Guidelines and Procedures to Accompany the Administrative Policy on Conducting Human Fetal Tissue Research

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University of Colorado Denver|

Anschutz Medical Campus

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I. Introduction

A. General Policy

The University of Colorado at Denver I Anschutz Medical Campus, herein referred to as the "University," has the responsibility to foster a research environment that promotes the responsible conduct of research. Specific federal regulations and policies have been issued regarding research that involves human fetal tissue (HFT) and human embryonic stem cells (hESC). Questions regarding procurement, storage, and disposal of such tissue are particularly at issue.

To fulfill its obligations and ensure the public trust, the University must monitor and oversee research using HFT or hESC tissues, ensuring that all federal, state, and local laws, regulations, and policies, as well as institutional policies and procedures applicable to said research will be followed. These guidelines and procedures are prepared to provide instruction for conducting research on human fetal tissue (as defined in Section II A below) at this institution.

The University has several regulatory bodies that may be used to review and approve the proposals and protocols of the applicable research projects. Through the submission process, it is determined which approvals are necessary and which entity will be ultimately responsible. If certain parameters of the research involve human subjects and informed consent, the project would be overseen by the Colorado Multiple Institutional Review Board (COMIRB), for example. Research using animals needs to be approved by the Institutional Animal Use and Care Committee (IACUC). The University also has established a Scientific Ethics Committee (SEC) to review, approve, and track research that uses HFT.

Nothing in these Guidelines and Procedures is intended to override or contradict provisions of other regulations or policies of the University of Colorado or of funding agencies.

While every effort will be made to follow the proscribed procedures, unanticipated situations including but not limited to the nature of the project and protocols related to its completion may necessitate additional or other reasonable changes in our approaches to ensuring ethical conduct of the research in consultation with the Vice Chancellor for Research.

B. Scope

These Guidelines and Procedures apply to any person engaged in research at this institution which falls under Administrative Policy *Conducting Human Fetal Tissue Research*. (See section "K" of this policy for federal statues and other policy references.)

In the event that these Guidelines and Procedures materially conflict with the requirements of any funding agency, the University will comply with the requirements of the funding agency, or whichever requirements are more restrictive.

II. Definitions

A. HFT Research

Research involving the use of human fetal tissue (HFT). HFT is defined as tissues or cells obtained from a dead human embryo or fetus after spontaneous or induced abortion, after a stillbirth, or from a potentially viable fetus. (Other terms used here are defined in the *Conducting Human Fetal Tissue Research* policy section "C".)

B. Regulatory Bodies Used in the Approval Process

1. Colorado Multiple Institutional Review Board (COMIRB)
   http://www.ucdenver.edu/research/comirb/Pages/COMIRB.aspx

2. Institutional Animal Use and Care Committee (IACUC)
   http://www.ucdenver.edu/research/ORCS/iacuc/Pages/default.aspx

3. Institutional Biosafety Committee (IBC)
   http://www.ucdenver.edu/research/EHS/Pages/EHS.aspx

4. Scientific Ethics Committee (SEC)
   http://www.ucdenver.edu/research/ORC/RI/Pages/SEC.aspx

III. Roles and Responsibilities

A. Research Integrity Officer

The Vice Chancellor for Research shall appoint the Research Integrity Officer (RIO). The RIO is the institutional official who has primary responsibility for implementing these Guidelines and Procedures.

B. Scientific Ethics Committee

The Scientific Ethics Committee (SEC) is a committee appointed by the AVC for Regulatory Compliance to ensure that the University of Colorado Denver I Anschutz Medical Campus (UCD) policy on "Conducting Human Fetal Tissue Research" is operationalized. The SEC has based its evaluation on an expansion of the NIH Guidelines on Human Stem Cell Research, July 7, 2008 (2009 guidelines: http://stemcells.nih.gov/policy/Pages/Default.aspx) as well as other applicable federal, state laws and regulations.

