UC Davis Guide for the Research Use of Human Biological Specimens: Collecting, Banking and Sharing Specimens

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I. Introduction

Who will use this Guide? This guidance is designed to support investigators and their staff who wish to use human biological specimens in their research, and/or those researchers who intend to establish or manage specimen banks and repositories for human specimens to be used by others for research. This Guide does not address topics related to the University's Body Donation Program (www.ucdmc.ucdavis.edu/bodydonation), tissue banking for transplantation purposes (www.ucdmc.ucdavis.edu/transplant) through the UC Davis Transplant Center, or UC Davis Stem Cell research (www.ucdmc.ucdavis.edu/stemcellresearch). Please use their respective websites for further information and procedures concerning these programs.

Specific topics covered in this Guide include:

- Accessing and using existing specimens residing in tissue banks and repositories
- Collecting biospecimens from human subjects for your own research use, or collecting to establish a specimen bank
- Sharing biospecimens with other researchers, institutions, or companies

What are the goals of this Guide? This Guide aims to provide practical information in a user-friendly format allowing researchers and staff to navigate University policies and approval procedures so that research projects can move forward. The Guide:

- Links to information about the IRB submission and review process at: http://research.ucdavis.edu/policiescompliance/irb-admin/irbnet/
- Provides practical information regarding important federal, state and local regulations, and when appropriate, lends real-world interpretation to important regulations governing the use of human biological specimens
- Provides links to more detailed information within the UC Davis system and elsewhere

II. Brief Overview

***Section Summary**: This section contains basic introductory information about human biospecimens, institutional oversight and the protection of private information.*

Types of Human Biological Specimens: Most human biological specimens come from tissue collected for diagnostic or therapeutic procedures, but other sources can include autopsies, volunteer donors, or materials collected and shared by other researchers.

- The term "biospecimen" is used widely and encompasses a full range of human specimen types including:
  - Sub-cellular components such as DNA or RNA
  - Cells or tissues from any part of the human body
  - Organs such as liver, bladder, kidney, heart, placenta, etc.
  - Gametes (ova and sperm)
  - Embryos and fetal tissues
  - Breast milk
  - Exhaled air
  - Bodily products such as teeth, hair, nail clippings, sweat, urine, feces
  - Blood and blood fractions: plasma, serum, buffy coat, red blood cells
  - Saliva and buccal cells
- Exceptions: Organisms, such as bacteria and viruses, isolated from human specimens are not human biological specimens.

Formats for Collecting and Storing Biospecimens: Depending on the type of specimen, researchers are usually given aliquots or sections of a specimen in a collection and not the entire specimen. The various formats for collecting and storing biospecimens include:

- Frozen
- Formalin-fixed, paraffin-embedded (FFPE) tissues
- Fresh (rapid distribution)
- Histological slides
- Aspirates, body fluids, swabs

Extracted DNA and RNA

Tissue Banks and Repositories: Various terms are used to designate the storage sites for human biological collections. An extensive but not all inclusive list of Tissue Banks and Repositories by location can be found at http://specimencentral.com/biobank-directory. The most common terms are defined below.

- **Repository** is a term usually applied to large formal collections of specimens and/or data. Examples include:

  The DoD DNA Specimen Repository for Remains Identification (*Example of Stored Collections*)
  http://www.afmes.mil/index.cfm?pageid=doddr.afrssir.overview

  The Cooperative Human Tissue Network (Example of Prospective Collections)
  www.chtn.nci.nih.gov

- **Tissue bank** generally refers to smaller collections of specimens, which may be specific to an institution, disease, or even to specimens in an individual researcher's freezer. Some examples at UC Davis include:

  The MIND Institute-Markers of Autism Risk in Babies (MARBLES Study**)**
  MARBLES is a longitudinal study for pregnant women who have a biological child with autism spectrum disorder. The MARBLES study investigates possible pre-natal and post-partum biological and environmental exposures and risk factors that may contribute to the development of autism.

  UC Davis Comprehensive Cancer Center Biorepository (CCB)
  The CCB maintains a centralized tissue bank for specimens collected from a variety of Cancer Center organ site programs (e.g. breast, prostate, lung, colon) and research efforts.

  IMPORTANT NOTE: "Tissue banking" also refers to tissues, cells and organs collected and processed for transplantation. Tissue banks engaged in transplantation services are subject to FDA oversight under Section 361 of the Public Health Service and 21 CFR Part 1270. The American Association of Tissue Banks is an excellent source of information regarding the regulatory standards, certification, and accreditation of tissue banks that provide materials for transplantation.

- **Banks with Extracted DNA and/or RNA** refer to facilities that store extracted nucleic acids. These banks can isolate and store DNA for approved studies in a monitored environment ensuring sample quality and data security.

Information Management: Regardless of specimen bank size, an inventory database is needed to track specimens and any associated data. Information is usually managed by a group of specific data fields, such as Specimen code/ID number, Specimen storage unit

location, Specimen type, condition and amount and Diagnosis, Demographics, Histopathology, Patient treatment/outcome, and Verification of informed consent.

- Typically, data fields are organized to facilitate sample storage and retrieval as well as to support efficient management of specimen-related data. Information management systems can range from a single spreadsheet to numerous, highly sophisticated enterprise-wide integrated informatics systems.
- The amount and type of data can vary widely among repositories and banks depending upon the mission and function of the organization.
- Information management and data security are discussed more fully in the section "Establishing, Operating and Maintaining a Biospecimen Repository".

Protection of Private Health Information: There are restrictions for accessing and using the personal identifying data that may be associated with human biospecimens.

- Researchers who manage human specimen data, and other investigators who have access to it, are legally and ethically obligated to protect data that is considered private information. (http://www.hhs.gov/ocr/privacy/hipaa/understanding/training/udmn.pdf)

- Researchers who obtain specimens from tissue banks and repositories often receive samples with a "limited data set." This is to protect the identity of the subject/patient without compromising the goals of conducting meaningful research. A limited data set must have all the direct identifiers removed, and may include but are not limited to some of the following information:

  Admission, discharge, and service dates;
  Year of birth, and if applicable, death;
  Age (including age 90 or over); and five-digit zip code or any other geographical subdivisions, such as state, county, city, precinct and their equivalent geocodes (except street address)
  Treatment response and outcome data
  Family history information (i.e. cancer risk, gene mutation, etc.)

Institutional Oversight of Research Involving Human Biospecimens: Specimen collection from subjects, use, and banking of human specimens for research may require approval by one or more of various regulatory committees at UC Davis. Some of these regulatory committees are:

Institutional Biosafety Committee (IBC)
Conflict of Interest Committee (COIC)
Cancer Center Scientific Review Committee (CCSRC)
Radiation Use Committee (RUC)
Stem Cell Research Oversight Committee (SCROC)

More information about the approval processes can be found at the UC Davis IRB website: http://research.ucdavis.edu/policiescompliance/irb-admin/

There are four Institutional Review Boards (IRBs) at UC Davis: Biomedical Committee A, Biomedical Committee B, Social and Behavioral Committee C, and Fast Track Committee D. For additional information, including the schedule of meeting dates, please visit http://research.ucdavis.edu/policiescompliance/irb-admin/researchers/meetings/

Categories of Human Specimen Information: Terms and Definitions: For regulatory purposes, human specimens are categorized based on the level of identifiers associated with them. Appendix A shows the designated categories which determine the level of IRB oversight.

III. Getting Started: Requirements for Working with Human Specimens at UC Davis

***Section Summary**: This section contains information about the approvals required before investigators can begin working with human biospecimens.*

What approvals do I need to work with human biospecimens?

- The Institutional Biosafety Committee (IBC)
- The UC Davis Human Research Committee – Institutional Review Board (IRB)
- Cancer Center Scientific Review Committee (CCSRC)
- Radiation Use Committee (RUC)
- Institutional Animal Care and Use Committee (IACUC)
- Conflict of Interest Committee (COIC)

What approvals do I need to work with human biospecimens? Approvals are needed from several departments and oversight committees before receiving and/or working with human biospecimens.

- Approval from the **Institutional Biosafety Committee (IBC)** in the form of a Biological Use Authorization (BUA) number is required to work with human-derived specimens (e.g., tissue, fluids, etc). A BUA is a prerequisite for approval by the Committee on Human Research (IRB) described below. Assistance with submitting and obtaining a BUA approval can be found at the BUA website.

