Report of the University of Utah Ad Hoc Committee on Tissue Banking Guidelines

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Chairman: Donald P. Alexander, Pharm.D.

Members: Jeffrey Botkin, M.D., M.P.H.
Leslie Francis, Ph.D., J.D.
Dana Hughes, Ph.D.
Larry Kraiss, M.D.
Greg Stoddard, M.B.A., M.P.H.

Ad Hoc Members: Kurt Albertine, Ph.D.
Chris Lehman, M.D.
Patricia MacCubbin, M.S.
Richard Wheeler, M.D.
1. The vocabulary used in the four options presented to patients is not clear and causes confusion in patient’s minds. Please rewrite the tissue banking options in a more user friendly language. The National Bioethics Panel has proposed 6 check boxes. Please review the National Bioethics Panel options and decide whether they can be used or whether another approach is needed.

Research in Human Subjects often involves the collection of tissue/blood/urine/body fluids. Patients/subjects are to be informed, with each protocol, what procedures and sample collections are to occur in the protocol. This should be clearly stated in the consent form document. What is not clear in the consent document, is what will happen to those samples after the completion of the research project. Many of these patient samples have been stored in University laboratories since the completion of the original research project. The donor patient has not authorized the use of these samples in future research. Future use of these stored samples may/will require locating the patient and obtaining consent for the new protocol. Therefore, it is IRB policy to require that all new protocols seek to identify the patient wishes for the disposition of these samples at the time of the original consent, so that future re-consenting of the patient is not necessary.

Current Tissue Banking Check Boxes being used by the IRB have been in place since 1998. The current revision of the TBG attempts to more clearly document the individual’s decision regarding the disposition of these samples. A proposed model document is included below. The use of the model check boxes in each consent document is not mandated but the essence of the information will be required in the official document used for patient consent. The members of the IRB reviewing the protocol will be responsible to evaluate the completeness of the questions posed for tissue sample disposition.

Specific questions that are required to be addressed:

1. At the end of this research project, can the specimen(s) be saved for future research?
2. Can the sample be stored with patient identifiers (coded or not)?
3. Can the specimen(s) be used for a wide variety of future research or for only designated types of research? (Research protocols using linked samples require IRB review and approval.)
4. Does the individual want to be contacted before any future research is conducted with this/these specimen(s) or can the samples be used without additional contact?
TISSUE BANKING CHECK BOXES

Please read each sentence below, think about your choice, and mark “YES” or “NO”. No matter what you decide to do, your decision will not affect your medical care.

May the University of Utah or its research partners retain your tissue/blood/urine/body fluid sample(s) after the end of this research project for use in future research?

☐ YES, my sample(s) may be saved for future _<specify a specific condition/disease>_< research

☐ NO, my sample(s) must be destroyed at the end of this research project

If yes, may the University of Utah or its research partners keep your name and other identifying information with your sample(s)?

☐ YES, my personal identifiers and medical information can be kept with my sample(s). All information will be kept secure and confidential.

☐ NO, my name and identifiers must be removed from my sample(s). My sample(s) cannot be linked back to me.

If you granted permission for the sample(s) to be used in future research by the University of Utah or its research partners, the Institutional Review Board will review and approve each new project. The Institutional Review Board may require that you be contacted for your permission prior to the use of the sample(s) in a new project if it determines consent is required for your protection.

You have the right to withdraw your consent in the future. You need to notify the investigator of your decision. If you decide to remove identifiers from your sample(s), you will not be able to withdraw your sample later because it cannot be linked back to you.
1a. Provide guidance as to the use/inclusion of “Tissue Banking Check Boxes” on the Autopsy Consent Form.

**Use of Autopsy specimens**

Review of research on human subjects is the primary responsibility of the IRB. The definition of a human subject in the Common Rule is someone that is currently alive. Research using human tissue/blood/urine/body fluids from autopsy or postmortem individuals is not generally covered under the Common Rule and may be exempt from IRB review and approval. The Common Rule is intended to provide guidance for the ethical and moral conduct of research for individual subjects and to address the potential harm to an individual or group(s) associated with the individual (ex. family, sect, race). Therefore, the IRB at the University of Utah is requiring the following process for the collection and use of tissue/blood/urine/body fluids from postmortem individuals in research:

1. If the tissue/blood/urine/body fluids collected for research are **unidentified**, the collection and use of these samples is not considered, under the Common Rule, human subject research that requires IRB approval. A limited amount of clinical information can accompany the sample(s).

