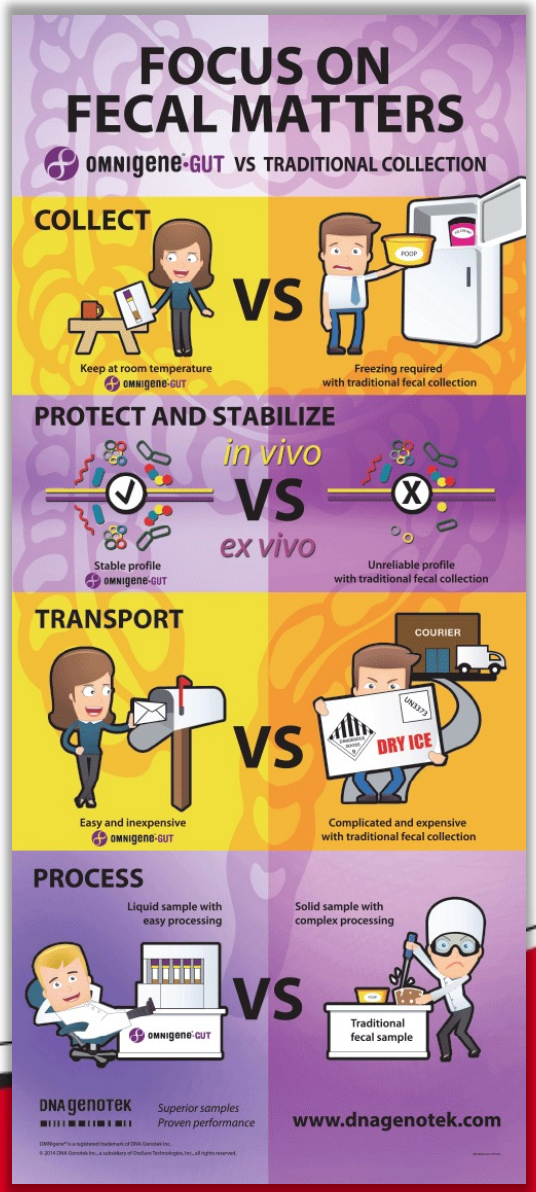
Chain of Custody

- Chain of custody (COC) is defined as the documentation of the chronological movement of biospecimen from the time of collection through analysis
  - Ensures the identity and the integrity of biospecimens
  - Allows for identification of potential sources of bias
  - Root cause analysis

Medical/ Surgical Procedures

Acquisition

Collection kits / containers



Medical/ Surgical Procedures

Acquisition

→ Daily Agenda

Fluid

Notify Clinic:

- Specimen collection kits
- Call/Page research personnel

→ **Transport:**

- Lab for processing

Tissue

Notify OR:

- Keep specimen fresh
- Call/Page research personnel

→ **Transport:**

- Pathology for processing

- Communication – communicate early and frequently with the clinical team in order to coordinate safe and timely collections
- Preparedness – ensure you have all the required materials needed for specimen collection (e.g., collection kits, forms, etc.)
- Documentation – ensure accurate and complete documentation

Collection Kits

UNIVERSITY OF Cincinnati


Medical/ Surgical Procedures

Acquisition

Challenges of Biopecimen Collection

- Timing of collection
  - Avoiding a separate stick for blood collection
- Delays in specimen processing may result in degradation of molecules such as RNA and phosphoproteins
  - Keeping specimen cold (4°C) and/or use of transport media and stabilizers
  - Rapid transport of biospecimens from collection to processing sites
- Limitations to the collection of tissue
  - Neoadjuvant therapy – tumor is very small or no viable tumor
  - More effective screening, detection, and diagnosis is resulting in smaller tissue specimen that are often entirely submitted for diagnostic purposes

Medical/ Surgical Procedures

Acquisition

Identifying Sources of Bias

- Pre-analytic variables may introduce bias
  - The physiology of the human research participants prior to biospecimen collection
  - Biospecimen collection and processing practices
- The larger the variation, the more difficult it is to identify treatment effects in clinical research
  - Use of central labs for quantitating laboratory parameters eliminates between-lab variation
  - Use of central evaluators to eliminate between-evaluator variation
- Careful record keeping can help identify and/or minimize bias