  If you have questions or need additional guidance, please contact EH&S-Biosafety at biosafety@ucdavis.edu for assistance.

  All staff must be trained annually in handling blood-borne pathogens.

  What is a BUA?

  A BUA is a document describing a Principal Investigator's (PI's) research at UC Davis. When approved by the IBC, it provides authorization for conduct of that research.

  Who must apply for a BUA?

  If the research involves recombinant DNA materials or technology, infectious agents, toxins, transgenic animals, human gene transfer, humans, sheep or Old World primates or their source materials, a BUA must be approved by the IBC before beginning laboratory research. Please see the UC Davis BIO Guide for more information. The BIO Guide and BUA forms are available on the IBC website.

  Can I Modify an Existing BUA?

  Yes but approval of changes to existing BUAs must be requested on the IBC website. Before you modify any research, you must have the modification approved.

- The UC Davis Human Subjects Committee is the federally mandated Institutional Review Board (IRB) at UC Davis and is part of the Human Research Protection Program in the Office of Research. The UC Davis IRB Committees fall under a Federalwide Assurance (FWA00004557) with the Department of Health and Human Services/Office of Human Research Protections (DHHS/OHRP).

  UC Davis has adopted a Human Research Protection Program Plan that outlines its responsibility to the UC Davis research community.

  All IRB approved protocols must be conducted in accordance with requirements in the UC Davis Investigator Manual. It is a document designed to guide researchers through policies and procedures related to the conduct of human research that are specific to UC Davis.

  - IRB approval is required for all projects involving any material covered under the human subject definition [45 CFR Part 46.102(f)].

    "*Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains

    (1) Data through intervention or interaction with the individual, or

    (2) Identifiable private information." [45 CFR Part 46.102(f)]

  - The IRB, not the investigator, determines whether specimen research involves "human subjects."

  - The level of IRB review and approval depends on the level of risk the study poses to subjects.
    - Studies that use existing specimens that are stripped of identifiers (unlinked or de-identified) pose less than a minimal risk and, generally, require less IRB oversight.

    - Study procedures that pose greater than minimal risk to subjects – collection of private information and/or collection of specimens by more invasive means than a blood draw - require greater IRB oversight.

    - IRB requirements are detailed in the UC Davis IRB guidelines.

- Cancer Center Scientific Review Committee (CCSRC) - The CCSRC is charged with the review and monitoring of protocols involving cancer patients and/or their data. The Committee provides a centralized mechanism for prospective evaluation of scientific merit, resource allocation, and clinical cancer research monitoring. The application requires that Principal Investigators contact the Cancer Center Scientific Review Committee for the review and approval of their research study, prior to submission of the protocol for IRB review and approval.

The IRB will not approve a protocol involving cancer patients and/or their data without the approval of the CCSRC. You can obtain further information on CCSRC policies by contacting 916-734-2596.

- **Radiation Use Committee**: If samples are radioactive you will need a Radiation Use Authorization (RUA) number from the Radiation Use Committee (requires campus username and Kerberos password). The RUC is responsible for the surveillance of all uses of radioactive materials and ionizing radiation (including diagnostic x-rays/fluoroscopy/ DEXA) in research involving human participants. Principal Investigators are required to identify, on "FORM: APPLICATION FOR INITIAL REVIEW (HRP-211)," all proposed radiation use. The application requires that Principal Investigators contact the Radiation Use Committee for the review and approval of their study, prior to IRB review and approval. The RUC may require amendments to the design of the study, restrictions, or specific wording in the informed consent document, to ensure conformance with the University's Radioactive Material License and state and federal regulations. The IRB will not approve a research study involving radiation without the prior approval/exemption of the Radiation Use Committee. (RUC Forms require your campus username and Kerberos password to access)

- Approval from the **Institutional Animal Care and Use Committee (IACUC)** is needed if the human tissues/specimens will be used in animal research. IACUC policies, procedures and guidelines can be found at the IACUC website.

- **Conflict of Interest Committee (COIC)** - Any actual or perceived conflict of interest as defined by institutional policy, consistent with applicable federal and state regulations is required to be reported to and reviewed by the Conflict of Interest Committee (COIC). The COIC will inform the IRB when investigators conducting human research have significant financial interests that constitute a financial conflict of interest. The IRB has the final authority and may grant final approval of research studies with a disclosed conflict of interest, provided that the IRB has taken appropriate steps to eliminate or manage the conflict, consistent with the Conflict of Interest Committee determination (see SOP: FINANCIAL CONFLICTS OF INTEREST [HRP-055]). Should the IRB or the Conflict of Interest Committee require changes in the research study to mitigate a conflict, the Principal Investigator will be required to submit the revised documents for IRB review and approval. You can find further information on the UC Davis Research Compliance and Integrity Office website.

- **Stem Cell Research Oversight Committee (SCROC)** – This Guide does not address SCROC but you can refer to their website for further information. SCROC: 1) provides oversight of all issues related to derivation and use of human adult and embryonic stem cell lines; 2) reviews and approves the scientific merit of research protocols; 3) reviews compliance of all human adult and embryonic stem cell research with all relevant regulations and guidelines; and 4) facilitates education of investigators involved in human adult and embryonic stem cell research. Principal Investigators are required to

identify, on "FORM: APPLICATION FOR INTIAL REVIEW (HRP-211)," all human adult and embryonic stem cell studies. The application requires that Principal Investigators contact the Stem Cell Research Oversight Committee for the review and approval of their research study.

- The Office of Research (OR) assists investigators with all contractual arrangements needed to provide clinical or laboratory services for a clinical study or to send and receive materials including human biological specimens. The list of all OR Forms can be located via the OR website.
    - Contact InnovationAccess in the OR and complete a Material Transfer Agreement (MTA) before sending or receiving human specimens.
        - An MTA is required for all exchanges of materials, incoming and outgoing, unless the specimens are purchased from a commercial entity.
        - More detailed information is provided in Sharing Biospecimens and Data with Other Researchers, Institutions or Private Companies.

IV. Accessing and Using Existing Specimens from Tissue Banks and Repositories

> ***Section Summary****: This section contains information for researchers who obtain existing specimens from biorepositories and who are not directly involved with subjects from whom the specimens originate.*

How do I get specimens from tissue banks (public, private and commercial repositories)? Before applying to any repository or specimen bank, you must first obtain approvals to work with human specimens at UC Davis. (see Getting Started)

Various types of tissue banks and repositories are described briefly below:

- **Federally funded or cooperative group banks** usually have well-defined prioritization and distribution methods. Be prepared to provide a Letter of Intent (LOI) or a study protocol describing your research plan. Applications are generally reviewed by an oversight committee and judged on scientific merit, statistical validity, the investigator's ability to conduct the proposed research, and the appropriateness of the sample size requested to accomplish the research goals.
- **Departmental/Division/ORU banks and investigator-maintained collections** may not have well-established application or distribution policies and may not be obligated to share specimen resources at all. Contact the tissue bank's administrator to find out how to obtain their specimens.

  If you are interested in cancer-related tissues, you may contact the UC Davis Comprehensive Cancer Center Biorepository (CCB). They have specific instructions on how to request their samples and services.
- **Commercial Tissue Banks:** Specimens may be available for purchase from commercial sources. The resource table below provides links to some companies providing a broad array of human specimens including tissues, blood and DNA.
- **Private Collections:** Individual researchers who are collecting specimens in your area of research may be willing to provide them. Contact the researcher directly to find out if collaboration is an option and the conditions for transferring or sharing specimens.

What are the informed consent and HIPAA authorization issues for accessing existing specimens? If you are obtaining human specimens from another source:

- Obtain source documentation stating that the specimens were obtained with either a valid informed consent or were deemed "hon-human subjects" under an IRB-approved protocol, and
- The study should adhere to the scope of research allowed by the original consent or IRB approval collection protocol.

IMPORTANT NOTE: Specimen repositories and sources from outside the United States should be able to supply comparable documentation regarding consent of research subjects and conditions for specimen use.

How do I locate specimen resources? The lists below represent a few of the growing number of specimen banks and repositories within the UC Davis system as well as publicly funded specimen banks and commercial sources of human tissues.