2. If the tissue/blood/urine/body fluids collected for research are **identified or coded**, an IRB application must be submitted for review and approval. A consent form is **not** required if the scope of the research does not include genetic testing for heritable traits.

3. If the tissue/blood/urine/body fluids collected for research are **identified and coded**, and the research involves genetic testing of these samples for **heritable traits**, an IRB application will be required for review and approval prior to autopsy collection of any samples. A consent form may be conditionally required. If the scope of the research and results generated by the research could have substantial adverse impact to the family or associated group(s), IRB approval as noted above is required and the responsible family member(s) **consent** may be required. Collection of specimens may not occur without IRB approval. Written consent from the responsible family member(s) should be gained concomitant with or sequential to the autopsy consent process.

The current University of Utah “Authorization For Performance of Autopsy” form used at the University of Utah Hospitals and Clinics should be revised to: 1) remove the current Tissue Banking Guideline check boxes, 2) remove the 3rd paragraph regarding the Pathology Department use of autopsy specimens, 3) to include the following statement: “The hospital through the pathology department may use autopsy tissues for clinical teaching purposes.”

**Veteran’s Administration (VA) samples**

The VA designates human subject research to include both living and deceased individuals. Therefore, **any** research involving tissue/blood/urine/body fluids from autopsy or postmortem sampling requires full IRB application and approval as well as a signed informed consent document by a responsible family member that meets VA requirements.

1. The **University policy is not clear on unidentified versus identified samples. Please define unidentified and identified specimens as well as what is meant by linkage and coded samples. (refer National Bioethics Advisory Committee (NBAC) Document)**

Investigators should be guided by a clear set of definitions of the Categories of Human Biological Materials. The definitions set forth in the NBAC document Table 1. should be adopted (see attached).

**Table 1. Categories of Human Biological Materials**

**Repository Collections**

1. **Unidentified specimens**: For these specimens, identifiable information was **not collected** or, if collected, was **not maintained** and **cannot be retrieved**.

2. **Identified specimens**: These specimens are linked to personal information in such a way that the person from whom the material was obtained could be identified by name, patient number, or clear pedigree location (i.e. his or her relationship to a family member whose identity is known).

**Research Samples**
1. **Unidentified samples**: Sometimes termed “anonymous”, these samples are supplied by repositories to investigators from a collection of unidentified human biological specimens.

2. **Unlinked samples**: Sometimes termed “anonymized”, these samples lack identifiers or codes that can link a particular sample to an identified specimen or a particular human being.

3. **Coded samples**: Sometimes termed “linked” or “identifiable”, these samples are supplied by repositories to investigators from identified specimens with a code rather than with personally identifying information, such as a name or Social Security number.

4. **Identified samples**: These samples are supplied by repositories from identified specimens with a personal identifier (such as a name or patient number) that would allow the researcher to link the biological information derived from the research directly to the individual from whom the material was obtained.

The committee recommends that for the unlinked samples to have usefulness, a minimal amount of information may accompany the unlinked specimen. Information that can accompany the specimen (not all inclusive) are 1) approximate date of collection (month/year) (ie. 5/01 vs. 5/18/01), 2) approximate date of surgery (month/year), 3) type of specimen, 4) diagnosis (some exceptions), 5) stage of disease, 6) gender, 7) age, 8) treatment status, 9) outcome, 10) race or ethnic group (exception: rare diagnosis that is identifiable). The inclusion of rare diagnoses is one exception to the above rule. A specific need for separate consent for these individuals would be required because of the opportunity for identification of individual information.

Information that should not be included with the sample are: 1) name, 2) medical record number, 3) social security number, 4) date of birth, 5) zip codes, 6) address and telephone. The committee recognizes that any combination of general information may provide a link to the personal information. We consider that good clinical judgement should be exercised in the provision of this information in select groups of patients. A full IRB application and approval will be required if the intent of the study is to demonstrate a previously unrecognized biological difference between races or ethnic groups. The IRB will determine whether there may be potential harm to the race or ethnic group being studied. If there is a question as to the use of certain information, the IRB should be consulted for advice prior to the use of such information.

