

**Regulatory Assessment of  
Human Fetal Tissue Research  
at the University of Pittsburgh**

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## **Executive Summary**

The University of Pittsburgh (the University or Pitt) engaged Hyman, Phelps & McNamara, P.C. (HPM) to evaluate the University's activities related to research involving human fetal tissue to determine whether the institution is in compliance with federal and state laws and regulations. Based on our thorough review of established procedures and the relevant studies conducted to date, we conclude that the University's activities related to the procurement, disbursement, and use of human fetal tissue in research are fully compliant with applicable laws.

Federal and state laws govern research involving human fetal tissue. The Public Health Service (PHS) Act (42 U.S.C. §§ 289g-1, 289g-2) prohibits the knowing acquisition, receipt, or any other transfer of human fetal tissue for "valuable consideration" if the transfer affects interstate commerce. The Federal Policy for the Protection of Human Subjects (Common Rule) (45 C.F.R. Part 46) applies to federally funded research involving human subjects, as that term is defined in regulation, and puts in place safeguards to protect their rights and welfare. The Pennsylvania Abortion Control Act (PACA) (18 Pa. Cons. Stat. §§ 3201 *et seq.*) imposes requirements for the procurement and use of fetal tissue for research, which include obtaining valid consent for tissue donation from the woman undergoing an abortion procedure. For consent to be valid, it must be obtained only after the decision to undergo an abortion procedure has been made and must be given without any exchange of consideration. Pennsylvania state law also mandates that the woman cannot designate the recipient of the donated tissue and that all researchers using the fetal tissue must be informed of how it was procured.

The University of Pittsburgh Institutional Review Board (IRB) is responsible for reviewing applications to conduct research involving human subjects that is conducted at the University. The IRB ensures that the research plan sufficiently protects the rights and welfare of humans participating as subjects in research and complies with applicable legal requirements. In general, a University of Pittsburgh researcher that seeks to conduct research using human fetal tissue must submit an application to the IRB containing, among other things, the study protocol and the method by which the researcher will obtain human fetal tissue. If the IRB is satisfied that the study will use de-identified human fetal tissue collected in a manner that does not involve the researcher interacting with the donor or obtaining identifiable private information, the study is deemed exempt from full IRB committee review because it does not involve a "human subject" as that term is defined by the Common Rule, 45 C.F.R. § 46.102(e)(1). In addition, research that involves the use of laboratory animals, including research involving fetal tissue, must be approved by the University's Institutional Animal Care and Use Committee (IACUC). The IACUC is responsible to ensure that the research plan minimizes animal harm, addresses any risks to humans involved in the research, and that there is a valid rationale for using an animal in research. HPM evaluated the IRB and IACUC processes for review and approval of research proposals involving human fetal tissue, and we conclude that they meet federal and state regulatory requirements.

If the IRB (and IACUC, if applicable) determine that the research may proceed, the researcher may request fetal tissue from the Pitt Biospecimen Core (PBC), which is a University entity that coordinates with the University of Pittsburgh Medical Center (UPMC) to procure tissue for research purposes from patients treated at UPMC and disburse it to researchers at Pitt. The

University is not involved in the underlying medical procedures or clinical care administered by UPMC. The PBC's collection and disbursement of fetal tissue is conducted pursuant to the University of Pittsburgh Fetal Tissue Collection Protocol, which is a standing protocol that has obtained separate IRB review and approval. The purpose of the Fetal Tissue Collection Protocol is to ensure that de-identified fetal tissue is accessible to researchers at the University in compliance with applicable laws. HPM reviewed the procedures set forth in the Fetal Tissue Collection Protocol, and we conclude that they specify the legal requirements necessary for PBC's full compliance when procuring and distributing human fetal tissue to be used in research. We also reviewed documentation related to the studies that have used tissue procured under the Fetal Tissue Collection Protocol to confirm the procedures were followed in practice.

In sum, our findings confirm that the University's activities in support of research involving human fetal tissue are conducted in compliance with federal and state laws.

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## **I. Scope of Review**

HPM focused its review on the activities for which the University has regulatory control and responsibilities. These activities are limited to review of applications involving research with human fetal tissue by the Institutional Review Board (IRB) and the Institutional Animal Care and Use Committee (IACUC); procurement and disbursement of fetal tissue for research purposes by the Pitt Biospecimen Core (PBC); and the conduct of research studies involving fetal tissue conducted by University investigators. HPM evaluated whether the University's activities comply with applicable federal or state laws and regulations, as well as the grants policies of the National Institutes of Health (NIH), which provides government funding for fetal tissue research in the United States. To conduct our assessment, we reviewed relevant written policies and procedures and documentation from pending and completed studies applicable to human fetal tissue research and conducted interviews with relevant Pitt personnel.

In the course of the review, HPM also considered whether there was any potential conflict of interest by the Pitt IRB in its review of human fetal tissue research protocols or any inappropriate interaction between Planned Parenthood of Western Pennsylvania and Pitt with respect to procurement of fetal tissue for research. We did not consider allegations relating to entities other than Pitt or to activities other than human fetal tissue research.

The scope of HPM's review was limited to Pitt research activities with human fetal tissue as that term is defined under applicable laws. Consistent with this focus, HPM did not review research involving embryonic stem cells. Nor did HPM review the regulatory compliance of independent third parties not affiliated with Pitt. In particular, we did not review the clinical decision-making or delivery of medical care, such as abortion, by individuals serving in their capacity as University of Pittsburgh Medical Center (UPMC) employees. UPMC is a private, nonprofit corporation that operates hospitals and employs physicians, residents, and fellows. In contrast, Pitt is a public, state-related institution that includes the School of Medicine, which provides medical education and conducts academic research. Pitt has no role in managing or supervising the provision of medical services by UPMC personnel; therefore, our review did not include the activities conducted by individuals acting in their capacity as a UPMC employee. We did, however, evaluate whether Pitt satisfied its independent duty to confirm compliance of specified activities related to fetal tissue undertaken by UPMC (e.g., UPMC's requirement to obtain informed consent for donation of fetal tissue from a patient).

## II. Legal and Regulatory Framework

Human fetal tissue research conducted in the United States is subject to the requirements of the Public Health Service Act (PHS Act)<sup>1</sup> and, in some cases, to federal regulations for the protection of human subjects of research, known as the “Common Rule.”<sup>2</sup> Human fetal tissue research conducted in Pennsylvania is additionally subject to the Pennsylvania Abortion Control Act.<sup>3</sup> Finally, human fetal tissue research that is supported by the NIH is subject to additional policies applicable to grants recipients.<sup>4</sup>

### a. Public Health Service Act

The PHS Act applies to all human fetal tissue research in the United States. The statute defines “human fetal tissue” as “tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion, or after a stillbirth.”<sup>5</sup>

The statute prohibits the knowing acquisition, receipt, or any other transfer of human fetal tissue for “valuable consideration” if the transfer affects interstate commerce.<sup>6</sup> “Valuable consideration” does not include “reasonable payments associated with the transportation, implantation, processing, preservation, quality control, or storage of human fetal tissue.”<sup>7</sup>

The PHS Act specifies additional prohibitions specific to the collection of human fetal tissue for human transplantation and specifies additional requirements applicable to research involving fetal tissue transplantation.<sup>8</sup> Since we understand that Pitt is not engaged in human fetal tissue transplantation research, we do not discuss those requirements in this report.

### b. Common Rule

The Common Rule applies to human subjects research conducted or supported by the federal government. It contains provisions intended to protect the rights and welfare of human subjects, including the obligation to obtain informed consent from research subjects and the requirement that proposed research be approved by an IRB. It also specifies additional requirements for research with vulnerable populations, which include women, neonates, and fetuses.<sup>9</sup>

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<sup>1</sup> 42 U.S.C. §§ 289g-1, 289g-2.

<sup>2</sup> 45 C.F.R. Part 46.

<sup>3</sup> 18 Pa. Cons. Stat. §§ 3201 *et seq.* Pennsylvania is one of many states that regulate human fetal tissue research. At least eighteen states have banned or placed strict limits on using human fetal tissue in research. 86 Fed. Reg. 2615, 2617 (Jan. 13, 2021).

<sup>4</sup> NIH Grants Policy available at: <https://grants.nih.gov/policy/nihgps/index.htm> (last accessed Dec. 9, 2021).

<sup>5</sup> 42 U.S.C. § 289g-1(g).