- Some of the banks that house specimens collected at UC Davis, as part of federally funded, multi-center trials (CALGB, COG, RTOG, AIDS and Cancer Center Bank), reside at national off-site locations.
- Each bank has policies and procedures governing the distribution of specimens to members, other UC Davis researchers, and outside entities.

UC DAVIS SPECIMEN BANKS (*partial listing*)

Comprehensive Cancer Center Biorepository (CCB) Shared Resource

(Revise by adding UC Davis banks who want to be included)
MARBLE
Etc.

PUBLIC and COMMERCIAL SPECIMENS BANKS (US and Global; *partial listing*)

Asterand
Cooperative Human Tissue Network
Coriell Cell Repository
AIDS and Cancer Specimen Resource
PrecisionMed Human Biological Material
RTOG Tissue Bank/Translational Research Program
National Human Radiobiology Tissue Repository
Tuberculosis Specimen Bank (WHO)

V. Collecting and/or Receiving Human Specimens for Banking

***Section Summary**: This section contains information for researchers engaged in prospectively collecting specimens from subjects and/or receiving specimens from clinicians for banking.*

What approvals do I need to prospectively collect and/or bank human specimens?
If you are involved in collecting specimens from research subjects or intend to receive specimens from clinicians for banking purposes, you will need to obtain protocol approval from the IRB as outlined in their Investigator Manual.

For more information on required approvals, refer to the section Getting Started: Requirements for Working with Human Specimens at UC Davis.

What kind of information can be collected with specimens? The type of information collected and retained with specimens will depend on the mission and objective of the repository. The table below shows the type of information that is considered personally identifiable (identified) or de-identified – both may be associated with banked specimens.

TYPE OR ASSOCIATED INFORMATION	EXAMPLES
IDENTIFIED	Patient Identifiers (Name, Medical Record Number)
	Family History (Pedigree)*
	Treatment and Outcome Data*
DE-IDENTIFIED	Histopathology
	Specimen Descriptors (Type, Condition, Amount)

*Patient identifiers may be needed to access long-term follow up information.

IMPORTANT NOTE: Information can be collected only as specified in the IRB-approved protocol.

What are the consent requirements for collecting and banking human specimens for research? Consent to collect, to use, and/or bank specimens for research can be obtained using a variety of different formats – all requiring IRB approval.

- Several factors determine the type of consent materials required to obtain specimens for research:

- Will the specimens be collected from surplus surgical material that would be otherwise discarded (Clinical Remnant Specimens)?
- Will the specimens be banked for future research use?
- Will the specimens be collected for research under a companion study that is part of a treatment or intervention study?
- Will the specimens be collected as part of a specimen banking protocol?
- Refer to the UC DAVIS BCR QUICK GUIDELINES for a detailed description of the various types of study protocols used to collect specimens and the consent requirements for each.

IMPORTANT NOTES:

The topics described above should be addressed, as applicable, in consent forms for research studies proposing to collect and bank biospecimens for research purposes. ***The study and the consent form must be approved by the IRB***.

What are the consent requirements for collecting research specimens from minors?
You will need to obtain permission (consent) from the minor's parents or guardian. The IRB decides whether permission is required from only one parent or both parents. You will also need to obtain assent (affirmative agreement) from the child if the child is capable. The IRB will decide how assent will be obtained and documented. In some instances a separate assent form can be used. For detailed information on obtaining informed consent/assent for minors, refer to the IRB guidelines. When the child turns 18 years of age, you will need to obtain consent from the new adult to continue to store and conduct any research using specimens previously collected from that participant.

VI. Establishing, Operating and Maintaining a Biospecimen Repository

> ***Section Summary***: *This section provides information for researchers who are interested in setting up, operating, and maintaining a specimen bank or repository.*

QUESTIONS to consider before creating a biorepository at UC Davis

Do I join or collaborate with an existing bank/repository or establish my own?
How do I establish a repository at UC Davis?

- What University Requirements are Involved?
- What Facilities and Equipment do I Need?
- What Operations are Involved?

What are some examples of model banks at UC Davis?
How do I handle information security?

- What is information security?
- What do the HIPAA security and privacy regulations require?
- What do I need to consider for physical security?
- What do I need to consider for electronic security?
- What if I am the systems manager of the database?
- How do I get rid of PHI storage devices?
- What if I suspect there has been a breach of security?
- Table: Information Security Do's and Don'ts

Do I join or collaborate with an existing specimen bank/repository or establish my own? The following resources may help you decide whether to use existing specimen repositories at UC Davis to store your samples or to set up your own bank.

- A discussion with your Department Chair, Program Director or MSO is a good place to start. It is important to understand the department/divisions resources, overall mission and policies regarding specimen banking.
- Becoming familiar with the operations of some already established biorepositories or large studies collecting specimens at UC Davis may be useful.

  MIND INSTITUTE (CHARGE Study, MARBLES, BEARS)
  Cancer Center Biorepository
  Molecular Pharmacology Shared Resource (specifically for Cancer Clinical Trials)
- An extensive report from the RAND Corporation, available for download or purchase, provides excellent information including best practices of model facilities within the United States.

How do I establish a repository at UC Davis? In addition to securing the necessary approvals required to have a specimen bank/repository at UC Davis, a successful operation requires robust management of all functional areas. The following section provides information regarding University requirements as well as points to consider for setting up the facility intended to house the specimen collection and the policy and procedures required to manage the facility's operation.

- **University Requirements:** You will need to obtain specific approvals from the various University oversight committees as described in the section Getting Started: Requirements for Working with Human Specimens at UC Davis.
- **Facilities and Equipment:** Although space and equipment needs may vary widely, the following lists provide some important points to consider and will likely apply to most facilities that house specimen banks:

  Specimen Banking Space [Appendix B]
  Specimen Banking Equipment [Appendix C]
  Specimen Storage and Labeling [Appendix D]
  Emergency and Backup Plans [Appendix E]

> **IMPORTANT NOTE:** An emergency action plan includes creating and maintaining a current contact list of key personnel. The list should be posted and/or readily available for all emergency responders.

- **Operations:** A successful specimen bank should have an effective operational plan for specimen acquisition, handling, tracking, distribution, and **final disposition**. A well-developed operational plan will include **written policies** and **procedures**, as well as a secure system for managing **records**. Some suggestions to consider for each area are shown below:
  - **Policies:** Written policies help establish and fulfill the mission and objective of the specimen bank.
    - Policies that govern specimen bank operations must be consistent with those of the University, including policies on:
      - **Confidentiality and Privacy:** Refer to the Compliance/HIPAA homepage for details.
      - **Certificate of Confidentiality**: To protect health data and biospecimens used in research from forced disclosure (subpoenas and court orders), investigators may apply to the Department of Health and Human Services for Certificates of Confidentiality. Certificates may be granted regardless of the funding source; the NIH encourages investigators to apply. For additional guidance see the NIH website describing Certificates of Confidentiality
      - **Safety:** Researchers and staff who handle human biological materials must receive appropriate safety training.
      - **Merging and/or closing specimen banks:** The University recommends that investigators who separate from UC Davis discuss transfer of all or part of their collections to another UC Davis biorepository. Please contact the BCR for further guidance at

biorepositories.initiative@ucdavis.edu.

- Other policies adopted by a particular specimen bank depend on the mission and objective of the bank. For example,
  - **Access and Utilization Review**: An informal policy for access and utilization review may be adequate for a small specimen bank serving a limited number of investigators within one department. However, a large repository with many applicants from scientifically diverse disciplines may require a more stringent and formal policy for access and utilization review. Suggested utilization review procedures are discussed below in **Procedures.**
  - **Staff Training:** With the exception of safety training, the specific type of staff training will be determined by the type of services provided by the specimen bank and may include specimen processing techniques, database management or quality assurance methods. The IRB will require staff to complete training from the Collaborative Institutional Training Initiative (CITI) or the NIH. More information about the training required for IRB submissions in the UC Davis Investigator Manual.

o **Procedures:** Written Standard Operating Procedures (SOPs) facilitate staff training and ensure specimen banking activities will be carried out consistently.