If research is conducted with unidentified or unlinked tissue samples, it is usually not considered human subject research requiring IRB review. The IRB will require the investigator(s) to submit an abbreviated IRB Application for the use of these tissue samples. This application should be reviewed for a Statement of Assurance from the investigator(s) regarding the unidentified nature of the samples. This application can be reviewed by the IRB Office or through an expedited review process. Although the use of unidentified samples is not regulated by the Common Rule, the IRB will be consistent in the oversight of how tissue samples are used within the institution.

2. Provide language for investigators to use in the consent document to state economic gain may be realized from the procurement of tissue samples.

The following statement should be included verbatim in the Consent document:

“Tissue or blood samples obtained from you in this research may help in the development of a commercial product by the University of Utah or its research partners. There are no plans to provide financial compensation to you should this occur.”

3. When are tissue samples “publicly available”, if ever?

There are few opportunities for tissue samples to be publicly available but there may be limited circumstances of tissue samples being made available to qualified researchers for valid research purposes at a reasonable cost. These samples must be characterized as unidentified samples. If the identity of the sample is known, the identity must be recognizable in the public domain and not entitled to a presumption of anonymity.

4. Define IRB standards for handling and use of samples from other institutions brought to the University for research?

Collaborative work - Samples sent from another institution or entity should be unidentified, unlinked or coded samples. These samples may or may not have accompanying medical information. The code key and “identities” should remain with the “home institution or entity”.

IRB requirements: 1) If the samples are unidentifiable or the samples are coded and/or unidentifiable to the University of Utah researcher, an abbreviated IRB Application should be completed including a signed Statement of Assurance as to the status of the samples. 2) If the samples are coded and identifiable to the University of Utah researcher, a full IRB Application is required. The University of Utah investigator/collaborator should include where the samples were obtained, the intended use of the samples and future storage or disposal of the sample(s). The IRB will review and verify the off-site IRB evaluation and approval of the protocol, consent document and tissue banking guidelines. This process will also pertain to the samples shared within the University of Utah as well. It is necessary for the University IRB to approve the study before the local investigator can use the sample(s).

Contract work – All tissue/blood samples received by faculty/staff at the University of Utah for contract work shall be required to be coded specimens and all means for identification removed prior to sample receipt by the University investigator. Policy and Procedures defining the handling, storage and disposal of samples should be developed by the local laboratory and the process for the return of the tissue sample to the original requestor or the process of destruction of the sample(s) should be clearly defined.

5. Define policies on how to handle samples collected at the University of Utah and then used for research in other institutions.

In general, identified tissue/specimen samples should not be shared with other institutions without the explicit consent of the subject as to the use and/or storage of the tissue sample/specimen in an IRB approved research protocol. Specific language identifying the samples as being owned by the University of Utah should be included in any collaborative work agreements and transfer of tissue sample/specimens for research in other institutions. The inclusion of the phrase “the University of Utah or its research partners” in the standard tissue banking consent document will permit sharing samples with other academic and commercial entities without ambiguity concerning the consent for this sharing if the direction of the research has been explicitly stated in the IRB approved protocol. The University of Utah will strive to have strict agreements with other institutions prohibiting the further distribution of samples that originated at the University of Utah.

Researchers at the University of Utah will take the necessary steps to assure the particular sample can be transferred and that the confidentiality of the subject providing any tissue sample/specimen collected at the University of Utah will be ensured. These steps include: 1) The University of Utah researcher will check the database and/or patient consent form(s) so that only those samples with appropriate authorization are considered for transfer to an outside entity; 2) All specific identifiers of these authorized samples selected for transfer will be removed and replaced with a code that will identify the sample for the University of Utah investigator; 3) The principal code of identity will be maintained at the University of Utah, shared with investigators of the outside entity unless the outside research investigator(s) is/are recognized research collaborators.

If the samples are unidentified, with all identifiers stripped and unretrievable, the investigator or responsible party is responsible to send a letter to the IRB office describing the number and type of sample(s) being transferred to an outside institution or cooperative group. This letter will serve as the Statement of Assurance that all effort has been made to ensure the confidentiality of the sample.

6. Should a separate informed consent be required for research for samples collected for clinical purposes only? In other words, when a patient consents for a sample collection for a clinical study, have they also consented for the sample to be used for any research subsequently conducted? If so, prepare a policy to deal with clinical samples that subsequently will be used for research.

The use of a clinical specimen collected for care of the patient may or may not have a requirement of a written consent form before the sample(s) is/are obtained and processed by the laboratory. There will be slightly different procedures required depending on the type of sample (blood, serum, urine or body fluid vs. tissue) and nature of the secondary need for the sample/specimen(s).

If the sample/specimen(s) is/are blood/serum/urine/body fluid or tissue sample(s) collected for the clinical management of the patient, there is usually not a consent form required for its collection. The blood/tissue sample cannot be used in research if it is an identified sample that can be linked to a specific individual’s clinical information unless the patient consents to its use and has signed a written consent form releasing the sample for an IRB approved research protocol. The investigator must gain written consent in order to obtain and use this sample. An exception to this rule is when the use of the
blood/serum/urine/body fluid or tissue sample(s) meets the criteria for a waiver of consent granted by the IRB for an approved research protocol. In either case, IRB approval for the use of the sample must be obtained. A blood/serum/urine/body fluid or tissue sample(s) may be used for research purposes if the sample(s) has/have been de-identified or unlinked by a third party other than the specific requesting researcher and IRB approval can be demonstrated. The specific unlinking of the sample(s) will be the responsibility of the laboratory before the sample(s) is/are released to an investigator and the process of unlinking of the sample(s) is approved by the IRB. Due to regulatory and legal requirements, and due to limited resources, investigators who want access to clinical specimens must also have the approval of the Medical Director of the laboratory in possession of the sample/specimen.

The use of archived tissue/blood/urine/body fluid samples for research that presents “minimal risk” to the patient may have consent waived if all four criteria required in the Common Rule are met and the protocol is reviewed by the IRB. This process may be handled under expedited review if the research presents no more than “minimal risk” to the study subjects. This situation should be addressed on a proposal by proposal basis by the IRB without the generation of a blanket approval for future research studies involving these samples.

When a research subject consents for sample collection for a clinical study, that sample may be used for additional investigations as long as the additional investigations are consistent with the original hypothesis and intent of the sample collection and design of the research. An exception to this rule would be to include genotyping and other genetic testing for heritable traits without obtaining additional consent. Additional patient consent should be requested because of the potential sensitive nature of this type of investigation. Testing for non-heritable genetic changes would be acceptable if investigation is consistent with the original hypothesis and design of the research.

Identified clinical specimens may be made available for research if the defined purpose of the research does not exceed “minimal risk” to the patient. An IRB application would need to be submitted and a waiver of consent requested from the IRB. Examples of this type of research may include but are not limited to: 1) laboratory assay validation, 2) experimental testing that has not been scientifically demonstrated to predict: a) the occurrence of an illness, b) an unexpected increase in the incidence of or recurrence of an illness, c) the complications of an illness, d) the incidence of mortality or the timing of mortality. The patient identifiers must be separated or unlinked from the experimental results once the study is complete. A limited exception to this rule will be in the situation of a formal written paper being prepared for publication. The patient identifiers will be required to be stripped or unlinked at the time of the galley proofs so that additional information may be used to clarify the information requested by reviewers prior to acceptance of the paper for publication. A written letter to the IRB by the investigator stating that the patient identifiers have been stripped will be required when the process is complete. Although the patient identifiers have been removed from the specimen, a limited amount of clinical information may continue to accompany the specimen.

In general, if the blood or tissue specimen(s) was/were collected with consent of the patient in accordance with applicable Tissue Banking Guidelines, the sample(s) may be used for future studies and may include specific identifiers according to the specific wishes of the patient as indicated on the signed informed consent form. The use of the specimens will require the submission and approval of a full IRB application for the project, disclosing the proposed use of the pre-designated tissue specimens.

However, when specimens are collected for research during a clinical procedure, the consent process for the collection of the tissue specimen for research should be separate from the consent process of the clinical procedure and conducted preferably by an individual different from the individual obtaining consent for the clinical procedure. This position is strongly suggested to eliminate the potential bias or the potential appearance of bias of a clinician/researcher requesting samples, and potential confusion by the patient as to the purpose of the sample(s) being collected for clinical care or for research.

If a researcher is conducting current research on coded or identified specimens collected prior to the implementation of the Tissue Banking Guidelines, it should not be presumed that the patient has given consent to all types of research with that specimen. If the original investigation has been completed, the archived patient sample(s) should not be used in additional research that has not been consented to by the patient, unless the additional research studies are consistent with the original intent of the study. A new IRB application is required including a new consent document, and the patient will need to be contacted for consent before the sample(s) is/are used. In limited circumstances, the IRB may entertain a waiver of consent if the investigator provides all supporting documentation and the circumstance meets all four criteria from the Common Rule. Large banks of archived identifiable tissue samples should not be used without the patients’ respective consent if the new investigation is outside the original intent of the sample collection and design of the research for which the patients previously consented.
7. For what types of markers (i.e. mRNA, protein, archived pathology specimens for confirming a new testing technique, etc.), if any, should the IRB consider a waiver of consent. In other words, are there types of research on tissues that carry a minimal risk of confidentiality issues.

Please refer to the response in Question #5. Samples of blood/serum/urine/body fluid and tissue collected for clinical purposes may be used in the development of the laboratory assays or new procedures if the results from this analysis is/are of “minimal risk”. The concern is whether the sample in question is/are linked or unlinked to specific patient clinical information. The use of samples collected for clinical purposes can be used to establish or confirm new testing procedures if the patient sample(s) is/are not chosen to specifically identify rare patient populations or identify a specific individual by the results. A waiver of consent may be given by the IRB if all four criteria are met in the Common Rule. A limited amount of clinical information may accompany the sample(s). The clinical information makes this sample valuable for future research. The limited amount of clinical information that could/may accompany the sample is/are (but not limited to): 1) diagnosis (some exceptions), 2) age, 3) date of collection (month/year), 4) date of surgery (month/year), 5) gender, 6) type of specimen, 7) treatment status, 8) stage of disease, 9) outcome, 10) race or ethnic group. One exception to this rule would be the use of these samples in any form of genetic testing for heritable traits. A full IRB application needs to be submitted and approved before the sample(s) can be used in research. This process may be handled under expedited review if the research presents no more than “minimal risk” to the study subjects. The methodology to separate the investigator from the identity of the patient (unlink the information) should be individualized to the laboratory and the procedure clearly and specifically written in the IRB application.

The use of archived pathology specimens is of a similar nature. The question is whether the sample is linked or unlinked to specific identifiable information. Research on specimens with linked data, without the consent of the patient, should not occur unless the criteria for minimal risk are met and IRB approval obtained. This is research without consent. To obtain access to these tissue specimens, the investigator should work with a second party to ensure the unlinking of the identifying personal information. Current Policy and Procedures in this area do not exist and should be developed.

Samples from previously completed research protocols are stored in many University of Utah medical research laboratories. These archived samples are an important set of blood and tissue samples. Many of these samples are linked to their specific clinical data about the individual patient. Since these samples were collected during a time when there was not a “Tissue Banking Guideline”, the individual patient gave consent for the original research but did not give official written consent for future research to be performed on these samples. Therefore, if future research is to be performed on these samples including the use of the linked information, a new full IRB Application must be submitted and approved including a new consent document before the research can begin, unless the new study is consistent with the intent of the original research. If the blood/tissue sample(s) is/are unlinked, meaning no identifiable information would accompany the sample(s), future research may be conducted with the unidentified sample(s). A limited amount of clinical information may accompany the sample(s). The clinical information makes this sample valuable for future research. The limited amount of clinical information that could/may accompany the sample is/are (but not limited to): 1) diagnosis (some exceptions), 2) age, 3) date of collection (month/year), 4) date of surgery (month/year), 5) gender, 6) type of specimen, 7) treatment status, 8) stage of disease, 9) outcome, 10) race or ethnic group, 11) cultural beliefs. A written Statement of Assurance should be submitted to the IRB concerning the use of unidentified samples.

