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Fetal Tissue Research: Frequently Asked Questions

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This report provides answers to frequently asked questions concerning the regulation and use of fetal tissue in research, including a description of what constitutes fetal tissue research, uses of fetal tissue for medical purposes, and how such tissue is acquired, along with rules and regulations governing the use and acquisition of fetal tissue.

What is fetal tissue?

Fetal tissue is any tissue or organ obtained from a fetus, which is the product of conception (egg and sperm) from the end of the eighth week of pregnancy onward. Prior to the ninth week, the product of conception is called an embryo.

What is fetal tissue research?

Researchers use fetal tissue to produce cell cultures, also called cell lines, which can be maintained in a laboratory environment for very long periods of time, in some cases indefinitely. Cultured cells mimic many of the properties that they have in a living body, and therefore can be used as a model for researchers studying basic biological processes. Research involving fetuses and fetal tissue has been conducted in the United States since the 1930s, and the National Institutes of Health (NIH) has been supporting research using fetal tissue since the 1950s.¹ NIH spent \$76 million on human fetal tissue research in FY2014, and will spend an estimated \$76 million in FY2015 and \$77 million in FY2016.²

What are the uses of fetal tissue in medicine and medical research?

Fetal tissue has been used “to identify and test the efficacy of vaccines and to examine the toxicity of drugs used by pregnant women. Vaccines for polio, measles, rubella and Rh disease were developed through the use of fetal tissue or cell lines derived from fetal tissue.”³ Human fetal tissue is used to study normal human development in order to gain insight into birth defects and other developmental diseases. Fetal tissue has been used in studies of genetic disease in the early stages of development, including organ formation.

¹ Patricia Donovan, “Funding Restrictions on Fetal Research: The Implications for Science and Health,” *Family Planning Perspectives*, vol. 22, no. 5 (September/October 1990), pp. 224-231; and, Dorothy E. Vawter and Arthur Caplan, “Strange Brew: The Politics and Ethics of Fetal Tissue Transplantation Research in the United States,” *Journal of Laboratory Clinical Medicine*, vol. 120, no. 1 (July 1992), pp. 30-34.

² At http://report.nih.gov/categorical_spending.aspx, putting “human fetal tissue” in the search box reveals the dollar amount spent or estimated by NIH for FY2011- FY2016. Clicking on the dollar amount for FY2011-FY2014 reveals the number of projects as well as details on each research project using human fetal tissue.

³ Donovan, “Funding Restrictions on Fetal Research,” p. 227.

What is human fetal tissue transplantation research?

Since the late 1920s, researchers in several countries, including the United States, “have grafted fetal liver, nerve, thymus and pancreas tissue into children and adults in efforts to reverse various neurological disorders, spinal cord injuries, diabetes, immune deficiencies, cancers and life-threatening blood diseases.”⁴ Perhaps the most widely known application in the field of human fetal tissue transplantation has been the treatment of Parkinson’s disease. The first such attempt, using the transplantation of human fetal brain cells, “took place in 1987 at Lund University in Sweden where the technique was pioneered.”⁵ Although controversial at the time, the approach “produced such striking results in some cases that by 1997 about 200 patients around the world had received the treatment.”⁶ However, because many patients did not benefit from the treatment, and it was unclear why this was the case, an international moratorium was imposed in 2003 on such replacement-therapy trials.⁷

In 2006, a retrospective analysis conducted by the original seven teams that had performed the transplant experiments “worked out that the procedure tended to be most effective in patients who were relatively young and whose disease was at an early stage.”⁸ In addition, “those who benefited the most had at least 100,000 dopamine-producing cells of fetal origin integrated into their brains. Cells from at least three fetuses are needed to achieve these numbers.”⁹ As a result, a new trial—called TRANSEURO, funded by the European Union—is being launched using dopamine-producing cells from fetal brains.¹⁰ The trial was scheduled to begin in July 2014 and expects to enroll 150 patients in the United Kingdom, Sweden, France, and Germany.¹¹

Similar trials involving the implementation of various types of stem cells into individuals with Parkinson’s disease are scheduled to begin in 2016 in Kyoto, Japan (using induced pluripotent stem cells); 2017 in New York; and 2018/2019 in Europe (both using human embryonic stem cells).¹² According to one source, many such human embryonic stem cell (ESC) lines “have now been generated that are well characterized and quality controlled and this includes two human ESC-based sources that have already been approved by the U.S. FDA for early stage clinical trials in humans.”¹³

⁴ Donovan, “Funding Restrictions on Fetal Research,” p. 227; and, Vawter and Caplan, “Strange Brew,” p. 30.

⁵ Allison Abbott, “Fetal-cell revival for Parkinson’s,” *Nature*, vol. 510 (June 12, 2014), pp. 195-196.