- **Specimen Handling:** Clearly defined procedures are needed to
  - Coordinate with any clinical team who may be assisting with collection of the specimens according to IRB-approved protocols.
  - Obtain informed consent for specimen use and/or banking.
- **Specimen Labeling and Storage:** Procedures should describe a consistent method for labeling:
  - Specimens must be labeled with a code or number
  - Initials are not permitted and should not be part of the code.
  - Any patient identifier must be separated from the specimen and kept in a separate secure file that is not linked to the specimen inventory database.
  - See the Specimen Storage and Labeling List **[**Appendix D**]** for guidance on the types of labels, marking pens and specimen containers to use.
- **Inventory and Database Management**: Specimen banks, regardless of size, should have established procedures for data collection, entry, retrieval, and verification.
- **Quality Assurance:** Written procedures describe the methods and criteria to use to assess the quality and suitability of specimens and associated data.
- **Utilization Review:** The process for utilization review – whether conducted by one person or a committee of diverse individuals – should ensure valuable specimens are used wisely. Some topics commonly considered by specimen utilization committees are described in the section Sharing Biospecimens and Data with Other Researchers, Institutions or Private Companies.

o **Records:** A secure system must be in place for keeping both paper and

electronic records.

- **Paper Documents**: Approvals from oversight committees usually are in the form of an electronic notification (letter or PDF) and must be filed in a secure place. Additional paper documents may include a variety of consents forms – surgical consents, clinical trial consents, or consents specifically for specimen banking. To maintain confidentiality and privacy paper files should be stored in locked cabinets.
- **Electronic Records**: Databases should be password-protected and access restricted to essential research personnel.

What are some examples of model banks at UC Davis? Several banks at UC Davis demonstrate model practices in specimen acquisition and processing, utilization review and distribution.

- **UC Davis MIND Institute:** The MIND Institute has multiple studies requiring biorepository services (CHARGE Study, MARBLES, BEARS). To learn more about clinical research at The MIND Institute, please contact 916-703-0299.

- **UC Davis Comprehensive Cancer Center Biorepository (CCB) Shared Resource**: The Cancer Center Biorepository is a diverse tissue bank with a well-established infrastructure that supports a broad range of services for cancer researchers. Best practices are demonstrated in their College of American Pathologist (CAP) Accreditation. For further CCB information, please contact 916-734-3026.

How do I handle information security? Several important topics are discussed below. Investigators must be aware that

Information security is the responsibility of all researchers who create, use, or distribute health-related data.

- **What is information security?** UC Davis policies on information security includes, but is not limited to the following:
  - The physical protection of hardware and data.
  - The electronic protection of records stored on permanent workstations and servers as well as on portable devices including laptops, PDA's, text pagers, and portable hard drives.
  - The protection of data transmitted via electronic means such as email, wireless, ftp, internet servers.

IMPORTANT NOTE: Sending secure Email messages at UC Davis is described *elsewhere*.

In addition to federal regulations governing privacy and confidentiality, such as the HIPAA privacy and security protection requirements there are also University computing standards, procedures and guidelines for information security both at the UC system wide level and for each campus. These are being updated to incorporate federal and state requirements.

Important links for UC Davis Medical Center IT procedures and policies are:

- UC Davis Campus IT Security Information

- UC Davis Health System IT Security Information

IMPORTANT NOTE: Know where your repository's server is located and which IT group supports it. If your repository is behind the Medical Center's firewall, follow the Medical Center's IT procedures and policies. Outside the Medical Center network, you will be required to follow the campus IT security policies and procedures, as well as your department's procedures.

- **What do the HIPAA security and privacy regulations require?** Databases that include protected health information must comply with HIPAA 's stringent requirements for security.
  - Security regulations require documentation showing that reasonable procedures and policies are in place for both the physical and electronic security of systems that contain electronic PHI, including administrative and technical standards.
  - Current UC Davis policies and guidelines for procedures:
    - UC Davis Compliance/HIPAA website
    - UC Davis Privacy policy and information (Legal Privacy Notices)

IMPORTANT NOTE: UC Davis information security policies and procedures must be addressed regardless of whether PHI or coded information is stored electronically in the database.

  - By having the three following plans, your registry systems can be adapted to address any additional security requirements:
    1. **Tracking System:** The specimen bank must be able to account for how its information, specimens, and data are accessed, used, transmitted, and shared, e.g. the actual flow into, within, and out of the system.
    2. **Recovery Plan:** The specimen bank must be able to recover its inventory database if it is lost due to physical destruction (fire, earthquake, or flood) or due to malicious electronic hacking.
       a. It can be in any format, such as a hard disk, backup hard drive, and rented commercial storage.
       b. Recovery/backup items must be kept physically separate from the database.
       c. It is critical that the recovery materials are tested for recoverability before an emergency.
    3. **Security Plan:** Both physical security and electronic security plans must address controlling physical and electronic access to your registry database. These should be designed to protect the database and collection from inadvertent

disclosure, loss, or theft.

- **What do I need to consider for physical security?** Physical security includes controlling access to the facility, the workstation, and any type of electronic device that may contain electronic PHI. However, for security reasons you should also consider controlling access to the specimens and any data on specimen labels as well as controlling disposal of portable media and devices or PHI.
    - **Specimens**:
        - Are identifiers physically located on sample container when it arrives?
        - Are identifiers marked on specimen for storage?
        - If receiving a data storage device or media, has it been screened with antivirus software prior to encryption or formatting?
    - **Physical site**:
        - How is access to the physical site restricted or controlled?
        - How is access to the database workstation controlled?
        - Is access to specimen storage containers controlled?
        - Are systems protected from inadvertent viewing of workstation screens?
        - Are hard copies of data (disk, paper, portable electronic devices) secured in an area completely separate from the main system?
        - What is the plan for destruction of any materials no longer in use, especially the disposal of old hard drives which must be wiped before disposal? This is also true for reuse of devices and media.
- **What do I need to consider for electronic security?** Never assume that a server, network or workstation is secured, especially if the system has electronic connectivity to other systems such as the internet or email.
    - You must know the level of protections for the network that your repository resides on. Always confirm with IT (not just the vendor) that your applications and hardware can be supported by IT and they will provide protection at a level expected by UC Davis.
    - Your department or IT can validate the security of your registry both for electronic access and electronic transmission of electronic PHI (ePHI). The UC Davis IT website contains further information about IT services.
    - California identity theft laws (California's SB1386) mandate that the loss of certain identifiers must be reported to every single individual involved in the loss. Know if these identifiers are in the database and how they are protected.
    - As information security procedures, policies, and guidance becomes available, they will be posted on various UC Davis websites.

      UC Davis HIPAA & Compliance Program

      IS-3 Electronic Information Security – UCOP Policy (43 pgs)

- **What if I am the systems manager of the database?** A database owner has many responsibilities and detailed guidelines are under development. However, if you are also the systems manager of the repository, you will be responsible for mandatory security procedures such as auditing, monitoring and documentation activities.
    - Management of Unique User ID and passwords for each user
    - Data access control (tracking and monitoring access to your system)
    - ePHI integrity and authentication activities
    - ePHI encryption and data transmission (accounting for where information went from your system)
    - Routine validation audits
- **How do I get rid of PHI storage devices?** Please remember that when you are upgrading or changing computer hardware, all your data still resides in the older computer. Once you copy the data file and transfer it to your new system, the old hard drive will need to be destroyed by one of the following methods:
    - Physically destroy the hard drive after it has been wiped clean of memory or reformatted, *or*
    - Run software specifically designed to wipe out hard drive memory, *or*
    - Reformat the older hard disk to remove all patient information (this is not necessarily a fool proof method).

IMPORTANT NOTE: When in doubt, always ask IT how to delete information from or how to destroy a hard drive or other device.

- ***What if I suspect there has been a breach of security?***
    - It is important to take action as soon as the security breach is suspected:

Report lost or stolen items to **UC Davis Campus Police** (530) 754-COPS (2677) immediately or UC Davis Medical Center Police at (916) 734-2555. Be prepared to answer questions on what type of identifiers stored on the device. UC Davis Police Department
The IT Express Computing Services Help Desk provides assistance with many topics, including software, campus Internet access, and activating and accessing your UC Davis email and computing accounts. Call for help at 530-754-HELP (4357).
For more information refer to the UC Davis Compliance Program website for requirements to disclose security breaches exposing PHI.