<sup>6</sup> *Id.* § 289g-2(a).

<sup>7</sup> *Id.* § 289g-2(e)(3).

<sup>8</sup> *Id.* §§ 289g-1, 289g-2(b), (c).

<sup>9</sup> 45 C.F.R. § 46.202(c) (defining “fetuses” as “the product of conception from implantation until delivery.”).

The Common Rule defines a “human subject” as:

[A] living individual about whom an investigator . . . conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.<sup>10</sup>

A living individual about whom a researcher obtains de-identified specimens is not considered a human subject. Similarly, an identifiable biospecimen obtained from a source other than a living individual is not a human subject. Therefore, research with fetal tissue from which all identifiers relating to a living individual have been removed is not considered human subjects research, is not subject to the Common Rule, and is exempt from IRB oversight. Said differently, a study is deemed exempt from full IRB committee review if it does not involve a “human subject,” as that term is defined by the Common Rule, 45 C.F.R. § 46.102(e)(1), and research with de-identified human fetal tissue that does not include interaction between the researcher and a living individual (e.g., the tissue donor) or the collection of identifiable information from a living individual is not considered to involve a “human subject.”

Although the Common Rule prescribes additional protections for pregnant women, fetuses, and neonates, the Rule excludes from its purview research involving tissue from the fetus after delivery.

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities.<sup>11</sup>

That section also confirms that fetal tissue research is subject to the Common Rule only if the research involves identifiable information about a living individual.<sup>12</sup>

### **c. NIH Grants Policy**

The NIH Grants Policy Statement (the “Policy”) applies to all NIH-funded research involving human fetal tissue derived from abortions.<sup>13</sup> The Policy defines human fetal tissue as “tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion or stillbirth. This definition does not include established human fetal cell lines.”<sup>14</sup>

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<sup>10</sup> *Id.* § 46.102(e)(1).

<sup>11</sup> *Id.* § 46.206(a).

<sup>12</sup> *Id.* § 46.206(b).

<sup>13</sup> NIH Grants Policy Statement (rev. Apr. 2021), [https://grants.nih.gov/grants/policy/nihgps/html5/section\\_4/4.1.14\\_human\\_fetal\\_tissue\\_research.htm](https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.14_human_fetal_tissue_research.htm).

<sup>14</sup> *Id.*

The Policy includes additional requirements applicable to research conducted by grantees using fetal tissue from elective abortions. Of relevance to this review, the Policy specifies that the informed consent for donation of human fetal tissue must include language acknowledging that:

- consent for donation was obtained by someone other than the person who obtained the informed consent for abortion;
- consent for donation occurred after the informed consent for the abortion;
- consent for donation will not affect the method of abortion; and
- no enticements, benefits, or financial incentives were used at any level of the process to incentivize a woman to undergo abortion and/or donate human fetal tissue.<sup>15</sup>

The Policy also requires that the consent form be signed by both the woman undergoing the abortion and the person obtaining the consent.

#### **d. Pennsylvania Abortion Control Act (PACA)**

The Pennsylvania Abortion Control Act is a state law that places conditions on the provision of abortion services to women within the Commonwealth of Pennsylvania.<sup>16</sup> The stated purpose of PACA is to “protect . . . the life and health of the woman subject to abortion and to protect the life and health of the child subject to abortion.”<sup>17</sup>

PACA includes requirements related to the “procurement and use” of any “fetal tissue or organ which is used in animal or human transplantation, research, or experimentation.”<sup>18</sup> Specifically:

- Written consent of the tissue donor is required before fetal tissue or organs may be procured or used;<sup>19</sup>
- Consent may be obtained only after the decision to abort has been made;<sup>20</sup>
- No consideration of any kind may be offered or given for such consent;<sup>21</sup>
- The person obtaining informed consent may not “employ the possibility of the use of aborted fetal tissue or organs as an inducement to a pregnant woman to undergo abortion.”<sup>22</sup>
- No remuneration, compensation, or other consideration may be paid to any person or organization in connection with the procurement of fetal tissues or organs,<sup>23</sup> although

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<sup>15</sup> *Id.* § 4.1.14.

<sup>16</sup> 18 Pa. Cons. Stat. §§ 3201 *et seq.*

<sup>17</sup> *Id.* § 3202(a).

<sup>18</sup> *Id.* § 3216(b).

<sup>19</sup> *Id.* § 3216(b)(1).

<sup>20</sup> *Id.*

<sup>21</sup> *Id.*

<sup>22</sup> *Id.* § 3216(b)(2).

<sup>23</sup> *Id.* § 3216(b)(3).



reasonable expenses related to actual retrieval, storage, and transportation of the tissues is permitted;<sup>24</sup>

- All participants in the procurement, use, or transplantation of fetal tissue or organs, including the recipients of such tissue or organs, must be informed as to whether the tissue or organ was procured pursuant to stillbirth, miscarriage, ectopic pregnancy, abortion, or other means;<sup>25</sup>
- The tissue donor may not designate the recipient of the tissue or organ, and no other person or organization may fulfill such designation, if made.<sup>26</sup>

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<sup>24</sup> *Id.* § 3216(b)(2).

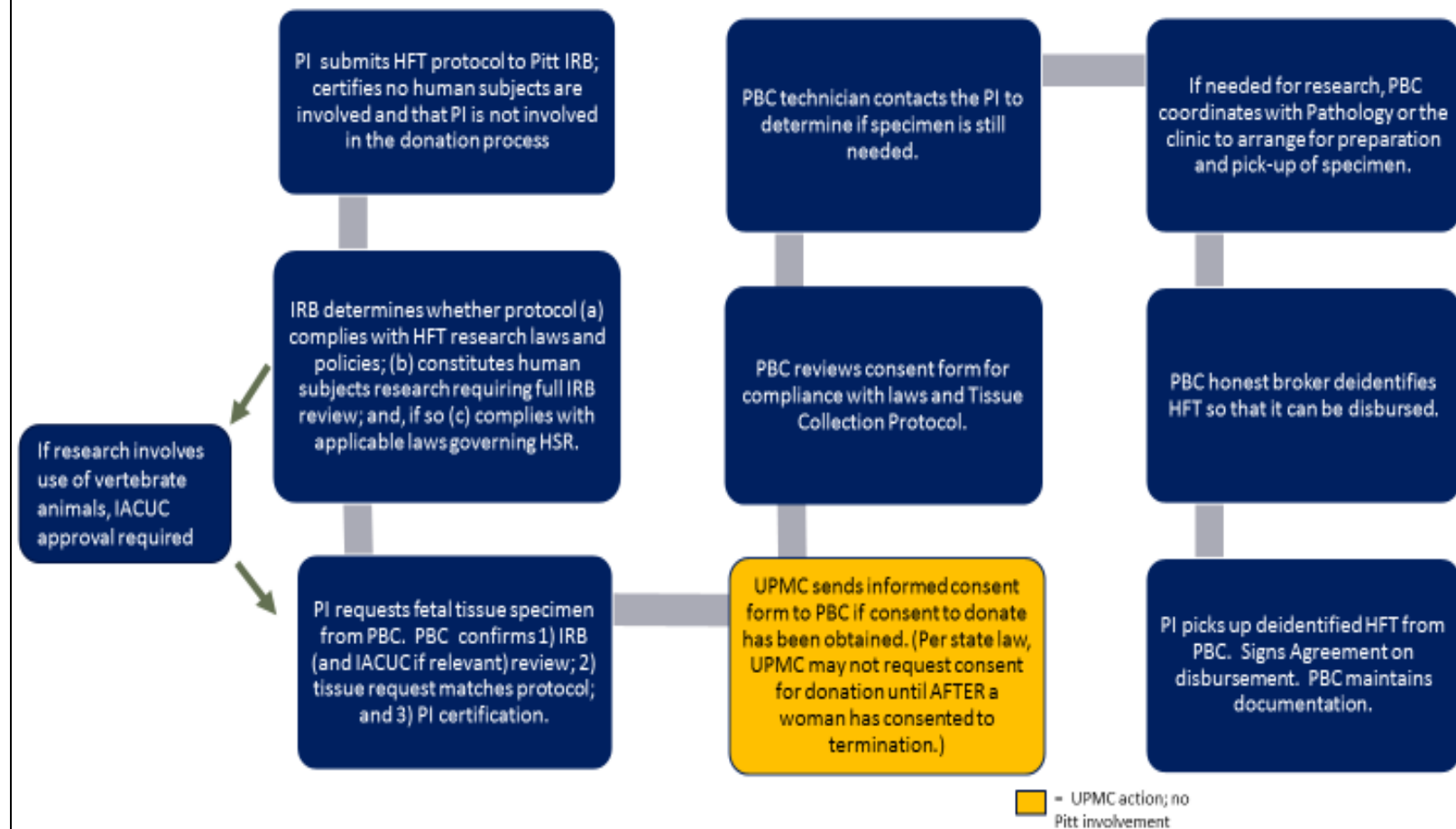
<sup>25</sup> *Id.* § 3216(b)(4), (5).