Information not to accompany the sample are: 1) name, 2) medical record number, 3) social security number, 4) date of birth, 5) zip codes, 6) address and telephone.

9. Develop a time-line where the IRB will no longer accept “archived samples”, collected solely for the purpose of research and obtained without informed consent for the stated research.

The committee recognizes that the large number of archived samples, in many University of Utah medical research laboratories, are a valuable asset to the University medical research community. Since most of these sample/specimens were collected prior to the requirement of the use of the “Tissue Banking check boxes” that guide the disposition of the tissue/blood samples, investigators should be educated to the issue(s) surrounding the access/use of this valuable set of biological samples. In addition, investigator(s) should be given direction as to the process to follow to access and use these samples in future research.

1. All future studies that collect blood/serum/urine/body fluid/tissue specifically for research studies (i.e. not collected for clinical diagnosis or management) will be required to state the intentions of the use of tissue/blood/urine/body fluid samples, including storage and disposal of the samples. (A specific section in the protocol should be included to cover this area or a specific Tissue Banking Guideline document developed.)
A system to formally track the consent form data is **not** currently developed or in place at the University of Utah. The IRB, through the support of the Vice President for Research, will need to develop such a system with specific mechanism(s) for tracking the responses of patients/subjects regarding the use of their sample(s).

2. If **new** research is planned on **identified/linked** samples previously collected and stored and the scope of the research is outside the original intent of the research consented to by the patient, the **original investigator** or, if not available, the investigator currently responsible for the specimens, (not the new investigator) will be the responsible person that will contact the patient to initiate the new consent process. The new investigator will need to initiate a new IRB Application and submit a new consent form for approval. IRB approval will need to be completed before the patient is contacted for consent. Written consent is needed before the samples can be used or transferred to a new investigator.

3. The IRB will be responsible, through supporting documentation from the investigator, to determine the intent of the patient as reflected in the old consent form so as not to require repeated patient contacts for re-consent unless clearly indicated. For patients who are deceased, the IRB will be responsible to assess the impact of the research on the surviving family and the need for additional contact and consent.

4. **If** the samples are **unlinked** from patient identifiers by the original investigator, these samples may be shared with other investigators who have received IRB approval for a new study. This may include a minimal amount of clinical information previously described that will not in any way lead to the identity of the patient. **In the transfer process**, the original investigator **must** submit a Statement of Assurance to the IRB office that these samples have been transferred **unlinked** to a new designated investigator for a study entitled: ____________________________, IRB # _____________ (if not a University of Utah investigator).

10. Develop suggested wording for investigators that addresses the right of the participant to withdraw consent for archived samples and the means to accomplish retrieval of the sample from the repository.

The patient should make verbal or written contact with the original investigator and state they want to withdraw consent to use the collected or archived tissue sample(s). The investigator should dispose of the sample(s) according to the wishes of the patient if the sample is archived locally. If the archived sample(s) is/are at an outside repository, the investigator should be responsible to contact the outside agency for withdraw and disposal of the specimen(s). A written letter stating the patient’s wishes to withdraw their consent to use the sample(s) in research should be requested from the patient to document their wishes and be maintained in the investigator’s file for reference. This is not mandatory. The investigator should be encouraged to place written documentation of the patient’s wishes of the sample(s) withdraw in the study file. In addition, a written record of what steps were taken to withdraw the sample(s) and the date(s) the steps were taken should be made and placed in the study file.

11. Develop suggested wording for the investigators that addresses the commercial use of tissues in research.

Please refer to the response in Question #3. The use of “the University of Utah and its research partners” should cover all involved.

12. **If** a minor (<18 y/o) originally consented to participate in a study through an Assent consent document, and now is >18 y/o, does an investigator need to re-consent the subject as an adult to use his tissue samples? **What guidance would you provide?**

In general, a re-consent process is not needed if the original consent/assent document was appropriate. The participant should be able to withdraw from the study and withdraw the specimen from the study/repository by the procedure in Q#10. One exception to the above process would be where genetic testing for heritable traits is to occur. A re-consent process would be considered prudent but not required.