C. Principal Investigator[s]

The Principal Investigator (PI), or named co-investigators (co-PI), is the University faculty /employee who is primarily responsible for the conduct of the research on any given project. The PI: prepares the proposal and its budget; discloses intended HFT research to the regulatory agencies of the University; obtains required approvals; follows all laws, regulations and policies applicable to the intended research; maintains accurate and complete records regarding procurement, storage, treatment, and disposal of any HFT materials; and is responsible for ensuring all personnel working on the project are properly trained in the protocols, procedures and ethical principles necessary to complete the project.

D. Departmental Administrator or Accounting Personnel

The University personnel (of whatever title) who process project-applicable financial or other procurement transactions must be aware of and work closely with the Office of Contracts and Grants, the Procurement Service Center, and the funding sponsor in following prescribed processes for obtaining FHT materials for the research project and in assigning any expenditures to the correct and allowable fund. This also includes separating and assigning facilities data such as lab space to appropriate funds (federal versus private).

E. Project Personnel

Project personnel includes students, Postdoctoral Fellows, Professional Research Associates, Research Associates, visiting scholars, and researchers of any other title who participate in an HFT-designated project. Project personnel are responsible to inform themselves and avail themselves of needed training related to procedures required to complete the conduct of research on the project and to be aware of the ethical considerations of using HFT in research.

IV. General Principles and Procedures

A. Obtaining Approval for HFT Research

Any PI who intends to conduct research, procure or share HFT must comply with the policies and procedures outlined by the applicable existing regulatory committees.

In addition, all research using HFT, collecting or procuring HFT or sharing HFT with external entities must be submitted to SEC for review and approval unless it is being submitted to COMIRB for review as a full board or expedited protocol.

Specifically:

1. If information associated with the HFT is recorded for research purposes in a manner that living individuals (e.g. living donor(s) of the material) can be identified, directly or indirectly through identifiers linked to those individuals (i.e. coded), those individuals are research subjects and as such require COMIRB full board or expedited review. If the protocol is being reviewed by COMIRB then it does not also need SEC review even if other categories below (2-7) also apply.

2. All research using HFT derived from viable fetuses or which otherwise meets the criteria for IRB full board or expedited review must be submitted to COMIRB for review and on-going approval**.**

3. For HFT that uses an external IRB rather than COMIRB for review and approval to meet the regulatory obligations, then the research must also be reviewed and approved by the SEC in accordance with its written procedures.

4. All research using HFT in living animals or which otherwise meets the criteria for Institutional Animal Care and Use Committee (IACUC) review must be submitted to IACUC for review and on-going approval**.**

5. All research using HFT or which otherwise meets the criteria for IBC review must be submitted to IBC for review and on-going approval.

6. Researchers who obtain HFT from an external third party regardless of whether this is a commercial supplier or academic institution, clinic, hospital, for free or for pay, must be reviewed and approved by the SEC in accordance with its written procedures.

7. Researchers who distribute HFT to an external third party regardless of whether this is a commercial supplier or academic institution, clinic, hospital, for free or for pay must be reviewed and approved by the SEC in accordance with its written procedures even if IRB/IACUC/IBC approval has been obtained.

B. Procuring and Distribution of HFT Materials for Research

1. A Materials Transfer Agreement (MTA) must be executed for HFT obtained from an external institution, clinic or hospital and must provide documentation that they are in compliance with the applicable Federal laws and policies or provide information on comparable restrictions in force in their country.

"External institution" does not include UCHA, CHCO, or DHHA. As such applicable research conducted in the affiliate hospitals may not need to obtain a MTA but the rest of these procedures still apply.

The following documents must be submitted to TTO in order for TTO to finalize a MTA involving HFT: SEC approval letter

2. A Materials Transfer Agreement (MTA) must be executed for HFT to be distributed by the University of Colorado Denver I Anschutz Medical Campus to a commercial entity or an academic institution, clinic or hospital.