<sup>26</sup> *Id.* § 3216(b)(5).

### **III. Process for Human Fetal Tissue Research at Pitt**

The following graphic depicts the process for the review of studies involving fetal tissue at Pitt and the process for procurement and disbursement of fetal tissue for research that has been approved or determined to be exempt. We discuss each of these steps below and include an assessment of whether each step meets regulatory requirements.

## Process for Fetal Tissue Research



## **a. Submission of Application**

The first step in the process is the submission of an application to the IRB proposing to conduct a study using human fetal tissue. The application must include information about the principal investigator (PI) and co-investigators involved in the study and provide a description of the research design and objectives and the significance of the proposed study. The PI also must disclose any financial incentives or sources of funding supporting the proposed research and individuals or institutions outside of Pitt that will have access to data from the research.

### ***1) Electronic Verification by PI***

For study protocols that intend to use fetal tissue, the computerized application process requires the PI to verify compliance with certain requirements designed to ensure the research is conducted in accordance with specified federal and state laws. Specifically, the PI must verify that:

- Fetal tissues or organs may be obtained for use in research only with the written informed consent of the woman undergoing the abortion procedure is obtained;
- Informed consent for the research use of fetal tissue will be obtained separate from, and after, the decision and consent to the clinical procedure has been made;
- No consideration of any kind (i.e., monetary or otherwise) will be offered to the woman in exchange for her consent to donate fetal tissue or organs for research;
- The woman may not designate a recipient of the fetal tissue or organs for use in research; and
- All persons who participate in the procurement or use of the fetal tissue or organs must be informed as to the source of the tissue (e.g., abortion, miscarriage, stillbirth, ectopic pregnancy).

### ***2) Research with Biological Specimens: Request for Exempt or No Human Subject Involvement Determination***

For the IRB to deem a study exempt from IRB review, the application for research involving fetal tissue also must include a form titled, “Research with Biological Specimens: Request for Exempt or No Human Subject Involvement Determination.”<sup>27</sup> The IRB must be satisfied that the study will use de-identified human fetal tissue collected in a manner that does not involve the researcher interacting with the donor or obtaining identifiable private information. This form requires the PI to certify that only de-identified fetal tissue will be used in the research, identify the source of the fetal tissue, and specify the type of specimens needed for the research. The form also requests that the researcher provide the IRB number associated with the tissue bank/repository from which tissue will be procured.

The request for exempt status also requires the PI to certify that no member of the research team has interacted, for research purposes, with the individuals whose specimens (and if applicable, data) will be studied and that no identifiable private information will be reviewed or

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<sup>27</sup> Redacted form attached as Appendix 1.

recorded. The form further requires that the researcher contact the Pitt Office of Research regarding any transfer agreements to the extent that specimens/data will come from, or will be sent to, another institution.

### ***3) Agreement Relating to Use of Fetal Tissue in Research***

The IRB submission also must include an “Agreement Relating to Use of Fetal Tissue in Research,”<sup>28</sup> in which the PI must agree to certain requirements to comply with federal and state laws, including that the researcher:

- will abide by all federal and state laws (specifically including PACA);
- has read and will abide by the IRB-approved policy for procuring fetal tissue for research (the Pitt Fetal Tissue Collection Protocol, discussed in section III.c);
- will advise all persons participating in the research involving fetal tissue of its method(s) of procurement;
- will use the fetal tissue solely for non-commercial medical research; and
- will maintain confidentiality of any medical information obtained from the use of fetal tissue.

The Agreement requires the researcher to identify the “Tissue Origin and Type” (e.g., fetus/fetal organs, placental tissue, maternal blood, or maternal urine) and the “Origin” (e.g., elective abortion, spontaneous abortion, intrauterine fetal death (IUFD), neonatal death, or ectopic pregnancy).

**Assessment:** The application process for research involving human fetal tissue includes built-in checkpoints to ensure the PI is aware of the legal requirements for conducting research using fetal tissue and requires the PI to certify that the research will be conducted in accordance with those requirements.

#### **b. IRB (and IACUC) Review**

Upon receipt of the completed application, IRB staff determines whether the PI’s application complies with all applicable human fetal tissue research laws and policies and whether the research is exempt from full IRB committee review because it does not involve identifiable information about a living individual. IRB staff members are not healthcare professionals who engage in medical procedures or conduct their own research, and they serve an administrative role for studies that are deemed IRB-exempt. If IRB staff determine that the research does involve human subjects research, full IRB committee review is required, and IRB staff will review the application for compliance with applicable laws governing human subjects research.

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<sup>28</sup> Redacted form attached as Appendix 2.

The IRB staff is responsible for confirming that the fetal tissue is obtained from a donor who did not designate the recipient of the human fetal tissue and who provided consent to donation separately from and only after giving consent to the abortion procedure, and that all researchers involved in the study are informed about the source of the tissue. If the researcher obtains the fetal tissue from the PBC, then the IRB staff can rely on the fact that the PBC is subject to the Fetal Tissue Collection Protocol as evidence that these conditions will be met. However, if the fetal tissue is obtained from a source other than the PBC, the researcher has the responsibility to submit documentation to the IRB demonstrating that the source complies with applicable legal requirements for procuring human fetal tissue.

If a proposed research study involves the use of laboratory animals (e.g., fetal tissue transplantation in mice) then approval by the Pitt IACUC also is required. The IACUC ensures that the research minimizes animal harm, that any risks to humans involved in conducting the research are adequately addressed (e.g., risk of exposure to pathogens), and that there is a valid rationale for using an animal in research. For animal research involving human fetal tissue, the IACUC also confirms that the IRB has assessed compliance with applicable federal and state laws and regulations governing fetal tissue research.

After the human fetal tissue research protocol has been determined to be exempt by IRB staff (or is approved by the full IRB committee), the IRB retains the authority to audit and monitor ongoing studies. The University of Pittsburgh Research Conduct and Compliance Office retains authority to periodically audit any research study, including those that are deemed exempt from IRB approval. To date, the IRB has not conducted any audits (routine or for-cause) of human fetal tissue research studies.

**Assessment:** Based on our review of the fetal tissue studies submitted to the IRB, the IRB staff appropriately evaluated whether these studies were IRB-exempt or whether IRB committee review was required.

### **c. Fetal Tissue Collection**

The PBC supports Pitt's research programs needing biospecimens for use in research, including fetal tissue obtained from abortion procedures conducted at UPMC. The PBC provides a mechanism to simplify and streamline the process of procurement of human tissue, including human fetal tissue, and disbursement of tissue to Pitt researchers, in compliance with applicable laws. While the PBC primarily supports researchers at Pitt and UPMC, collaborative relationships between the PBC and other institutions are permissible provided that any required institutional approvals or agreements (e.g., Material Transfer Agreements and Sponsored Research Agreements) are in place.

#### ***1) Fetal Tissue Collection Protocol***

The process for collection of fetal tissue from UPMC and disbursement to researchers at Pitt typically is governed by the University of Pittsburgh Fetal Tissue Collection Protocol (TCP).

The objective of the TCP is to “provide access to de-identified fetal tissue for research in a manner that is expeditious for patients and researchers and in compliance with applicable rules and regulations.” The protocol implements a consent form that allows a woman to be approached only once to permit the donation of tissue for use by multiple researchers. The TCP is IRB-approved (e.g., the Pitt IRB reviewed the 2005 protocol as IRB702050; Study 19070406), and it has been in effect, as amended, under the aegis of successive PIs. Dr. Stefan Kostadinov is the current PI for the TCP.

Because the TCP is intended to ensure regulatory compliance in the procurement and disbursement of fetal tissue, the procedure aligns closely with the federal and state requirements. Specifically, the TCP ensures the following requirements are met with respect to tissue collection and disbursement:

<b><u>TCP Provision</u></b>	<b><u>PHS Act</u></b>	<b><u>Common Rule</u></b>	<b><u>PACA</u></b>	<b><u>NIH Grants Policy</u></b>
Specifies that women will not be compensated for donating human fetal tissue.	X		X	X
Requires that the attending physician retain the responsibility for determining the procedure to be used for the abortion and that choice of procedure not be influenced by the patient’s decision to donate, or not to donate, fetal tissue.	X			X
Specifies that the patient may not designate the recipient of the tissue or the specific research project in which it will be used.	X			
Requires researchers proposing research with human fetal tissue to first submit their protocol to the Pitt IRB and obtain approval or an exemption determination.		X	X	
Permits fetal tissue to be accepted for donation only from patients who have had a stillbirth or who have undergone an induced (surgical or medical) or spontaneous abortion before 24 weeks of gestation. The TCP also permits collection of tissue obtained post pathology review in the autopsy suite after stillbirth or miscarriage.			X	
Specifies that consent for donation of fetal tissue may be obtained only after the patient has consented to the abortion procedure. <sup>29</sup>			X	X

<sup>29</sup> The TCP does not specify a minimum waiting period between a woman’s consent to abortion and the request for donation of fetal tissue. However, the TCP notes that, because PACA requires a waiting period of at least 24 hours between when consent to abortion is given and the abortion procedure is performed, in practice consent for donation will typically be requested approximately 24 hours after consent to abortion has been obtained.

Requires researchers obtaining fetal tissue from the PBC to sign an agreement acknowledging that they have been informed of the origin of the fetal tissue (e.g., from an elective abortion, spontaneous abortion, or stillbirth) and that they will provide this information to all personnel involved in the research.			X	
Requires that the consent to donate fetal tissue be signed by the patient and the UPMC healthcare provider who obtains the consent.			X <sup>30</sup>	X
States that the person obtaining consent for fetal tissue donation cannot be the surgeon or care provider overseeing the abortion procedure.				X
Requires that the person obtaining consent for fetal tissue donation be different from the person who obtained consent for the abortion procedure.				X

The protocol also requires that the person obtaining consent for the donation of fetal tissue be a clinician involved in the care of the patient who did not oversee the abortion procedure and who will not be part of any research in which the donated tissue is used.<sup>31</sup>

The TCP contains a template form for the “Consent to Act as a Participant in Research (Fetal Tissue Consent Form).”<sup>32</sup> This form states that:

- The current and future care that the woman will receive will not be affected by her decision regarding donation of fetal tissue for research;
- The donor will not be charged for the costs of any procedures performed as part of the research;
- The donor will not be paid for donating tissue for research;
- The researchers receiving the fetal tissue will not be provided any identifiable medical information, samples, or data/information about tests done on the samples; and
- The research will not involve the use or disclosure of the donor’s identifiable medical information.

The TCP applies only to abortion procedures being performed at UPMC, and not to abortions performed by UPMC physicians at a non-UPMC facility. Were tissue to be collected for research purposes following a procedure conducted at a non-UPMC facility, the TCP would

<sup>30</sup> PACA requires written consent from the patient, but does not require the consent be signed by the healthcare provider.

<sup>31</sup> The TCP cites the Health Insurance Portability and Accountability Act (HIPAA) to support this requirement. HIPAA governs the disclosure of health care records by health care institutions. Pub. L. 104-191 (1996).

<sup>32</sup> Redacted form attached as Appendix 3.



not govern the process. It is HPM’s understanding that no fetal tissue is collected from abortions performed at Planned Parenthood of Western Pennsylvania.

**Assessment:** HPM reviewed the TCP and confirmed that it complies with applicable federal and state requirements and internal Pitt policies with respect to the collection of human fetal tissue for research purposes. We note that there is some ambiguity in the signature field of the consent forms that has led to errors by the healthcare professional describing their role in the tissue collection process. We recommend clarifying the form to make clear what information is being requested from the healthcare professional.

## 2) GUDMAP

Although the vast majority of fetal tissue collection is conducted pursuant to the TCP, the PBC also, for about five years, collected fetal tissue pursuant to a separate protocol that supported the Genitourinary Development Molecular Anatomy Project (GUDMAP). The GUDMAP consortium was formed by the National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK) to conduct research on kidney and genitourinary development.<sup>33</sup> One stated goal of GUDMAP is to develop a basis for the advancement of future research into the prevention and treatment of chronic kidney disease—a disease that is particularly prevalent in African Americans.<sup>34</sup>

Around 2016, Dr. Rajiv Dhir, the Director of the PBC, submitted a proposal for the PBC to collect fetal genitourinary tissue specifically to support the federally funded GUDMAP research program. This proposal was reviewed by the IRB (IRB 17030614, Study19020213), and the University received NIH grant monies as part of its participation in GUDMAP: between September 2016 – June 2020 Pitt received \$1,499,961. In 2021, the University discontinued its participation in the GUDMAP program, primarily because GUDMAP obtains fetal genitourinary tissue from other sources, but the PBC continues to collect fetal tissue pursuant to the TCP.

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<sup>33</sup> See <https://www.gudmap.org/about/> (last accessed Dec. 7, 2021).

<sup>34</sup> Chronic kidney disease in African Americans has been described in medical literature as “one of the most dramatic examples of racial/ethnic disparities in health in our nation.” Moreover, “African Americans are 3 times more likely to require renal replacement therapy than their non-Hispanic white counterparts.” Laster M., Shen J., & Norris K., *Kidney Disease Among African Americans: A Population Perspective*, 72(5) Am. J. of Kidney Diseases S3 (2018).

**Assessment:** HPM confirmed that the GUDMAP protocol complied with federal and state law and regulations. In particular, the GUDMAP protocol required that fetal tissue be collected in accordance with the TCP (IRB702050; Study 19070406). It further specified that all fetal tissue must be de-identified by honest brokers, the researchers receiving the fetal tissue would not have the ability to identify the source of the tissue, and there would be no subject interaction with the researchers. The only annotating data that the researchers would receive was clinical, pathological, and patient demographic information. Specimens could be distributed by the PBC only to NIH/NIDDK-approved researchers and projects. Non-Pitt researchers were required to have their own IRB-approved study in place, as well as an executed material transfer and data use agreement, before the PBC would transfer any fetal tissue.

#### d. UPMC Independent Activities

UPMC is a private healthcare institution that delivers medical services to patients. UPMC has independent responsibility to ensure its employees comply with all laws, and UPMC has a written policy that sets forth the procedures UPMC follows to determine when and how abortions can be performed.<sup>35</sup> The procedures are intended to ensure that UPMC meets applicable federal and state laws, including PACA, which, among other provisions, requires that consent to an abortion procedure be obtained from a woman at least 24 hours in advance of the procedure.

Under the UPMC policy, “[n]o fetal or placental tissue may be used for research purposes except in compliance with the Abortion Control Act of the Commonwealth of Pennsylvania, the Fetal Tissue Procurement Program approved by the Institutional Review Board and all applicable Institutional Review Board policies.”<sup>36</sup> Thus, any fetal tissue collected from abortion procedures conducted at UPMC must follow the procedures set forth in the TCP (described above). According to the TCP, “the person obtaining consent for fetal tissue procurement must be a clinician involved in the care of the patient to comply with HIPAA.”<sup>37</sup> Thus UPMC is responsible for obtaining informed consent from a woman interested in donating fetal tissue for research. UPMC personnel may not request consent to donate human fetal tissue until after the patient has consented to the abortion procedure. In practice, we understand that the donation option is discussed with patients when they arrive for the abortion procedure, which is at least 24 hours after consent to the abortion has been obtained.

UPMC must ensure that the person obtaining consent for the abortion is different than the person obtaining consent to donate fetal tissue and that the person obtaining consent for donation

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<sup>35</sup> Magee-Womens Hospital of UPMC, Abortion, Policy #ADM36 (Sept. 13, 2014).

<sup>36</sup> *Id.* at 11.

<sup>37</sup> TCP, Study Design, Number 2.

is not the medical professional performing or overseeing the abortion procedure. We understand that, in practice, informed consent for donation is usually obtained by a nurse.

**e. De-Identification and Disbursement**

Upon initial receipt of a request for human fetal tissue from a Pitt researcher, the PBC confirms that: the protocol has been approved or determined to be exempt by the Pitt IRB; IACUC approval has been obtained, if animals are included in the protocol; and the PI has signed the Agreement Relating to the Use of Fetal Tissue in Research. Once a UPMC patient consents to donate human fetal tissue, UPMC transmits the patient's Fetal Tissue Consent Form to the PBC, and the PBC reviews the Fetal Tissue Consent Form to ensure that the fetal tissue has been collected from the donor in compliance with the TCP. The PBC will notify the researcher that tissue is available and confirm that the PI is ready to receive the tissue.

The TCP requires that the person collecting fetal tissue for research from UPMC (termed the Designated Procurement Individual, or DPI) be a certified "honest broker." An "honest broker" is a PBC employee who undergoes training to de-identify tissue samples (including human fetal tissue) and maintain the confidentiality of such samples, such that they are not made available to the researchers using the tissue. The honest broker function allows the PBC to provide investigators with de-identified tissue and biological specimens. All PBC employees are certified honest brokers.

The honest broker will de-identify the fetal tissue and assign it a code. The researcher will be provided only the de-identified fetal tissue. Per the TCP, the PBC honest broker also has responsibility for maintaining a copy of the Fetal Tissue Consent Form and a copy of the IRB approval or exemption letter and a log of all fetal tissue provided for research;<sup>38</sup> for ensuring that the Agreement Relating to Use of Fetal Tissue in Research, signed by the PI, is attached to all project requests; and for providing appropriate notification to researchers involved in the study. Documentation must be stored by the PBC in a secure database.

After de-identification, the PBC contacts the researcher to schedule a pickup. To receive the tissue, the researcher must sign a disbursement receipt supplied by the PBC that confirms distribution of fetal tissue to a researcher that requested such tissue.

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<sup>38</sup> For tissue procured from fetal autopsy, the honest broker must confirm that a consent to fetal autopsy was obtained.

**Assessment:** The procedures for disbursement of fetal tissue comply with applicable federal and state requirements, and in some cases go beyond legal requirements. For example, the TCP specifies the use of an honest broker to ensure that only de-identified specimens are disbursed to researchers and requires the PBC to securely maintain patient identifiable information, thereby preventing access to such information by the researcher. Assigning responsibility for procurement and disbursement solely to the PBC also ensures that there is no direct contact between a researcher and UPMC personnel involved in obtaining informed consent or the patient from whom consent is being requested. Although these measures are not required by applicable laws and policies, they protect patient confidentiality and eliminate the possibility of improper influence by the researcher interested in obtaining fetal tissue on UPMC personnel or the patient.

Moreover, the TCP has multiple layers of verification to ensure legal compliance. Namely, the PBC honest broker checks to ensure that UPMC has obtained a signed Fetal Tissue Consent Form from the donor and that the researcher has an IRB-approved protocol and has signed the Agreement Relating to Use of Fetal Tissue in Research.

#### IV. Analysis of Completed or Pending Fetal Tissue Research Studies

HPM evaluated all research protocols involving the use of human fetal tissue and corresponding consent documents provided by Pitt. There have been 31 individual research studies using human fetal tissue since 2001.<sup>39</sup>

HPM reviewed all consent documents associated with each of the studies and confirmed that consent to donation had been obtained for all tissue used in the studies. A handful of the consent documents contained administrative errors.<sup>40</sup> Specifically, four consent forms for donation of human fetal tissue for research were not signed.<sup>41</sup> One consent form was signed by the surgical resident.<sup>42</sup> Because the PBC was not able to confirm that the surgical resident had not been involved with the procedure, the PBC did not accept the tissue for research use and it was discarded. Two consent forms were signed by Dr. Beatrice Chen. In an interview with Dr. Chen, she stated that it was her practice to discuss with patients the option to donate fetal tissue, but that a nurse was responsible for obtaining informed consent if a patient expressed interest in donating.<sup>43</sup>

HPM also evaluated the IRB process for review of studies involving human fetal tissue and determined it appropriately assessed compliance with applicable laws, regulations, and policies applicable to human fetal tissue research, and also appropriately evaluated the source of the fetal tissue as required by the TCP. Of the 31 individual studies involving human fetal tissue that were submitted to the IRB, 30 were determined to be exempt because they involved the use of de-identified fetal tissue only and, therefore, did not involve research with human subjects. One study was referred for IRB committee review because a portion of the study (that was unrelated to fetal tissue) involved sequencing the genome of individuals of a specific genotype on a patient-identifiable basis.

Of the 31 studies reviewed, five involved the use of fetal tissue from a source other than the PBC. Two of the five studies used tissue from the University of Washington, through an “NIH-funded program instituted to provide fetal tissues to NIH-funded investigators.”<sup>44</sup> One study, originally approved in 2004, used tissue from the Allegheny Reproductive Health Center (ARHC).<sup>45</sup> ARHC utilizes an honest broker system to distribute fetal tissue, and it certified to the

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<sup>39</sup> Note that, pursuant to Pitt’s document retention policies, Pitt retains records for at least seven years post conclusion of a research study.

<sup>40</sup> Note that sixteen consent forms require follow-up likely due to scanning errors when the document was digitized.

<sup>41</sup> Consent forms TP05-1012, TP12-334, TP15-M641, and TP16-M539.

<sup>42</sup> Consent form TP18-M58.

<sup>43</sup> Consent forms TP06-1464 and TP06-1870.

<sup>44</sup> The Pitt studies have the following identifiers: PRO10020037; PRO12040628. The University of Washington honest broker system is supported by NIH Award Number R24HD000836 from the Eunice Kennedy Shriver National Institute of Child Health & Human Development and has an Honest Broker system identifier: HB 000836.

<sup>45</sup> PRO07090092.

Pitt IRB that it would provide only de-identified tissue and would abide by PACA.<sup>46</sup> The other two studies used fetal tissue procured from Advanced Bioscience Resources, Inc. (ABR), a commercial tissue supplier. In those cases, the PI disclosed the proposed source of the tissue, and the IRB reviewed the information to ensure that the source was compliant with applicable laws.

- The Scientific Reports Study,<sup>47</sup> submitted to the IRB by Dr. Moses Bility, involved grafting fetal tissue from the scalp and dorsum onto immunodeficient mice and rats, in order to provide a means of studying human immune response to skin infection. Dr. Bility disclosed to the IRB that fetal tissue for the study would be obtained from ABR and submitted the terms and conditions under which ABR would procure the tissue, which included compliance with PACA. Specifically, ABR certified that it would adhere to PACA, including that no remuneration, compensation, or other consideration of any kind would be offered to a woman to consent to the use of fetal tissues for research and that the donor would not designate the recipient of fetal tissue. IRB staff reviewed the ABR process for collection to determine adherence to federal and state laws and regulations and reviewed the Terms of Service with ABR (which the PI confirmed with the ABR President). The IRB determined that tissue could be procured from ABR and that the study was exempt because it involved only de-identified tissue and therefore did not involve human subjects.<sup>48</sup>
- A research study titled, “Human fetal liver cell in vitro studies” studied fetal liver cells to “identify and characterize hepatic progenitor in human fetal liver.”<sup>49</sup> The study was intended to provide a basis for future studies involving extracorporeal biartificial liver support systems and/or cell transplantation, as a means to develop new treatment options for patients suffering from liver failure. The PI for this study, Dr. Gerlach, submitted the required application forms to the Pitt IRB in which he identified ABR as the source for fetal tissue. Dr. Gerlach stated in his application documents that ABR complied with PACA, had an IRB-approved fetal tissue protocol in place, and that ABR would de-identify any samples before providing them to researchers. The Pitt IRB determined that the source of the fetal tissue was acceptable and that the study was exempt.

HPM identified three studies that the IRB did not approve, for various reasons. One study was not approved because the application did not provide detail regarding the entire clinical program that was sufficient for the IRB to evaluate its risks and benefits. A second study was not

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<sup>46</sup> This certification was signed by the ARHC medical director (Dr. Morris E. Turner) and clinic director (Claire Keyes).

<sup>47</sup> Agarwal Y., Beatty C., Ho S. et al., *Development of humanized mouse and rat models with full-thickness human skin and autologous immune cells*, 10 Sci. Rep. 14,598 (2020).

<sup>48</sup> Due to compliance issues subsequently identified at ABR, the IRB is no longer permitting the use of tissue obtained from ABR.

<sup>49</sup> PRO012020516.

approved because it did not comply with PACA. A third study was not approved because the PI did not submit sufficient supporting data and because the IRB determined that it did not have jurisdiction over the study because it was conducted outside the United States.

HPM also interviewed numerous Pitt personnel to understand the IACUC process for review of studies involving human fetal tissue. IACUC evaluates scientific validity of the research and considers successful completion of the federal grants process as an indication of scientific merit, or, alternatively, support of the department chair. HPM concluded that IACUC review was conducted as needed for studies involving both fetal tissue and laboratory animals and that the IACUC process for reviewing the use of fetal tissue in animal studies was appropriate.

Two studies involved the use of rodents. The Scientific Reports Study,<sup>50</sup> described above, demonstrated successful co-engraftment of fetal tissue in a rodent model. A second study, for which Dr. Bility also served as the PI, involved the development of humanized mouse models using human fetal cells and thymus for the purpose of elucidating the “pathogenic mechanisms of hepatitis virus infections, HIV infections/co-infections and fatty liver disease,” with the goal being to then use the model to develop treatments for patients with these diseases.<sup>51</sup> Both of these studies were submitted for review and approved by the IACUC.

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<sup>50</sup> Agarwal Y., Beatty C., Ho S. *et al.*, *Development of humanized mouse and rat models with full-thickness human skin and autologous immune cells*, 10 Sci. Rep. 14,598 (2020).

<sup>51</sup> PRO18070556. For this study, Dr. Bility used human fetal tissue obtained from the PBC.

## V. Conclusions

Although the use of human fetal tissue in research may not be universally accepted, federal and state laws, as well as NIH grants policy, permit these activities as long as certain requirements are met. We have completed our assessment of Pitt's activities involving research using human fetal tissue and conclude that the University is fully compliant with federal and state regulatory requirements.

HPM can make several observations from its review. First, because the University researchers are blinded to a patient's abortion decision and the procedure itself, there is no pathway for the researcher to influence a woman to terminate her pregnancy or to donate fetal tissue for research. To receive fetal tissue, the PI must certify there will no communication with the healthcare provider performing the termination or the patient undergoing the termination procedure. Further, established procedures ensure that the UPMC clinician's decision on how the procedure is performed is independent from the woman's decision to donate fetal tissue. The Tissue Collection Protocol specifically states that the "attending physician retains the responsibility for determining the procedure to be used for termination of the pregnancy or treatment of a spontaneous abortion." We confirmed that the decision to donate fetal tissue post-dates the woman's decision to terminate, and that the healthcare provider does not know which researcher or research project will ultimately receive the donated human fetal tissue.

Second, there is no inherent conflict of interest in the IRB process for reviewing study protocols involving human fetal tissue. Upon submission of an application requesting the use of fetal tissue for research purposes, the IRB staff (who are not medical professionals) review the submission to confirm that the study is exempt from IRB review (i.e., that it does not involve the use of identifiable specimens or information from a human subject). IRB committee members review only those studies that are not deemed to be IRB-exempt. Based on our review, all but one of the studies involving human fetal tissue were deemed IRB-exempt. We confirmed that Dr. Beatrice Chen, a medical practitioner at UPMC and a Pitt IRB committee member, has not been involved in the IRB's review of any protocols involving human fetal tissue. IRB procedures are adequate to permit IRB committee members to recuse themselves in the event of any potential or perceived conflict. We note that the Pitt Audit Committee conducted its own review of a perceived conflict of interest by Dr. Chen and concluded that no conflicts or violations existed.

Third, our assessment did not find any illegal arrangement or quid pro quo between Pitt and Planned Parenthood of Western Pennsylvania. Pitt has no contractual arrangement with Planned Parenthood of Western Pennsylvania, nor would it be inherently unlawful for Pitt to have such an arrangement. There is no law preventing Pitt from supporting Planned Parenthood of Western Pennsylvania if it chooses to do so. We also confirmed that Planned Parenthood of Western Pennsylvania does not even collect human fetal tissue for research purposes, which undermines any allegation that Pitt engages in a relationship with Planned Parenthood to obtain fetal tissue.

Some confusion may exist about the role of certain individuals that work at Planned Parenthood. As noted, UPMC is an independent entity that provides medical services, and there



are some UPMC physicians who provide medical services at Planned Parenthood of Western Pennsylvania. OB-GYN residents or complex family planning fellows (who are employed by UPMC) also conduct rotations at Planned Parenthood. Pitt does not have oversight or responsibility for the clinical activities conducted by these individuals.

Fourth, Pitt does not use its access to fetal tissue from abortions conducted at UPMC as a mechanism to obtain NIH grant money. NIH grant money is not tied to the source of human fetal tissue. Pitt researchers could receive NIH funding for studies using human fetal tissue from sources other than the PBC, such as the two studies that used tissue obtained from the University of Washington.

Fifth, the process for obtaining informed consent from donors of human fetal tissue is proper and is intentionally silent as to the ultimate research use for the donation. Federal and state laws do not permit the donor to be told how donated human fetal tissue will be used because the doctor performing the abortion procedure, along with supporting medical personnel, are blinded as to the ultimate use of the donated human fetal tissue.

## **VI. Recommendations**

Although Pitt’s human fetal tissue research program is conducted lawfully, there are areas for improvement. The following recommendations can clarify and reinforce the requirements for researchers and other employees involved in the procurement, distribution, and use of human fetal tissue, and can help Pitt document its continued compliance with applicable laws.

### ***1) Tissue Collection Protocol***

It may be helpful to provide more detailed instructions for how to complete the Consent Forms that are used as part of the Tissue Collection Protocol. Issues for clarification can include: 1) identification of who may obtain the consent (e.g., that the consent cannot be obtained from the clinical provider performing the abortion procedure); 2) the categories of individuals who may obtain consent from the woman (e.g., non-operating room nurse; intake nurse); and 3) legal terminology for accuracy (e.g., that an IRB “approval” is not the same as an IRB “exempt” determination).

### ***2) Enhanced Oversight***

Although not required by law, it could be prudent for Pitt to use its audit authority through the Education and Compliance Committee, or other designee, to conduct periodic audits of the Tissue Collection Protocol, including the Fetal Tissue Consent Form, and of its implementation in individual fetal tissue studies conducted at Pitt. Because the Tissue Collection Protocol is unique in that it is intended to ensure compliance with applicable laws and policies, the audit function may need to include legal or regulatory review beyond the IRB. Periodic auditing could verify that the University continues to meet legal requirements for fetal tissue research.

Also, the Pitt IRB could, as part of the application process, further reinforce to researchers, the relevant requirements for the use of human fetal tissue. Although the IRB already has many safeguards in place, a reminder to experienced researchers and training for new researchers can be helpful. Documentation of periodic audits and training activities also may be useful to respond to any future allegations of noncompliance.

### ***3) Documentation of Process for Fetal Tissue Research***

Our assessment summarizes the activities for which the University is responsible related to human fetal tissue research. The University does not have a formal procedure that comprehensively documents this process (i.e., from submission of an application to the IRB through disbursement of tissue by the PBC). This documentation can be used for training purposes and could also provide good evidence of Pitt’s compliance with federal and state laws. A formal procedure could facilitate periodic reviews to ensure that the procedure reflects any changes in laws.

### ***4) Administrative Corrections to Consent Forms***

HPM identified consent forms that were not fully completed. These forms primarily appear to involve technical issues that are not material to legal compliance. We understand that around 2018 the PBC implemented a quality review process for evaluation of consent forms used in tissue

collection, so it is unlikely that any issues in the proper completion of Consent Forms will recur. Nevertheless, we recommend that the PBC review the forms that contain gaps and follow-up, if needed.

\* \* \*

## **Appendix 1**

# Research with Biological Specimens

## Request for Exempt or No Human Subject Involvement Determination

Principal Investigator: [REDACTED]

Study Title: [REDACTED]

1. Will de-identified frozen specimens (and if applicable, data) be obtained exclusively from the [Health Sciences Tissue Bank \(HSTB\)](#)? ☒ No ☐ Yes If Yes, **STOP** and submit directly to the HSTB using their application.
2. Is this research limited solely to the use of an FDA-regulated in vitro diagnostic (IVD) device study with leftover human specimens (or specimens from an IRB-approved repository) that are not individually identifiable? ☒ No ☐ Yes If Yes, **STOP**. Do not use this form. Instead submit the 'In Vitro Diagnostic Device - Informed Consent Exception Exempt form' displayed under [Exempt forms](#) on the HRPO website.
3. Will any information from this project be submitted to the FDA or held for inspection by the FDA? ☒ No ☐ Yes If Yes, **STOP** and contact [REDACTED]

### Part A - Source of Materials

Each source of materials should only be listed in one section based on the current location of the materials.