⁶ Constance Holden, “Fetal cells again?,” *Science*, vol. 326 (October 16, 2009), pp. 358-359.

⁷ Abbott, “Fetal-cell revival for Parkinson’s,” p. 195.

⁸ *Ibid.*

⁹ *Ibid.*

¹⁰ *Ibid.*, p. 196.

¹¹ *Ibid.* For further information about the trial, see <http://www.transeuro.org.uk/>.

¹² Abbott, “Fetal-cell revival for Parkinson’s,” p. 196.

¹³ Janelle Drouin-Ouellet and Roger A. Barker, “Stem cell therapies for Parkinson’s disease: are trials just around the corner?,” *Regenerative Medicine*, vol. 9, no. 5 (2014), pp. 553-555.

How is fetal tissue acquired for research?

Fetal tissue used in research is obtained from elective abortions. Under certain rare circumstances, fetal tissue may also be obtained from a miscarriage, also called a spontaneous abortion, or following the removal of an ectopic pregnancy, which occurs when an embryo has implanted outside the uterus. Because the timing or recognition of a spontaneous abortion or ectopic pregnancy is unpredictable, and both conditions may result in a serious health emergency for the woman, the fetal tissue collected under these circumstances is often not suitable for research purposes.

According to a Government Accountability Office (GAO) report published in October 2000, most biomedical researchers at that time obtained human fetal tissue from a “central tissue supplier”; three identified as receiving NIH funding included the Birth Defects Laboratory at the University of Washington, the Brain and Tissue Banks for Developmental Disorders at the University of Maryland, and the University of Miami School of Medicine/Children’s Hospital of Orange County.¹⁴ According to a 1992 journal article, NIH had funded such a center for collecting fetal tissue for many years.¹⁵ Another source of human fetal tissue mentioned in the GAO report was “private, nonprofit central tissue supply organizations that did not directly receive federal funds.”¹⁶ Those identified by GAO in 2000 were Advanced Bioscience Resources, Inc. (Alameda, CA), and the Albert Einstein College of Medicine Human Tissue Repository (New York, NY). Alternatively, some researchers obtained fetal tissue directly from an academic medical center hospital or a health clinic.¹⁷

A recent media article states that “many researchers buy tissue from two small California companies,” StemExpress, in Placerville, and Advanced Bioscience Resources Inc. (ABR), in Alameda, “a nonprofit that has 12 employees and recent sales of about \$1.4 million.”¹⁸ According to the article, fetal tissue accounted for about 10% of StemExpress’s business and the tissue “has been used in studies of leukemia, Hodgkin’s lymphoma and Parkinson’s disease.”¹⁹

Can fetal tissue be sold for research purposes?

Under the NIH Revitalization Act of 1993, it is “unlawful for any person to knowingly acquire, receive, or otherwise transfer any human fetal tissue for valuable consideration if the transfer affects interstate commerce.”²⁰ While this provision prohibits the sale or purchase of fetal tissue itself, the term *valuable consideration* “does not include reasonable payments associated with the

¹⁴ U.S. General Accounting Office, *Human Fetal Tissue: Acquisition for Federally Funded Biomedical Research*, GAO-01-65R, October 4, 2000, p. 4.

¹⁵ Vawter and Caplan, “Strange Brew,” p. 30.

¹⁶ U.S. General Accounting Office, *Human Fetal Tissue: Acquisition for Federally Funded Biomedical Research*, GAO-01-65R, October 4, 2000, p. 5.

¹⁷ U.S. General Accounting Office, *Human Fetal Tissue: Acquisition for Federally Funded Biomedical Research*, GAO-01-65R, October 4, 2000, pp. 4-5.

¹⁸ Denise Grady and Nicholas St. Fleur, “Shadowy Trade in Fetal Tissue,” *The New York Times*, July 28, 2015, pp. D1, D3.

¹⁹ *Ibid.*

²⁰ PHS Act §498B; 42 U.S.C. §289g-2(a).

transportation, implantation, processing, preservation, quality control, or storage of human fetal tissue.”²¹ Thus, tissue companies may charge researchers to recover the costs associated with these types of activities.

Persons violating these provisions shall be subject to fines, imprisonment for not more than 10 years, or both.²² Violations involving the payment of valuable consideration shall result in fines reflecting not less than twice the amount of the valuable consideration received.²³

According to the founder of StemExpress, the fetal cells are difficult to isolate and involve “expensive processes that take millions of dollars of equipment. Just to attempt to do some of these isolations can cost us thousands of dollars, and it may not even work.”²⁴ As an illustration of just how expensive, “a vial containing five million frozen fetal liver CD133+ stem cells can cost more than \$24,000 ... and an overnight shipment to Germany, for example, can cost thousands of dollars.”²⁵ Another supplier of fetal tissue, ABR, charged “\$300 a specimen for tissue from a second-trimester fetus, and \$515 if the fetus was first-trimester,” according to a 2013 price sheet.²⁶

Who investigates the illegal sale of fetal tissue?

On the federal level, the Department of Justice, and more specifically the Federal Bureau of Investigation (FBI), would open investigations into individuals and entities suspected of violating federal law with respect to the illegal sale, or trafficking, of human fetal tissue and other organs. As noted earlier, federal law prohibits the sale or purchase of human fetal tissue in interstate commerce.²⁷ In 2000, the FBI reportedly investigated a Kansas clinic affiliated with Planned Parenthood for allegedly selling—and profiting from the sale of—fetal tissue; ultimately, no laws were found to have been broken.²⁸

What federal regulations govern the collection and use of fetal tissue for research?

Federal law permits the Department of Health and Human Services (HHS) to fund *research on new therapies that involve the transplantation of human fetal tissue* using tissue derived from an elective or spontaneous abortion, or from a stillbirth.²⁹ However, human fetal tissue may be used for such purposes only if the following conditions are met:

²¹ PHS Act §498B; 42 U.S.C. §289g-2(e)(3).

²² 42 U.S.C. §289g-2(c)(1).

²³ 42 U.S.C. §289g-2(c)(2).

²⁴ Grady and St. Fleur, “Shadowy Trade in Fetal Tissue,” p. D3.

²⁵ Ibid. See also a StemExpress price list at <http://stemexpress.com/product-category/fetal-liver/>.

²⁶ Ibid.

²⁷ PHS Act §498B; 42 U.S.C. §289g-2(a).

²⁸ Sandhya Somashekhar and Danielle Paquette, “Undercover video shows Planned Parenthood Official Discussing Fetal Organs Used for Research,” *The Washington Post*, July 14, 2015.

²⁹ PHS Act §498A(a); 42 U.S.C. §289g-1(a).

- The woman must provide her written consent that she is donating the fetal tissue for research, that the donation is being made without any restrictions on who may receive the tissue, and that she has not been informed of the identity of any such recipients.³⁰
- The attending physician must declare in writing that, in the case of an induced abortion (1) the woman's consent for the abortion was obtained prior to requesting or obtaining consent to donate the fetal tissue for research; (2) the timing, method, or procedures used to terminate the pregnancy were not altered in order to obtain the tissue; and (3) the abortion was performed in accordance with applicable state law. In addition, the attending physician must declare that the tissue has been donated with the woman's consent and that the woman has been fully informed of the physician's interest, if any, in the research, and of any medical or privacy risks associated with the tissue donation.³¹
- The principal researcher must declare in writing that (1) he or she is aware that the tissue is human fetal tissue that may have been obtained from an elective or spontaneous abortion, or a stillbirth, and that it was donated for the purposes of research; and (2) prior to obtaining the informed consent of a research subject to be a recipient of the transplanted tissue (see discussion of Common Rule, below), he or she will provide the same information about the fetal tissue to the research subject and get written acknowledgement of receipt of such information.³²

In addition to the above statutory requirements, fetal tissue research that involves human subjects is subject to the Common Rule.³³ Under the Common Rule, research protocols must be approved by an Institutional Review Board (IRB) to ensure that the rights and welfare of the research subjects are protected.³⁴

The Common Rule lists several criteria for IRB approval, including the requirement that researchers obtain the informed consent of their research subjects.³⁵ In addition, it sets out the types of information that must be provided to prospective research subjects during the informed consent process, including an explanation of the purpose of the research, a description of the research procedures, and a description of the risks and benefits of the research.³⁶ An IRB may decide to waive the informed consent requirement if it determines that (1) the research poses no more than minimal risk to the subjects, (2) the waiver will not adversely affect the rights and welfare of the subjects, and (3) the research is not practicable without a waiver.³⁷

If the human fetal tissue to be used in the research is identifiable, such that information associated with the material links it to one or more living individuals (which often may be the case), then

³⁰ PHS Act §498A(b)(1); 42 U.S.C. §289g-1(b)(1).

³¹ PHS Act §498A(b)(2); 42 U.S.C. §289g-1(b)(2).

³² PHS Act §498A(c); 42 U.S.C. §289g-1(c).

³³ The Common Rule is the informal name given to core federal regulations governing the protection of human subjects in research supported or conducted by the federal government. The regulations were first promulgated by HHS at 45 C.F.R. Part 46, Subpart A.

³⁴ 45 C.F.R. §46.109.

³⁵ 45 C.F.R. §46.111(a)(4).

³⁶ 45 C.F.R. §46.116(a).

³⁷ 45 C.F.R. §46.116(d).

those individuals also become research subjects under the Common Rule.³⁸ Thus, an IRB may have to review the protocol for collecting and testing the human fetal tissue, and the woman who is donating the tissue may have to provide informed consent (unless waived by the IRB).