IMPORTANT NOTE: Remember, if you suspect that your system has been compromised or hacked, ***stop***

using the system until IT has cleared the machine.

INFORMATION SECURITY DO'S AND DON'TS

DO'S	DON'TS
SECURITY NEEDS AND ASSESSMENT	
Work with your local IT and department to determine the real security risks and the necessary protections for your system.	Do not assume system security based on its location or product/vendor security claims.
SYSTEM PROTECTIONS	
Use firewalls supported by your IT group. Use antiviral protections at all times.	Do not operate systems without understanding limitations of security protections.
SECURITY PLAN TO CONTROL ACCESS	
Develop and use a security plan to control the physical access to system and the electronic access to data.	Do not operate registry databases without a security plan.
PHYSICAL ACCESS SECURITY	
Control access to the facilities housing database, workstations, and specimens using: ID cards, locked doors, sign in sheets.	Do not leave a database server or workstation accessible to non-authorized personnel.
ELECTRONIC ACCESS SECURITY	
Password protect computers allowing access to only authorized personnel access. Terminate passwords of separated staff.	Do not leave workstation terminals open. *Even in highly secured areas, unique user ID and a password provide audit trails.*
TRANSMISSION SECURITY	
Validate security of method (encryption) used for ePHI transmission. VPN is secure. Medical Center intranet is secure for email transmissions. Ensure all registry staff understand security policies. Web portals need approval.	Do not send ePHI in campus email as password protected attachments; *If Medical Center email goes to the campus side, it is no longer secure. Wireless transmissions are not secure. See Secure Email solution: Campus.*
ACCESS TO PHI	
Limit PHI displayed on terminals. PHI should be sequestered from specimen inventory using study codes or accession numbers.	Do not make PHI readily available on the database.
INTERNET CONNECTIVITY	
Not recommended.	Do not have internet, email, ftp, or wireless applications on the main registry terminal.
RECOVERY PLAN	
Have a data recovery plan that includes validation and testing of all recovery processes.	Do not store backup data at the same physical site as the original database. Do not use untested backup media or devices.
PHI DISPOSAL PLAN	
Establish procedures for disposing of PHI labels, electronic devices, media, and for reusing media.	Do not use trash bins for PHI disposal. All computer equipment must have the hard drives/memory erased.

VII. Sharing Biospecimens and Data with Other Researchers, Institutions or Private Companies

***Section Summary**: This section provides information for researchers who share specimens and/or associated data with other researcher within UC Davis and entities outside the University system. Some suggestions on how to optimize specimen utilization through well planned collaborations and transfers are included.*

How are biospecimens shared **within the UC Davis system**? Topics covered:

- Evaluating research plans
- Recouping costs
- Disposition of unused specimens
- Publications
- Verification of IRB approval
- Obtaining Consent to Share Biospecimens

How are biospecimens shared with researchers **outside the UC Davis system**? Topics covered:

- Written agreements:
  - Material Transfer Agreements
  - Clinical Trial Agreements
  - Clinical Services Agreements
- Financial concerns when transferring biospecimens outside UC Davis
- Protecting intellectual property (IP) rights

What are the HIPAA privacy issues when sharing biospecimens for research?

How are biospecimens shared within the UC Davis system? The University encourages collaborations between UC Davis colleagues. The following topics should be considered before collaborations begin involving human specimens:

Evaluating Research Plans
Recouping Costs
Disposition of Unused Specimens
Publications
Verification of IRB Approval
Obtaining Consent to Share Biospecimens

- **Evaluating Research Plans:** The following topics - considered by many specimen utilization review committees - may be useful whether you are preparing a specimen request or evaluating requests from potential collaborators:

SCIENTIFIC MERIT	**Is the research plan well designed and likely to provide meaningful results?**
	It is very important to provide reviewers with a strong scientific rationale to justify use of specimens that are often a scarce resource. Justification should include reasons why established human cell lines and/or animals tissues cannot be used. Applicants should thoughtfully consider the justification if requesting valuable or rare specimens, such as tumor specimens with 5+ years of follow-up data.
PRIORITY	**How does the request rank with those competing for similar specimens?**
	Many program banks give priority to researchers within the program. Approval for a request for large numbers of valuable specimens (e.g. rare or limited resource, especially those with a large amount of correlative follow-up data), will be carefully considered if the request will deplete the resource.
STATISTICAL POWER	**Is the number of specimens requested adequate to meet the stated aims?**
	The research plan should have adequate statistical power to achieve meaningful results. This issue applies more to larger projects and less to pilot studies or efforts in assay develop.
DATA REQUESTED	**What kind of specimen-associated data is needed to achieve the stated goals?**
	An applicant requesting 10 aliquots of tumor for assay development would not need to receive detailed demographic and follow up data with the specimens. It would be appropriate to supply detailed demographic and follow up data to a researcher looking for prognostic markers for breast cancer recurrence.

- **Recouping Costs:** Although UC Davis banks and investigators are not allowed to sell specimens for profit, investigators involved in specimen banking are permitted to recover the costs within the UC Davis re-charge system for expenses associated with collection, processing, storage, and distribution.
  - The table below shows many of the general activities to consider when estimating costs.

> **IMPORTANT NOTE**: Your departmental manager or budget analyst may be able to provide financial guidance to help determine appropriate costs for staff-time and materials involved in specimen collection, storage, and distribution. Costs should be included in contract negotiations and grant proposals.

RECOVERING COSTS FOR ACTIVITIES INVOLVED IN HANDLING SPECIMENS

Specimen Collection
• Tracking of patients and operating/procedure schedules
• Coordination with collaborators/providers: OR, pathology, laboratory staff

• Specimen Sampling at Site of Collection:
• Examples:
  ○ For solid tumor specimens, multiple tissue samples (tumor, adjacent benign, nodes, and possibly normal) are prepared according to protocol
  ○ Fine Needle Aspirations (FNAs)
  ○ For whole blood specimens, isolation/fraction blood components

• Documentation of signed consent
Specimen Processing
• Paraffin embedding of fixed tissues
• Preparation and staining of control slides for FNAs
• Preparation and staining of H&E controls for all tissues to document QC on sampling and presence of tumor
• Trimming of blocks to maximize tumor volume
• Special tissue preparation for investigators, including thick sectioning, collodian bag preparation,   ○ cystospins, filter preparations, preparations for laser microdissection
• Maintenance of frozen and paraffin banks
• Pulling tissues and preparing for distribution
• Database maintenance of inventory, demographic and pathology data
Pathology Activities
• Review of QC slides
• Review and marking of slides for trimming
• Selection of cases for specific studies in collaboration with investigators
• Retrieval of archival tissues from pathology tissue banks (formalin-fixed tissues) or banked frozen tissues

- **Disposition of Unused Specimens**: Many established banks stipulate that unused portions of specimens be returned to the bank. Others specify that leftover portions of extracted DNA/RNA should be shared with other investigators. Researchers releasing specimens should consider what should be done with any remaining portions of specimens and come to an agreement with the requestor prior to release of the specimens.

- **Publications**: Requestors should agree to acknowledge the repository or bank as the specimen source in all publications, abstracts, and presentations that result from research using the specimens. The option of co-authorship may be appropriate if the bank provides scientific input.

- **Verification of IRB Approval:** Anyone who plans to share specimens with other researchers should have a plan for verifying that the requestors have obtained approval from the Committee on Human Research, UC Davis's Institutional Review Board.

IMPORTANT NOTE: Sharing specimens with researchers outside the UC Davis system and Material Transfer Agreements are discussed at the UC Davis InnovationAccess website. Verification should be obtained from the applicant that the protocol has approval from the appropriate institutional review board.

- **Obtaining Consent to Share Biospecimens:** The consent form used to obtain specimens should inform participants that their specimens will be shared and with whom. For a template consent form from the UC Davis IRB with suggested standard wording, refer to the IRB HRP-502 (Consent Form).

ƒ ***How are biospecimens shared with researchers outside the UC Davis system?*** A written agreement, executed by InnovationAccess, is required before human biospecimens collected at UC Davis can be shared with researchers outside the UC Davis system.

InnovationAccess carefully negotiates and executes contractual agreements with academic institutions, non-profit organizations, and industry to ensure the University's and the researcher's financial concerns and intellectual property rights are protected.

- **Written agreements** pertinent to sharing human biospecimens with outside entities include:
  - **Material Transfer Agreements (MTA)** are required to transfer any research material, including human biospecimens, *from* UC Davis *to* researchers outside UC Davis (termed an outgoing MTA).
    - MTAs are negotiated and executed by InnovationAccess of the Office of Sponsored Research.
    - All MTAs (incoming and outgoing) are reviewed by InnovationAccess OR regardless of funding source.
    - The MTA process is initiated by completing an MTA Document.
    - The Office of Research (InnovationAccess) provides important information about MTAs, including contacts, resources and detailed procedural information for researchers to facilitate prompt execution of the agreement.
    - If both the provider and recipient of materials are academic or non-profit institutions, a UC Davis Bilateral Confidentiality Agreement (BCA) may also need to be signed.
  - **Clinical Trial Agreements** are required to conduct a clinical trial with an outside entity. The provisions for collecting and transferring human biospecimens that are part of a clinical trial would be described in the Clinical Trial Agreement. If you have any questions concerning biological specimens collected under a formal clinical trial rather than generic biobanking, please contact the Office of Research or CTSC Clinical Trials Unit.

- ***Financial concerns when transferring biospecimens outside UC Davis:*** As discussed above, although **specimens cannot be sold for a profit**, investigators can recover time and material costs associated with obtaining, processing, shipping, and tracking samples. It is important that researchers include these costs in contract negotiations and grant proposals, as well as for cost recovery in the UC Davis recharge system (see below).
  - Your departmental manager or budget analyst may be able to provide financial

guidance to help determine appropriate costs for staff-time and materials involved in specimen collection, storage, and distribution

- External revenue of recharge activities [UC Davis Recharge Policy (Recharge Activities & Rates]:
  - Recharge Activity may charge a rate in excess of full direct plus indirect costs to one or more external users.
  - The surplus revenue above the direct and indirect costs generally must be transferred out of the Recharge Activity's operating fund to a reserve fund at least annually. Such surplus revenue may be used in any manner that supports the Recharge Activity, including subsidies to lower costs charged to other users, paying for unallowable costs, purchasing equipment, or expanding the Recharge Activity.
  - If the surplus revenue is used to subsidize allowable costs, it may be retained and utilized within the Recharge Activity's operating fund.

- ***Protecting intellectual property (IP) rights:*** Researchers should be aware of the UC Davis Intellectual Property (IP) policy to ensure IP rights are protected in collaborative research projects involving human biospecimens. However, the UC Davis IP policy is only one of a number of UC policies that address intellectual property. The best way to protect IP rights when transferring human specimens to another institution is for the investigator to contact the Office of Research InnovationAccess and it will negotiate a specimen transfer agreement with the appropriate IP terms (as well as other terms that are important to the University).

- ***What are the HIPAA privacy issues when sharing biospecimens for research?*** The type and extent of private information that can be transferred with shared specimens must be consistent with your IRB-approved research protocol, HIPAA authorization from the participant, data use agreements, and, if applicable, Clinical Trial Agreements.
- Investigators are asked to address HIPAA privacy issues applicable to their research throughout the IRB application process. For example, investigators must describe the type of information that will be created, used, and distributed as part of the study, as well as the safeguards that will be implemented to protect the PHI from inappropriate disclosure. Although each study will be reviewed individually, the IRB generally recommends the following:
  - Investigators should only supply the minimum amount of health information to meet research objectives.
    -
    - Only limited PHI should be associated with specimens collected at UC Davis and sent elsewhere as part of clinical trials. The specimens should be coded and direct identifiers (name, medical record number, or social security number) must not be associated with specimens unless specifically documented in the signed consent form.
- HIPAA compliance must be maintained throughout the research study while sending and receiving all specimen and/or data formats, including:

- Physical media such as paper, disks, images, CD ROMs, DVDs, memory sticks, computers, laptops, and portable devices; and
- Any form of electronic transmission: email, internet, FTP, electronic facsimile, web portals, digital, audio, and video.

VIII. Using Human Stem Cell Lines

This section is under construction. Current policies and procedures are described on the UC Davis Stem Cell Research homepage.

IX. A Brochure for Prospective Tissue Donors

Donating Tissue for Medical Research:

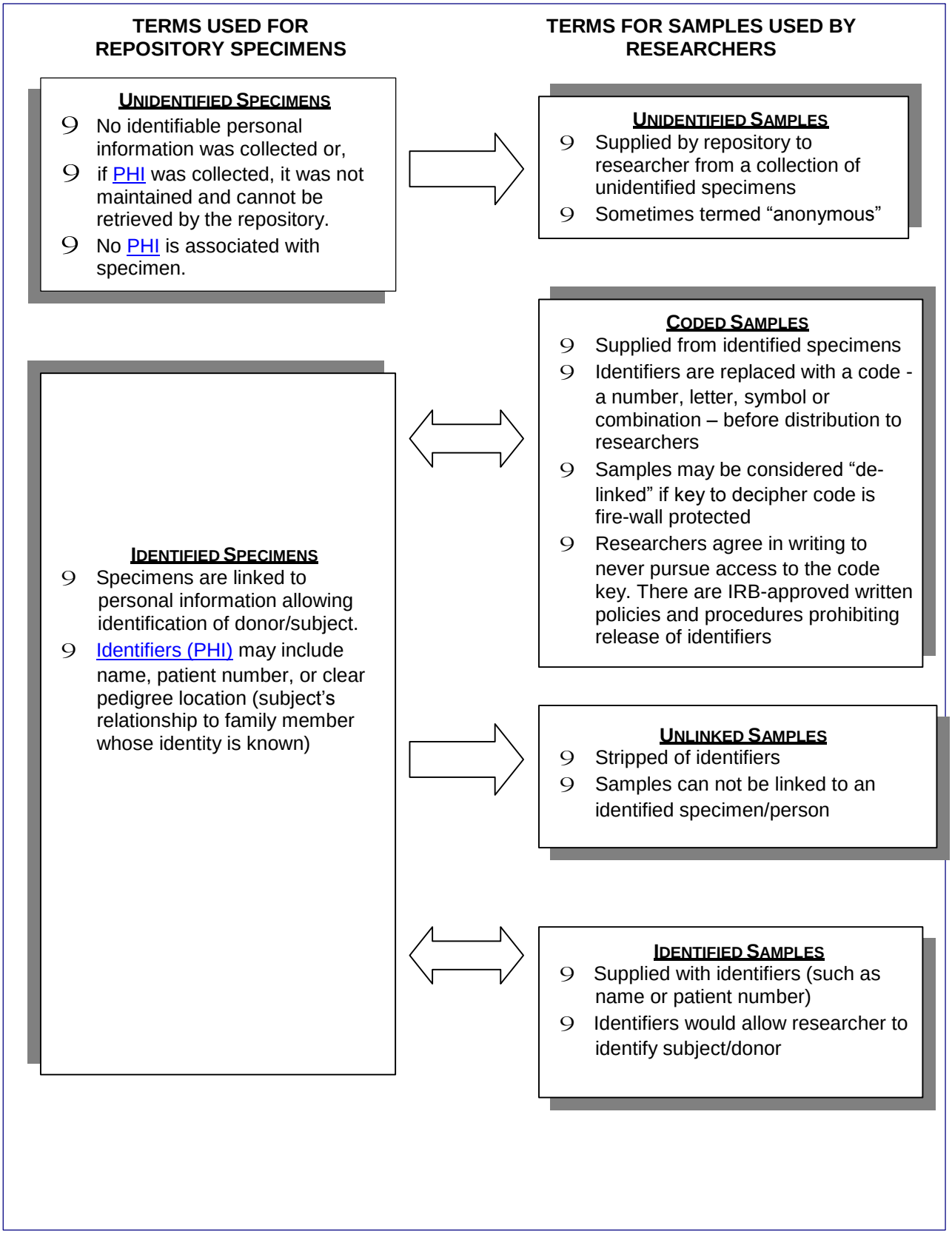
National Cancer Institute: Donating Tissue for Research (Brochure in PDF)

Example of UCSF Tri-Fold Brochure for Tissue Donation.pdf

X. BCR "QUICK GUIDE" Link

This is a link to the BCR Quick Guide that identifies some common types of research involving specimens and what IRB requirements may be involved.

Appendix A: Terms and Definitions Categories of Human Biospecimen Information



Appendix B: Specimen Banking Space: Points to Consider

SPECIMEN BANKING SPACE: POINTS TO CONSIDER
1. Is the overall space sufficient for housing storage equipment?
2. Can the height and depth of each storage unit fit in the space?
3. Is there clearance for opening and closing doors and for safe entry and Exit?
4. Is there adequate ventilation to handle heat generated by equipment?
5. Is there sufficient clearance at doors and hallways for delivery of the storage equipment?
6. Is space sufficient for operations: receiving, processing, storing, transferring specimens, cleaning storage unit, and data entry?

Appendix C: Specimen Banking Equipment: Points to Consider

SPECIMEN BANKING EQUIPMENT: POINTS TO CONSIDER

Ultra-low Temperature Freezers:

1. The range of sample types and what samples will be used for. Some specimens can be highly sensitive to temperature fluctuations.
2. How frequently will the freezers be opened and closed?
3. Upright versus chest freezers: Upright units are more space economical than chest freezers, but chest freezers can maintain ultra low temperature longer. Power fluctuations can be a problem with temperature variance for types.
4. Voltage requirements – 110 or 208,
5. Temperature recorder type, voltage regulator – optional or standard?
6. Seismic issues - Does the unit have locking wheels? Units must be secured to wall.
7. Extended warranty available on compressors-make sure it covers labor and parts
8. Alarm systems for freezers are a necessity. Need local and remote alarm system to contact staff 24 x 7 in the event of equipment or power failure. Local alarms are only good if people are present in the laboratory. Will they work in a power loss situation?
9. Plan at least 5 years out for equipment replacement or repairs. You must calculate this into your budget in order to protect the collections.

Liquid Nitrogen Units:

1. Size of unit – number of vials a unit will hold
2. Weight of a full rack – a completely filled rack if it had to be lifted out of the freezer may weight 30-50 pounds or more.
3. Alarm system that is programmable. This will warn you that the liquid nitrogen level is low in your freezer or your source of liquid nitrogen needs to be replenished. Otherwise, someone must check the levels daily.
4. Automatic refill system for liquid nitrogen: – note the smaller units are manually fed but automatic systems can fail to refill tanks.
5. Racking and inventory system – metal boxes are best with a lid.
6. Liquid nitrogen freezers should be in an open area, not in a confined space
7. Face shields, safety goggles, and cryogenic gloves must be available for lab personnel.
8. Protective floor matting: Liquid nitrogen is so cold that it will shatter/crack your vinyl flooring.
9. Seismic issues- Does the unit have locking wheels? Units must be secured to wall. Are source canisters tied down? Check with EH&S.
10. Electrical requirements: for the units that have alarms or other sensors

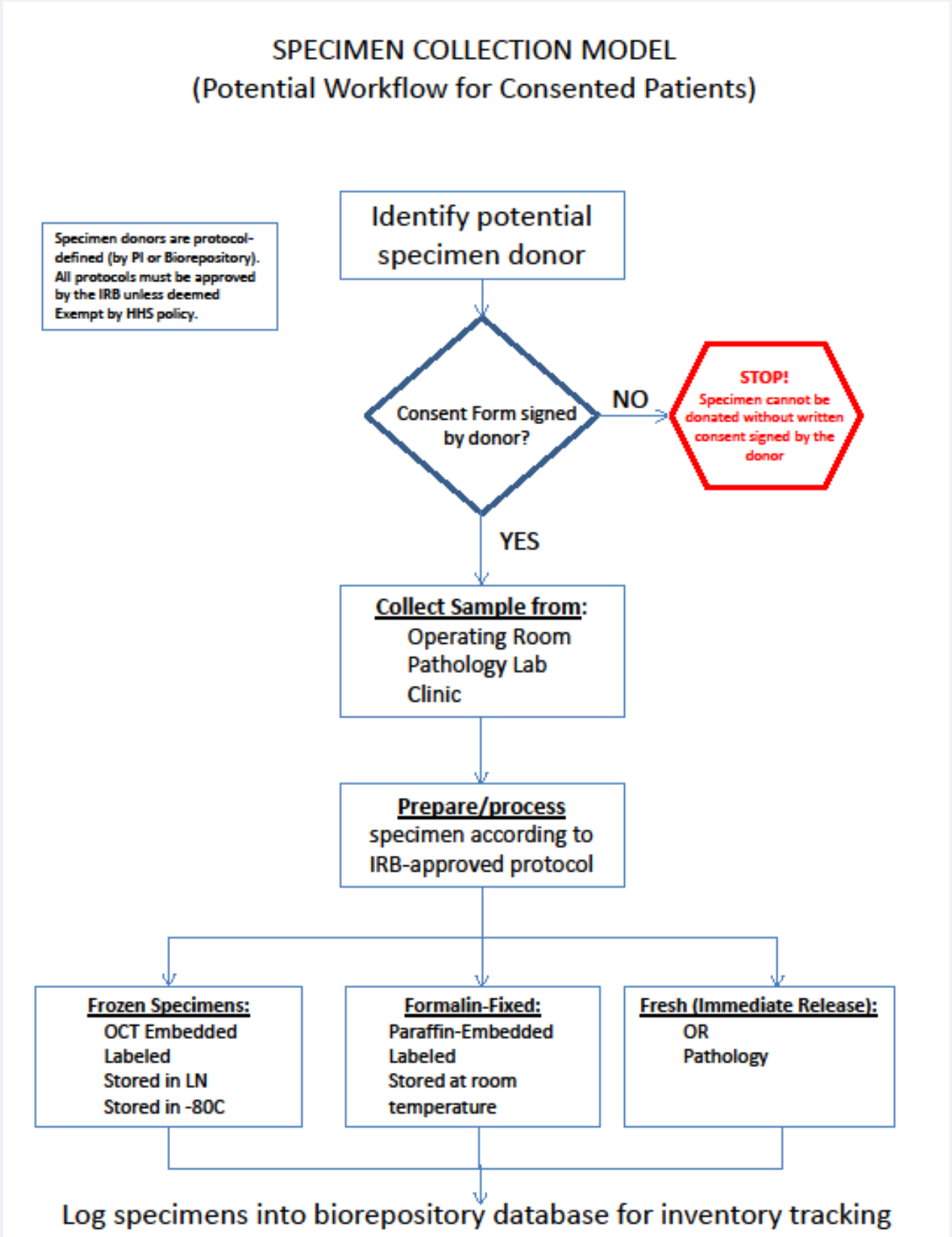
Appendix D: Specimen Storage and Labeling: Points to Consider

Specimen Storage and Labeling: Points to Consider
Specimen Storage
1. **Freezer storage system:** Racks and cryo boxes suitable for individual storage containers: Do you want to store 96 well plates, 2 ml, 5 ml cryovials, or 15 ml, 50 ml conical tubes? Liquid nitrogen racks vs canes, plates, vials, dishes, and tubes?
2. **Safe specimen distribution:** Ideally if there is a large amount of freezer space and floor space, each specimen should be distributed in different freezers to prevent loss of all specimens from one subject. Without this luxury a scanning alarm system is required to inform staff of equipment failure and/or electrical power outages.
Specimen Labeling
1. **Label type:** Use only labels specifically designed for liquid nitrogen and ultra-low temperature storage because general-use labels will detach when exposed to ultra-low temperatures. Do not use scotch tape.
2. **Computer labels**: Consider labeling by computer and not by hand. This eliminates the problem with poor handwriting styles and limited space on the label. Proper inventory systems should have a labeling program to prevent hand labeling of cryovials.
3. **Bar coding:** Thermal transfer labels are resistant to many chemicals and are durable in both hot water baths and liquid nitrogen freezes. Some manufactures/suppliers are: Brady, Zebra (Eltron), Shamrock, and Intermec. You need a thermal transfer printer to use these labels.
4. **Labeling pen**: Pencil will smear over time, some inks actually smear or bleed when exposed to liquid nitrogen or ice. Test all markers before using them in your specimen bank.