4. Will this study use residual specimens (and if applicable, data) obtained for clinical treatment or pathology purposes independent of this research project? ☐ No ☒ Yes If Yes, answer the following questions:
  - a. Name the clinical source of materials: The University of Pittsburgh Health Sciences Tissue Bank
  - b. Will the specimens (and if applicable, data - e.g. medical record information) be provided to this research team without personal identifiers or linkage codes? ☐ No ☒ Yes If No, explain:
  - c. Will an Honest Broker be used to de-identify these specimens (and if applicable, data)? ☐ No ☒ Yes If No, describe how the research team will receive specimens (and if applicable, data) without identifiers:
  - d. If paraffin tissue blocks from UPMC will be studied, provide the name of the pathologist who has reviewed this project and approved the allocation of tissue:  
Name: E-mail:
5. Will this study use specimens (and if applicable, data) obtained from a tissue bank or repository? ☐ No ☒ Yes If Yes, answer the following questions:
  - a. Name of the bank/repository: [REDACTED] The University of Pittsburgh Health Sciences Tissue Bank Provide the IRB number and attach the bank/repository consent to item E2.0 in OSIRIS. If not applicable, explain: [REDACTED] consent on file at IRB office
  - b. Will the specimens (and if applicable data) be provided to this research team without personal identifiers? ☐ No ☒ Yes If No, explain:
  - c. If paraffin tissue blocks from UPMC will be studied, provide the name of the pathologist who has reviewed this project and approved the allocation of tissue:  
Name: E-mail:
6. Will this study use specimens (and if applicable, data) obtained from a prior research study? ☐ No ☒ Yes If Yes, answer the following questions:

- a. Did the consent form signed by the subjects restrict the use of their samples in any way? ☒ No ☐ Yes  
If Yes, describe restrictions:
- b. Is copy of initial consent form attached? ☒ No ☐ Yes If No, explain why not: On file in the IRB office
- c. Information from the prior research study:
- i. Study Title: [REDACTED]
  - ii. PI name: [REDACTED]
  - iii. IRB number: [REDACTED]

7. Will this study use specimens (and if applicable, data) obtained directly from a commercial vendor?  
☒ No ☐ Yes If Yes, identify the vendor by name:

Part B

8. Will this study team access (look at) identifiers or identifiable information? ☒ No ☐ Yes  
If Yes, explain:

9. Will this study team collect or receive specimens (and if applicable, data) with identifiers or identifiable information? ☒ No ☐ Yes  
If Yes, **STOP**. This is not an exempt study. Submit a new expedited protocol for review.

10. Will this study team record subject identifiers and link them to the specimens (and if applicable, data)?  
☒ No ☐ Yes  
If Yes, **STOP**. This is not an exempt study. Submit a new expedited protocol for review.

11. Do the specimens (and if applicable, data) have a numerical code such that a link exists that could allow the specimens (and if applicable, data) to be re-identified? ☐ No ☒ Yes  
If Yes, is there a written agreement that prohibits the PI and research staff from accessing the link? ☐ No ☒ Yes  
If No, explain:

12. Are all specimens (and if applicable, data) in existence as of the date the application is submitted to the IRB?  
If No, this form should not be used unless this project qualifies for a "No Human Subjects determination" (see question 13). Otherwise, this project must be submitted for expedited review.

☒ **No; Address the following:**

- a. **Over what time period will the specimens/data be collected?** The samples will be collected for a period of at least two years
- b. **From what source?** From the Magee-Womens Hospital as part of the [REDACTED]
- c. **Who will collect the specimens (and if applicable, data)?** The Health Sciences Tissue Bank will collect all samples [REDACTED]

☐ **Yes; List the specific date range of records to be studied:** [Click here to enter start of date range](#) to [Click here to enter end of date range](#)

13. Does your study meet both of the following requirements: ☐ No ☒ Yes

- i. No member of the research team has interacted, for research purposes, with the individuals whose specimens (and if applicable, data) will be studied (note: if any members of this study team are/were affiliated with a research project you will obtain specimens (and if applicable data) from, you may not qualify for this determination)

**AND**

- ii. No identifiable private information will be reviewed or recorded

14. Are you explicitly requesting a “No Human Subject determination”? ☐ No ☒ Yes

[Note: If this project is NIH-funded, the grant application must explicitly indicate that at least a component of the study does not involve human subjects.]

15. If applicable, in what format will medical record information be provided to this study team?

Information about the HIPAA requirement can be found [here](#).

- a. ☒ De-identified (HIPAA “safe harbor”; none of the 18 HIPAA identifiers will be included)

- b. ☐ Limited Data Set (includes dates and certain geographic information)

i. Justify why dates and/or geographical information from medical record are needed to perform this study:

ii. Justify the need for each of the requested medical record data elements that are specified under item 17d below:

iii. For UPMC and/or University of Pittsburgh medical records: A completed Data Use Agreement for Limited Data Sets must be uploaded in the “other attachments” section of OSIRIS.

**Note:** This application cannot be processed without this form, signed by the recipient. For a copy of this form, contact [REDACTED]

- c. ☐ N/A – No medical record information will be collected

### Part C

16. How will the study be conducted? Fetal organs (Brain, gastrointestinal, placental) samples will be provided by the Magee Womens Hospital as part of the [REDACTED]  
[REDACTED] Fetal cells/tissues will be analyzed with immunofluorescence, flow cytometry, RNA and protein extraction.

17. Types of specimens (e.g., tissue, blood, bodily fluids) and if applicable, data to be studied:

- a. What specimens/data will be accessed? Human brain, small and large intestine, and placentas will be accessed. They will be provided by the Magee-Womens Hospital as part of the [REDACTED]  
[REDACTED]

- b. Describe the original collection of the specimens/data (how, where, and by whom): The samples will be collected for a period of 2 years from the Magee-Womens Hospital as part of the [REDACTED]  
[REDACTED] The Health Sciences Tissue Bank will collect the samples and distribute to the research team.

- c. If specimens/data are still being collected, who will be responsible for obtaining the specimens/data? The Health Sciences Tissue Bank [REDACTED] will collect specimens under consent of the IRB [REDACTED]

- i. Is that person a member of this research team? ☒ No ☐ Yes

d. If applicable, provide a list of data variables that will be collected (e.g., diagnosis, age, laboratory results, etc.): Gestational age and location of sample (i.e. small or large intestine)

e. Are personal identifiers associated with the original specimens/data? ☐ No ☒ Yes

If Yes, address the following questions:

i. Who will access the specimens/data and what is their right to do so? HTSB Staff as certified honest brokers

ii. Describe the process of obtaining specimens/data: [REDACTED]

iii. Describe how the specimens/data will be de-identified prior to being provided to this study team (if applicable): All specimens will be coded upon receipt in the HTSB

1. If specimens/data will be obtained from the University and/or UPMC, specify the identity of the IRB-approved Honest Broker System/Process that will be used in obtaining the specimens/data in section 2.13 of OSIRIS

OR

2. If a non-approved Honest Broker is used, provide a justification:

a. Name the person or group, independent of this research team, who has agreed to serve as the honest broker and has completed the honest broker assurance form:

b. Attach the signed honest broker assurance form in OSIRIS item E2.0.

18. If specimens/data will come from, or will be sent to, another institution, you must consult with the University of Pittsburgh Office of Research regarding any necessary transfer agreements ([www.research.pitt.edu](http://www.research.pitt.edu)). If you intend to share specimens/data, this must be addressed in OSIRIS item 5.8.

19. Additional Information, Clarification, or Comments for the IRB Reviewer:

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#### Final Process:

- Save this document to your computer and then upload into OSIRIS item E2.0
- If a certified honest broker will be used to provide de-identified specimens/data, answer YES to items 2.13 (honest broker) and 2.14 (medical records) in OSIRIS.
- If a certified honest broker or an independent individual (not associated with this research study) will de-identify specimens/data prior to providing it to this study team, attach a completed and signed Honest Broker Assurance form (found [under "Honest Broker Assurance Form" on the HRPO web site](#)) in OSIRIS item E2.0.