The researchers must also obtain prior approval from the Food and Drug Administration (FDA) by filing an Investigational New Drug (IND) application if the research is testing a new diagnostic or therapeutic intervention that the researchers hope will receive FDA marketing approval. One of the IND requirements is that the researchers obtain IRB approval.

Importantly, if the purpose of the human fetal tissue research is simply to acquire new biomedical knowledge, and it is not being conducted under an IND or involving human research subjects, then the research is not subject to the Common Rule or FDA regulation.

Finally, the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule applies if the researchers want access to medical information about the woman from whose fetus the fetal tissue was obtained. Under the Privacy Rule, an individual's medical information may not be used or disclosed for research without the individual's written authorization unless an IRB (or equivalent Privacy Board) waives the authorization based on certain specified criteria.³⁹

What federal regulations govern the clinical use of fetal tissue?

Currently, fetal tissue is not being used in any clinical applications involving transplantation. Any such therapeutic use of human fetal tissue that received approval from the FDA would be regulated under the agency's Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) regulations.⁴⁰ An HCT/P is an article "containing or consisting of human cells and tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient."⁴¹ HCT/Ps include bone, ligament, skin, dura mater, heart valves, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, and semen or other reproductive tissue.⁴²

FDA regulates HCT/Ps primarily under its general authority to control the spread of communicable diseases.⁴³ The HCT/P regulations are focused on (1) preventing the use of contaminated cells and tissues with the potential for transmitting infectious diseases, (2) preventing the improper handling or processing of cells and tissues that might contaminate or damage them, and (3) ensuring the clinical safety and effectiveness of cells and tissues.

³⁸ 45 C.F.R. §46.206.

³⁹ 45 C.F.R. §164.512(i).

⁴⁰ 21 C.F.R. Part 1271.

⁴¹ 21 C.F.R. §1271.3.

⁴² *Ibid.* HCT/Ps do not include vascularized human organs for transplantation, which are regulated by the Health Resources and Services Administration (HRSA). Nor do they include plasma and blood or derivative products regulated by FDA under 21 C.F.R. Parts 606, 607, 630, and 640.

⁴³ PHS Act §361; 42 U.S.C. §264.

The regulations require establishments that recover, handle, store, and distribute HCT/Ps for clinical purposes to register with FDA and submit a list of their products.⁴⁴ The regulations also establish eligibility criteria for donors of HCT/Ps, including donor screening and testing.⁴⁵ Finally, the regulations include a set of good tissue practices (GTPs) that govern the methods, facilities, and controls used to deal with HCT/Ps.⁴⁶ The GTPs address personnel, procedures, environmental control and monitoring, equipment, supplies and reagents, recovery, processing and process controls, storage, shipment and distribution, records, tracking, and complaints.

Is the system for collecting non-fetal organs and tissue different from that for fetal tissue?

The federal government has established policies and a system for procuring organs that are separate from policies for the acquisition of fetal tissue. Organs are procured (or acquired) from living persons or cadavers. An organ is “[a] human kidney, liver, heart, lung, pancreas, or intestine (including the esophagus, stomach, small or large intestine, or any portion of the gastrointestinal tract), or vascularized composite allograft.” The National Organ Transplant Act (NOTA of 1984; P.L. 98-507) created the Organ Procurement and Transplantation Network (OPTN), which is the federally supported system for organ sharing in the United States. The Health Resources and Services Administration (HRSA) oversees organ procurement by way of the OPTN’s operations.

Does the Department of Veterans Affairs (VA) allow the use of human fetal tissue in research conducted by VA researchers?

No. The Veterans Health Administration (VHA) states that “research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue), cannot be conducted by VA [researchers] while on official duty, at VA facilities, or at VA-approved off-site facilities.”⁴⁷ Additionally, the use of stem cells are governed by the policy set by NIH for recipients of NIH research funding.

Does the Department of Defense use fetal tissue in medical research?

No. The Department of Defense medical research programs are not using fetal tissue in medical research at this time. However, there is not a blanket ban on the use of such tissue. Under

⁴⁴ 21 C.F.R. Part 1271, Subpart B.

⁴⁵ 21 C.F.R. Part 1271, Subpart C.

⁴⁶ 21 C.F.R. Part 1271, Subpart D.

⁴⁷ Department of Veterans Affairs, Veterans Health Administration, “Requirements for the Protection of Human Subjects in Research,” VHA Handbook 1200.05, November 12, 2014.

Department of Defense Instruction 3216.02, entitled Protection of Human Subjects and Adherence to Ethical Standards in DOD-Supported Research, any “research involving human subjects using fetal tissue shall comply with sections 289g–289g-2” of title 42, United States Code.⁴⁸

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⁴⁸ <http://www.dtic.mil/whs/directives/corres/pdf/321602p.pdf>.