   The following documents must be submitted to TTO in order for TTO to finalize a MTA involving HFT: SEC approval letter

3. Financial Transactions related to the procurement and / or distribution of HFT must include these additional procedures or restrictions:

   a. All commercial suppliers of HFT must provide documentation that they are in compliance with the applicable federal laws and policies and complete the SEC attestation form. (see Appendix A)

   b. All commercial transactions for the procurement of HFT must be transacted through the University of Colorado Procurement Services Center (PSC) in accordance with relevant PSC rules under Sensitive Expenditures.

   c. PSC will require a copy of the following documents to complete the transaction and will maintain a copy of these documents with the related transaction records:

      A copy of the MTA

      A copy of the approval from the SEC

   d. **HFT cannot be purchased using a university procurement card regardless of the value of the proposed purchase.**

C. Certificate of Confidentiality

If identifiable HFT will be collected or used in a research study then the Principal Investigator should apply to NIH for a Certificate of Confidentiality to provide additional privacy protection. A Certificate of Confidentiality allows researchers to refuse to disclose names or other identifying characteristics of research subjects in response to legal demands. More information is available at: http://grants.nih.gov/grants/policy/coc/index.htm

D. Maintenance and Retention of Records

PIs must maintain and retain a complete set of records of all procurement, attestation, storage and disposal records in relation to the project and use of the HFT materials. No documents may be destroyed until at least three years after the close of the project or longer if other federal, state or university policies also apply.

The University's PSC and OCG must maintain and retain all required documents related to the MTAs or purchase transactions and required attestations for seven years after the close of the project.

V. The Scientific Ethics Committee

A. Applicable Principles

To ensure adherence to ethical standards and social norms for research projects that are not required to undergo scientific and/or regulatory review in accordance with federal or state regulations, the Scientific Ethics Committee has been established.

Failure to have such research reviewed may be unethical; create an unsafe environment at the University of Colorado Anschutz Medical Campus; result in the loss of federal funds; cause the institution to incur financial or other penalties; and/or cause the public to lose confidence in the institution's research programs.

In 2009, NIH released guidelines on the ethical conduct of research utilizing human embryonic stem cells. A registry was created with existing hESC lines, and research using these established cell lines is acceptable. For hESC lines that are not part of this registry, the guidelines center around four key themes regarding tissue derivation: 1) embryos are not created for research purposes, 2) the decision to donate embryos was voluntary and uninfluenced, 3) embryos were not created or donated for donor's personal gain/agenda, and 4) donors were aware of what they were doing when donating. **While the NIH guidelines apply specifically to hESCs, UCD expects that research conducted with any fetal and / or embryonic tissue meets these same ethical standards, regardless of tissue type.** NIH Guidelines on Human Stem Cell Research, July 7, 2009 (http://stemcells.nih.gov/policy/Pages/Default.aspx)

Finally, federal law prohibits the use of federal money to destroy embryos; UCD, being a federally-funded institution, will comply with this law by ensuring that no UCD-related activity leads directly to the destruction of embryos.

B. The Goals of the Committee

- To promote an ethical framework for research involving human embryonic cells or fetal tissues, or other similar research that may have social implications
- To ensure that the science to be conducted has potential benefit to society
- To ensure that other alternative resources are not available to adequately address the research question
- To ensure that the proposed research is in compliance with all applicable regulations
- To ensure that such samples will be handled in an appropriate and respectful manner throughout the conduct of the research
- To promote fair policies and procedures to maximize scientific endeavor while minimizing needless use of such resources

C. Membership of the SEC

Members will be appointed by the Associate Vice Chancellor for Regulatory Compliance and will represent a broad range of researchers, physicians in obstetrics, and individuals with advanced training in law, philosophy and/or research ethics. There is no number limit for the Committee, but no fewer than five persons must contribute to the assessment and decision for approval or denial of the proposed research. The AVC will also name the Chair of the Committee. Determinations of the SEC will be made by a majority vote. Any person who is conflicted with a specific project will recuse themselves from the review of that research project.

D. Documents to be Submitted

The researcher will provide the following documents for review:

- Protocol or summary of research to be conducted
- Completed SEC application form (Appendix B)
- Copy of the consent form used to obtain the HFT or a copy of the completed attestation from if HFT to be provided by an external vendor. (Appendix A)
- Budget for the research project
- Copy of Standard Purchase Order if applicable
- Copy of draft MTA if applicable

E. Convening the SEC

A meeting of the SEC will be scheduled within 2-3 weeks of a protocol being submitted. Standing members of the committee will be invited to participate as well as additional experts as needed to assess the particular proposal submitted.