## **Appendix 2**

AGREEMENT RELATING TO USE OF  
FETAL TISSUE IN RESEARCH

The undersigned, having received approval by the IRB for use of fetal tissue, intending to be legally bound, hereby acknowledges and agrees that:

1. The use of human fetal tissue in research is governed by provisions of Pennsylvania's Abortion Control Act, 15 Pa. C.S.A. § 3216 and by the regulations of the Department of Health and Human Services and the Food and Drug Administration regarding the protection of human subjects in research (45 C.F.R. Part 46 and 21 C.F.R. Part 50). The undersigned agrees to abide by and comply with all applicable provisions of such state and federal laws as they now exist or may hereafter be amended in conducting the approved research project and to cause such compliance by all persons who may participate in the conduct of the research project.
2. The undersigned acknowledges that the undersigned has read the IRB approved policy on 'Research on tissue from an elective or spontaneous abortion < 24 weeks' of the source or sources of the fetal tissue and agrees to advise all persons participating in the research involving such tissue of the method(s) of its procurement.
3. The undersigned agrees that the fetal tissue will be used solely for medical research and that such fetal tissue and any products derived there from, will not be used for any commercial purposes.
4. The undersigned agrees to maintain the confidentiality of the medical information, if any, acquired by the undersigned in connection with its use of fetal tissue.
5. The undersigned hereby agrees to indemnify and hold Magee-Womens Hospital, its officers, directors, employees and medical staff harmless from and against any and all damages or losses it or they may suffer or incur, including reasonable attorneys' fees, arising of or as a consequence of the undersigned's use of fetal tissue in violation of applicable state or federal laws, including without limitation Pennsylvania's Abortion Control Act, or this Agreement.

**TISSUE ORIGIN AND TYPE**

**TYPE**

☐ Fetus/Fetal organs ☐ Placental tissue ☐ Maternal blood ☐ Maternal urine

**ORIGIN**

☐ Elective abortion ☐ Spontaneous abortion  
☐ Fetal death (IUFD) ☐ Neonatal death  
☐ Ectopic pregnancy

Date

Signature

Print Name



## **Appendix 3**



# Magee-Womens Hospital

of the University of Pittsburgh Medical Center

300 Halket Street  
Pittsburgh, PA 15213-3180

## CONSENT TO ACT AS A PARTICIPANT IN RESEARCH (FETAL TISSUE CONSENT FORM)

TITLE: [REDACTED]

PRINCIPAL INVESTIGATOR: [REDACTED]  
Magee-Womens Hospital, [REDACTED]

### ***Why is this research being done?***

Some researchers are performing studies of fetal tissue within the limits of the laws of Pennsylvania. For these studies, the researchers need to use tissue from pregnancies. This protocol allows us to collect and store tissue and facilitate the distribution of fetal tissue samples to those who have approved research protocols.

### ***Who is being asked to take part in this research?***

You are being asked to submit tissue for this research study after you have experienced a loss of pregnancy and have consented to a fetal autopsy.

### ***What procedures will be performed for research purposes?***

You are being asked to allow researchers at the University of Pittsburgh to use any of the tissue from the pregnancy, as needed, for research projects. We may collect a sample of your urine (about 6 tablespoons) and blood (about 1 tablespoon), if possible, to use for research projects. Your samples may undergo genetic analysis (DNA/RNA), including genotype and phenotype. The tissue and samples may also be used by other researchers. These research studies are approved by an ethics review board (Institutional Review Board or IRB) and are subject to oversight to make sure that they are conducted appropriately and within the laws of the Commonwealth of Pennsylvania and/or the state in which the research is being conducted.

We are also requesting your authorization or permission to review your medical records. We will obtain the following information: data related to pregnancy, tissue and maternal health. Your signed consent form will be placed in your medical record. This research will involve collecting information from your medical records but your identity will only be known to the person (honest broker) collecting this information. Identifiable information will never be provided to any researchers.

Your participation is completely voluntary. If you agree to allow your samples to be included as part of this collection protocol, they will become the property of the University of Pittsburgh. Your medical information and samples will be stored at the University of Pittsburgh and/or at other federal research repositories until such time that the samples are used up or no longer felt to be appropriate for use in research studies. Your voluntary decision to provide these samples and identifiable medical information to the inclusion of this study, or to later withdraw from it, will not affect your current or future medical care at UPMC.

Your samples will be stored in a way that will permit the people responsible for the samples (honest brokers) to connect your identity with your samples. However, when your medical information, samples, and data/information about tests done on your samples (including genotype and phenotype) are made available for actual use in research studies, they will be provided to researchers without personal identifiers. Researchers will not be able to connect your identity with the data, samples, or medical information. Your de-identified samples, results (genotype and phenotype) from samples and medical information may also be shared with other federally-funded tissue banks, shared data bases (both unrestricted-access and controlled-access repositories) and researchers, who may also share samples and medical information with other researchers. You will not be contacted when your samples or information are sent to researchers. Note that these samples will be released only after it is ensured proper research approvals are received (i.e. IRB approval). Because it will not be possible to connect your identity with your tissue/biological sample when the sample is being used for research, it will not be possible to inform you of the results of such research.

***What are the possible risks, side effects and discomforts of this research?***

If you agree to allow us to collect blood, we will collect blood by putting a needle into one of your veins and letting the blood flow into a tube. You may feel some pain and experience some bleeding when the needle goes into your vein. Although rare, there is a risk of fainting and infection from taking blood. You may have a small bruise where the needle went under the skin.

There is a risk of breach of confidentiality. The risks associated with genetic studies include the potential for a breach of confidentiality which could affect future insurability, employability, or reproduction plans, or have a negative impact on family relationships and/or result in paternity suits or stigmatization. However, we have put measures in place to reduce these risks. No information will be given to any researchers that would allow them to identify you in any way. A federal law called the Genetic Information Nondiscrimination Act (GINA) helps protect you from being treated unfairly because of your genes.

***What are the possible benefits from taking part in this research?***

There is no personal or direct benefit to you from participating in this research. However, a potential benefit to society from this research is a gain in knowledge.

***What treatments or procedures are available if I decide not to take part in this research?***

You do not have to agree to participate in this study. Your participation is completely voluntary. Your care and benefits will be the same whether you agree to participate in this study or not.

***Will my insurance provider or I be charged for the costs of any procedures performed as part of this research?***

There are no costs to you or your insurance provider for participating in this research (urine sample, blood sample, medical record information, fetal tissue collection). You will be charged in the standard manner for any clinical care/clinical procedures.

***Will I be paid if I take part in this research?***

You will not be paid for allowing your fetal tissue to be used for research or for your participation. Your samples may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by researchers and the University of Pittsburgh for use in other research or the development of new products. You will

not retain any property rights nor will you share in any money which researchers, the University of Pittsburgh, or their agents may realize. There are no costs to you for participating.

***Who will pay if I am injured as a result of participation in this research?***

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

***Who will know about my participation in this research?***

The honest brokers will have access to identifiable information linking you to your samples. However, no researchers will be provided with any identifiable information or samples. The University of Pittsburgh Research Conduct and Compliance Office may have access to your records (including your identifiable medical information) for the purposes of monitoring the conduct of this project.

This authorization is valid for an indefinite period of time.

You may withdraw your authorization to review your medical records, and your consent for the collection and use of your fetal tissue, blood, and/or urine. However, once data or samples have been shared with researchers, there will be no way to get the data/samples back as researchers are not provided with any identifiers. To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

***How long will records be maintained?***

Research records will be kept indefinitely but at least 7 years after completion of the research.

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**VOLUNTARY CONSENT**

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research during the course of this research, and that such future questions will be answered by the researchers listed on the first page of this form. Any questions which I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research and provide my authorization to share my medical records, as described above. I agree to donate one or more of the following samples. A copy of this consent form will be given to me.

☐ Tissue

- ☐ Urine
- ☐ Blood
- ☐ All of the above

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Participant's Signature

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Date

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Participant's Printed Name

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research to the above-named individual, and I have discussed the potential benefits and possible risks of the research participation. Any questions the individual has about this research have been answered, and we will always be available to address future questions as they arise.

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Printed Name of Person Obtaining Consent

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Role in Research

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Signature of Person Obtaining Consent

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Date

Hyman, Phelps & McNamara, P.C. has completed its written assessment for the University of Pittsburgh. If you have any questions or require discussion, please contact us at:

Anne K. Walsh

[awalsh@hpm.com](mailto:awalsh@hpm.com)

202-737-4592 (office)

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