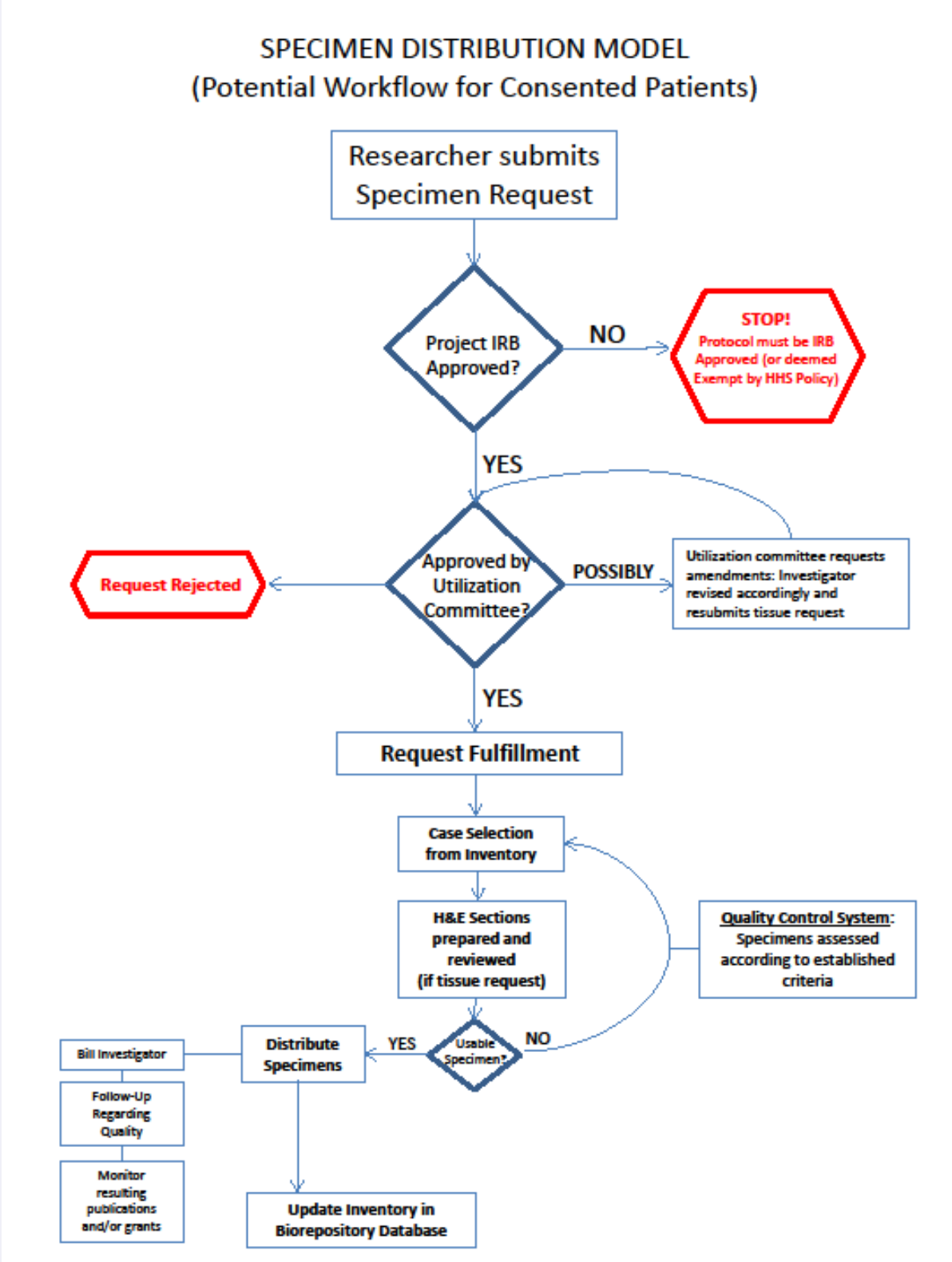
Appendix E: Emergency and Backup Plans: Points to Consider

EMERGENCY AND BACKUP PLANS: POINTS TO CONSIDER
1. **Electrical backups:** If your laboratory experiences a loss of electrical power, does your facility have an electrical generator? If not, what are your plans in the event there is no power for more than 24 hours?
2. **Backup freezer:** If you will have a large specimen bank, then include in your budget at least one empty freezer as a backup in the event of a unit malfunction.
3. **Backup freezer loaners:** know what is available for backup freezers, such as ultra low freezer rentals. Check out available sizes and rental requirements such as recharge account before an emergency occurs.
4. **Liquid nitrogen backup:** Can the vendor deliver on short notice? Does the campus have a reserve supply for emergencies that you could use? Who can you either borrow a container from or who has extra space for you to temporarily store your samples? Extra canisters are rare at UC Davis.
5. **Dry ice availability:** Who supplies it and how often? Can you get an emergency delivery? Who can you borrow dry ice from at UC Davis? In some emergencies, UC Davis will provide a large stock of dry ice for campus.

Appendix F: Potential Specimen Collection Workflow



Appendix G: Potential Specimen Distribution Workflow



Appendix H: HIPAA Information

What is HIPAA?

The Health Information Affordability and Accountability Act is a law that gives rights to patients with respect to their identifiable health information (PHI). With a few exceptions, it requires health care providers to obtain an authorization from the patient before that patient's health information can be used for research. It also requires providers to protect identifiable health information. UC Davis Health System employees must comply with all of the requirements of HIPPA. The following is a summary of the requirements at UC Davis.

What is PHI?

Protected health information (PHI) is any information in the medical record or designated record set that can be used to identify an individual and that was created, used, or disclosed in the course of providing a health care service such as diagnosis or treatment. For example, PHI is used in research studies involving review of medical records to obtain research data, such as a retrospective chart review study. Also, studies that create new medical information because a health care service is being performed as part of research. Examples include diagnosing a health condition or investigating a new drug or device to treat a health condition.

What is not PHI?

Examples of research health information not subject to HIPAA include studies analyzing only de-identified or anonymous data or that use a limited data set with a data use agreement. Some genetic basic research can fall into this category such as the search for potential genetic markers, promoter control elements, and other exploratory genetic research. In contrast, genetic testing for a known disease that is considered to be part of diagnosis, treatment and health care would be considered to use PHI and therefore subject to HIPAA regulations.

Health information by itself without the 18 identifiers is not considered to be PHI. For example, a dataset of vital signs by themselves do not constitute protected health information. However, if the vital signs dataset includes medical record numbers, then the entire dataset must be protected since it contains an identifier. PHI is health information that includes anything that can be used to identify an individual such as private information, facial images, fingerprints, and voiceprints. These can be associated with medical records, biological specimens, biometrics, data sets, as well as direct identifiers of the research subjects in clinical trials.

The HIPAA Privacy Rule provides for a "safe harbor" to help researchers determine whether specimens and health information is de-identified. To meet the safe harbor requirements,

the following information must not be included on the specimen label or the health information accompanying the specimen:

1. Names;
2. All geographical subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code, if according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and (2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;
4. Phone numbers;
5. Fax numbers;
6. Electronic mail addresses;
7. Social Security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate/license numbers;
12. Vehicle identifiers and serial numbers, including license plate numbers;
13. Device identifiers and serial numbers;
14. Web Universal Resource Locators (URLs);
15. Internet Protocol (IP) address numbers;
16. Biometric identifiers, including finger and voice prints;
17. Full face photographic images and any comparable images; and
18. Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data)

There are also additional standards and criteria to protect individual's privacy from re-identification. Any code used to replace the identifiers in datasets cannot be derived from any information related to the individual and the master codes, nor can the method to derive the codes be disclosed. For example, the unique code cannot include the last four digits (in sequence) of the social security number. Additionally, the researcher must not have actual knowledge that the research subject could be re-identified from the remaining identifiers in the PHI used in the research study. In other words, the information would still be considered identifiable is there was a way to identify the individual even though all of the 18 identifiers were removed.

At UC Davis, researchers can access and use PHI when necessary to conduct research under four circumstances.

- With an authorization from the patient or the patient's legally authorized representative;
- With a waiver of authorization from an IRB;
- With clearance from the UC Davis Health System Compliance; and
- With clearance from UC Davis Health System Compliance for activities preparatory to research.

For more information, contact the UC Davis Health System Office of Compliance.