F. Review of the Proposal & Protocols

1. PIs must submit the documents listed above and any other documents requested by the SEC or the University's RIO.
2. The Committee's members will individually review the proposal packet prior to the convened meeting.
3. The Committee will meet together to discuss the proposed research and to determine the ethical appropriateness and scientific worth of the project in order to make a designation of approval or rejection, and to perhaps place restrictions, ask questions or request modifications to the proposal and its protocols in order for approval to be obtained.
4. The Chair of the Committee will complete the Committee's "Checklist", which provides space for designating the Committee's decision[s].
5. Decisions must be completed and delivered to the RIO in a timely manner, within no more than five work days from the first Committee meeting.

G. Notification of Decision[s]

1. The Chair of the Committee will forward the completed Checklist to the RIO.
2. The RIO or delegate will inform the PIs of the decision[s] of the Committee in writing.

    a. If the research project is approved, the PI may then proceed to submit the SEC approval letter to the relevant regulatory compliance committee as needed as well as to TTO and/or PSC so that necessary processing can be completed.

    b. If the proposal is denied, the PI may make revisions and re-submit for review.

    c. If the Committee has made other stipulations or requests additional information, the PI needs to resubmit with the appropriate modifications to the proposal or with additional information.

H. Modifications and Resubmission

1. Any resubmissions are processed the same as outlined above in sections F and G.
2. Any pertinent modifications to the approved research protocol and plan must be submitted to the SEC for prior approval. Such modifications would include:
   - A new external supplier of HFT
   - A significant change in the process to obtain HFT locally such as a new clinic
   - Substantial revisions to the consent form
   - Addition of a new Principal Investigator
3. Any submitted modifications to a formerly approved proposal must undergo the entire submission, review, and decision process again. Modifications must **not** be implemented without approval.

I. Closure

SEC must be notified when a research project closes for tracking purposes.

VI. Other Considerations

A. Internal Routing of Information

All offices or entities who review research proposals are required to include within their required forms for review, a method of identifying research using HFT, and the category or source of HFT.

The reviewing compliance committee must include in their processes the stipulation that HFT related research cannot be finally approved by that regulatory committee without submission of an approval from SEC.

Research teams can also follow the instructions on the Office of Regulatory Compliance website and in this policy document to initiate review of an applicable research project by SEC if no other regulatory committee review is required or the research team wants to initiate a parallel review by SEC to minimize delay.

B. Internal Tracking

The AVC for Regulatory Compliance is responsible for ensuring that the campus has a centralized means for tracking all procurement, use or external distribution of HFT by University of Colorado Denver I Anschutz Medical Campus faculty, employees or agents or

if the institution is contracting with an external third party to obtain and or use HFT on behalf of the institution for research purposes.

All research projects approved by the SEC or COMIRB will be entered on an excel spreadsheet by Office of Regulatory Compliance or COMIRB staff for reporting purposes. A copy of the spreadsheet will be stored on the COMIRB K drive and will be available to representatives from each of the compliance areas (ORC, COMIRB, IACUC, IBC and legal) to enter tracking data.

An annual report of research projects approved to use HFT will be made to the VC for Research.

APPENDIX A

Scientific Ethics Committee (SEC)

Attestation Form:
For the proposed use of Human Fetal Tissue (HFT) by researchers at University of Colorado Denver

If HFT is to be provided by an external commercial vendor or an external institution, clinic or hospital then that entity providing the tissue must complete a separate attestation form and include with this application.

To ensure adherence to ethical standards and social norms for research projects that are not required to undergo scientific and/or regulatory review in accordance with federal or state regulations, the Scientific Ethics Committee has been established.

The SEC has adopted the NIH guidelines apply specifically to hESCs more broadly so that UCD expects that research conducted with any human fetal and / or embryonic tissue meet these same ethical standards, regardless of tissue type.