Examples of potential sources of bias in tissue sets

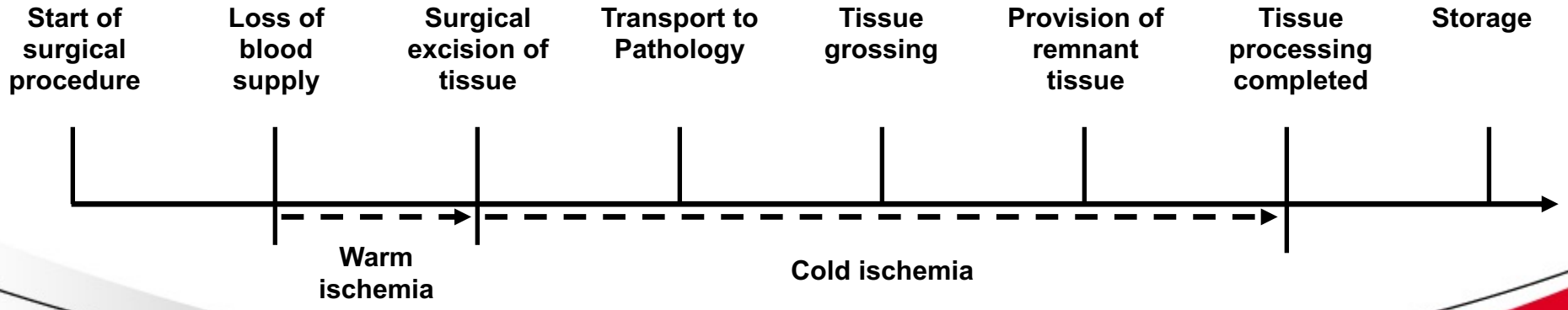
1	Systematic differences among the sites of sample collection
2	Population (e.g., racial mixtures, differences in sex and age, ethnicity)
3	Diurnal variations (i.e., time of collection)
4	Homeostasis (e.g., fed or fasting state)
5	Stress of donors
6	Comorbidity (diabetics versus hypertensive patients)
7	Collection container (red top vs. tiger separator or type of plasma)
8	Time from processing to freezing
9	Temperature and length of storage
10	Freeze thaw cycles

Grizzle et al., Cancer Biomark, 2010

Handling/
Processing

Tissue Ischemia

- Prolonged tissue ischemia will negatively impact tissue quality
- The clock starts during the procedure:
  - Warm ischemia: the amount of time that a tissue or organ remains at body temperature after its blood supply has been stopped or reduced
  - Cold ischemia: the amount of time a tissue or organ is chilled (below body temperature) after the blood supply has been stopped or reduced



Handling/
Processing

Biospecimen Processing

- Biospecimen should be processed and/or preserved as quickly as possible following established SOPs
- Ideally processing methods are determined based on the intended use of a particular biospecimen
  - Sometimes unknown at the time of collection and processing of biospecimen
- Processing procedures should be optimized to minimize molecular changes

Handling/
Processing

Common Processing Methods

- Centrifugation
- Stabilizers (RNAlater)
- Snap freezing (LN_2 or isopentane)
- Controlled rate freezing (required for viable specimens)
- Tissue processing and embedding
  - Embedded in freezing media (OCT)
  - Formalin-fixed paraffin-embedded (FFPE)
- Nucleic acid extraction
- Protein extraction

Handling/ Processing

Biospecimen are processed per SOPs

Prospective

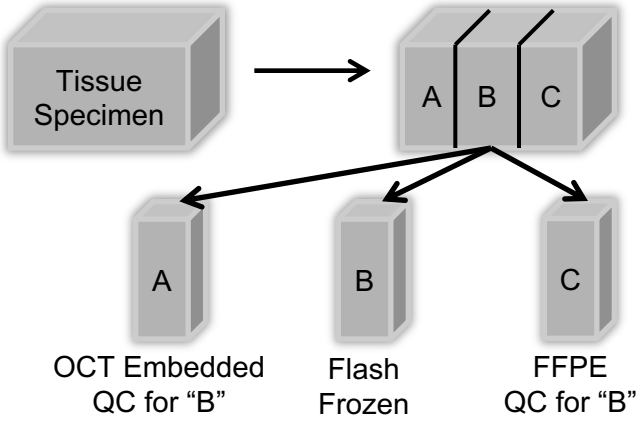
Banking

Per investigators study specific requirements

Per UCB SOPs

Processing Sheets

Biospecimen are processed in a standardize manner to minimize variability amongst samples and help assure sample quality



UC Cancer Institute
UNIVERSITY OF CINCINNATI | UC HEALTH
Tumor Bank

SOP # - APPENDIX A
Tissue Processing
Tissue Processing Sheet

REGISTRY: HDN / HDS / MAL / THO / URS Other: _____

DATE	SUBJECT ID	PATIENT INITIALS	COORDINATOR INITIALS	SAMPLE LOGGED

TIME POINTS:	Time	Notes
1. Excision:	AM PM	
2. Tissue arrived at Path:	AM PM	Specimen Container ID:
3. Tissue received in Path:	AM PM	
4. Processing started:	AM PM	
5. Processing completed:	AM PM	
6. Tissue arrives at UCCITB:	AM PM	
7. Placed in Formalin:	AM PM	
Total Processing Time (Time 5 – Time 4):	____hr ____min	
Total Ischemic Time (Time 5 – Time 1):	____hr ____min	☐ > 1 hour

	Time	Date	Notes
8. Placed in processor:	PM		
9. Placed in paraffin:	AM PM		

TISSUE RECEIVED:	No. of Sample(s)	Weight (g)	Tissue Origin
Normal			
Tumor			

COLLECTION SITE: Grossing Room | Frozen Section Room | OR

ALIQUOT: (by priority)	Fresh			OCT			Flash Frozen			FFPE		
	#	TR #	Weight (g)	#	Box	Position	#	Box	Position	#	Box	Position
Normal												
Tumor												

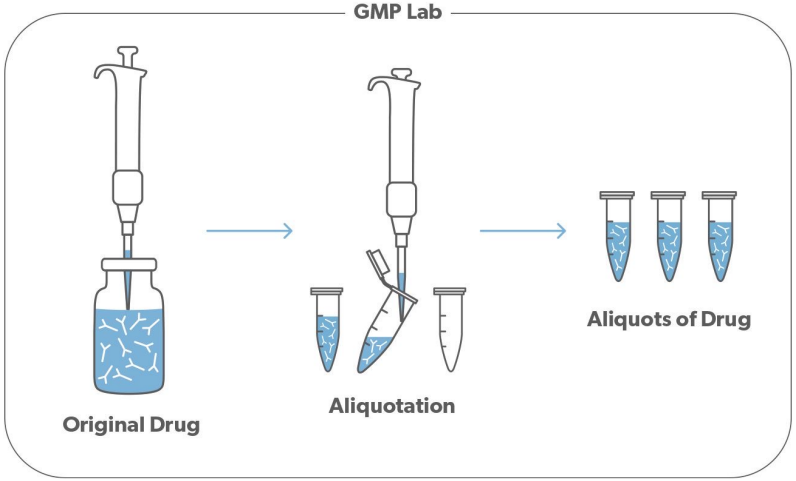
NOTES:

Version 6, 2015 UCCITB@uc.edu, Phone: (513) 558-7111, Location: MSB 1001 Page 1 of 1

Handling/
Processing

ALIQUOT! ALIQUOT! ALIQUOT!

- Prepare appropriately sized aliquots in order to avoid unnecessary freeze-thaw cycles
- Storage containers should be stable under planned storage conditions (e.g., -80°C)



Storage

Storage of Biospecimen

- The use of frost-free (self-defrost) freezers should be avoided
- The location of each sample should be tracked to facilitate sample retrieval and minimize fluctuations in freezer temperature
- Freezers should have regular preventative maintenance and be connected to a monitoring system that alerts research personnel to power and temperature failures
- Specimen should be stored in a secure location and access should be limited to authorized personnel

Storage Conditions

- Selection of storage methods balances the costs of storage and the limitations in the methods of storage
  - All methods of storage have limitations
- In selecting storage conditions, consideration should be given to:
  - Type of biospecimen
  - Anticipated length of storage
  - Biomolecules of interest
  - Preservation of viable cells
    - Cryoprotectants and controlled-rate freezing
- Common storage conditions:
  - Room temperature – storage of FFPE tissue
  - -80°C – storage of biofluids and tissue
  - Vapor phase LN_2 (-150°C) – storage of viable tissue/cells

Storage

Biospecimen are labeled and stored per SOPs → Freezers are monitored 24/7

Data is stored in a secure database

Storage Equipment

- -20°C Freezer
- -80°C Freezers
- LN_2 Freezers

Biospecimen Storage

- Each sample is assigned a unique ID
- Appropriately sized aliquots prevent freeze-thaw cycles
  - Aliquots are split between different freezers to prevent total loss in the event of freezer failure
- Freezer Monitoring System
  - Alerts biobank staff to power and temperature failures

Data Storage

- CTMS / LIMS / REDCap
  - Track consent
  - Specimen collection and processing information
  - Specimen storage locations
    - Freezer > Shelf > Rack > Box > Position
  - Associated clinical data

Storage

Data Collection and Storage

- Well-documented collection/storage data and proper clinical annotation are essential to ensuring the value of biospecimen
- The two main types of data that may be associated with biospecimens include:
  - Specimen-specific data: processing conditions, quantity, quality, etc.
  - Donor-specific data: clinical or biological data gleaned from medical records such as diagnosis, medical history, family history, etc.
- The minimum clinical annotation of biospecimens should include age, race and sex of the donor and relevant diagnosis at the time of biospecimen collection
  - Beyond this, the extent of annotation required for a specimen will vary with the primary intended use and the goals of the clinical research study

Quality Management System

Quality Assurance

- Policies and procedures are documented in SOPs following best practice recommendations
  - Personnel are trained in all SOPs
- An extensive audit trail (chain of custody) is maintained for all specimen from receipt to analysis / distribution
- Equipment maintenance and calibration procedures are performed and documented
- Access to the biospecimen database is limited and controlled

Quality Control

- Histopathology
  - Histologic tissue slides are reviewed by a Pathologist to confirm agreement with associated clinicopathologic data
  - Used to confirm diagnosis, % tumor, % necrosis, etc. of the tissue collected for research
- Nucleic acid quantity / quality
  - Used to confirm that collection, processing, and storage procedures do no negatively impact sample quality
- Cell viability
  - Used to demonstrate effectiveness of collection, processing, and storage procedures for viable specimens (e.g., PBMCs)

Distribution

Biospecimen Shipping Regulations

- Packaging and shipping should conform to applicable regulations:
  - International Air Transport Association (IATA)
    - Air shipping
  - U.S. Department of Transportation (DOT)
    - Ground shipping
  - International Civil Aviation Organization (ICAO)
    - International shipping
- All personnel involved in shipping biological materials should be appropriately trained

Distribution

Shipping Considerations

- How to classify the shipment
  - Are you shipping “dangerous goods”?
    - Infectious?
    - Flammable?
    - Dry ice?
- Temperature
  - Ambient
  - Refrigerated (2 to 8°C)
  - Frozen (-20°C, -70°C, -150°C)

- Shipment of cold / frozen biospecimen should be shipped with sufficient and appropriate refrigerant to maintain temperature throughout shipping and allow for at least a 24-hour delay
  - Temperature recording devices may be used to confirm acceptable temperatures are maintained during shipment
- Communication
  - Notification of shipment and expected delivery date with tracking information
  - Shipping manifest
  - Confirmation of receipt

Summary

- Biospecimen are a critical component of all clinical research
- The use of biospecimens for research purposes should remain within the scope of the consent
- Biospecimen should be handled in a standardized manner that ensures their identity and integrity
  - Following established SOPs for collection, processing, storage, and shipment
  - Document chain of custody
  - Quality management plan
- ALIQUOT! ALIQUOT! ALIQUOT!
  - Avoid unnecessary freeze-thaw cycles