Name of External third party providing the HFT:

Attestation section of the application

If HFT is to be provided to any faculty, employees, or staff of UCD from an outside entity, prior to procurement an authorized individual from that entity must attest in writing as follows:

☐ **The embryos are not created for research purposes**

☐ **The decision to donate embryos and / or fetal tissue was voluntary and not coerced**

☐ **Embryos and / or fetal tissue were not created or donated for donor's personal gain/agenda**

☐ **Donors were aware of the implications of donating embryos and / or fetal tissue and signed an IRB or Ethic Committee approved consent form**

☐ **UCD funds will not lead to the destruction of embryos or fetuses**

☐ **No payments and/or valuable consideration were made to any third party for the conduct of, inducement of, or the product of an abortion, including without limitation any parent(s) of any unborn fetus. Valuable consideration includes money, gifts in lieu of money, barter arrangements or exchange of services that do not constitute reasonable payment associated with the transportation, implantation, processing, preservation, quality control or storage of human fetal tissue.**

☐ **None of the tissue provided has been or will be obtained from any Planned Parenthood site.**

I hereby attest that:

- **The information provided above is accurate**
- **All human fetal tissue provided was collected in accordance with all applicable laws and policies governing the procurement and distribution of HFT.**

Signature of representative for the external entity providing the HFT:

Date:

APPENDIX B

Scientific Ethics Committee (SEC)

Application Form:
For the proposed use of Human Fetal Tissue (HFT) by researchers at University of Colorado Denver

To ensure adherence to ethical standards and social norms for research projects that are not required to undergo scientific and/or regulatory review in accordance with federal or state regulations, the Scientific Ethics Committee has been established.

The SEC has adopted the NIH guidelines apply specifically to hESCs more broadly so that UCD expects that research conducted with any human fetal and / or embryonic tissue meet these same ethical standards, regardless of tissue type.

Documents to be submitted with this application form:

- Protocol or summary of research to be conducted;
- Copy of the consent form used to obtain the HFT or a copy of the completed attestation from if HFT to be provided by an external vendor.
- Budget for the research project
- Copy of SPO if applicable
- Copy of draft MTA if applicable
- Attestation form if applicable

Name of UCD Researcher:

To assist the Scientific Ethics Committee (SEC) with its review please provide the following information:

1. Describe the plan to obtain or procure the human fetal tissue or embryonic stem cells:

2. Justify why the research cannot be conducted without use of this tissue:

3. Describe why this research is important and how it will advance this field of science:

4. Describe who will conduct the various components of the study and document how each individual has the appropriate expertise to conduct that work:

5. Provide additional information as needed regarding any limitations relating to the budget and describe how these will be overcome:

6. Provide the data points of personal and/or clinical information that will accompany the HFT

7. Describe where the samples will be stored and who will have access to them.

8. Describe the plan for disposal of the tissue once the research is completed:

Attestation section of the application
If HFT is to be provided to any faculty, employees or staff of UCD from an outside entity, prior to procurement an authorized individual from that entity must attest in writing by completing a separate attestation form which must be included with this application.

If HFT is to be provided or procured by faculty, employees or staff of UCD then please attest to the following:

☐ **The embryos are not created for research purposes**

☐ **The decision to donate embryos and / or fetal tissue was voluntary and not coerced**

☐ **Embryos and / or fetal tissue were not created or donated for donor's personal gain/agenda**

☐ **Donors were aware of the implications of donating embryos and / or fetal tissue**

☐ **UCD funds will not lead to the destruction of embryos or fetuses**

☐ **No payments and/or valuable consideration were made to any third party for the conduct of, inducement of, or the product of an abortion, including without limitation any parent(s) of any unborn fetus. Valuable consideration includes money, gifts in lieu of money, barter arrangements or exchange of services that do not constitute reasonable payment associated with the transportation, implantation, processing, preservation, quality control or storage of human fetal tissue.**

☐ **None of the tissue provided has been or will be obtained from any Planned Parenthood**

I also attest that:

- **I will be conducting research that uses human fetal tissue as described in the attached protocol, and**
- **I am aware of and will comply with the relevant legal and UCD policy requirements governing the procurement and distribution of HFT.**

UCD Researcher Signature:

Completed by:

Date: