RESEARCH ON HUMAN FETAL TISSUE: LEGAL ANALYSIS

A. HISTORICAL OVERVIEW

Since at least the 1930s, American biomedical research has involved ex utero fetal tissue as both a medium, and increasingly, an object for experimentation. The 1954 Nobel Prize for Medicine, for example, was awarded to American immunologists using cell lines obtained from human fetal kidney cells to grow poliovirus in tissue cultures other than nerve tissue. It was not until 1972, in a period that coincided with a larger societal debate over elective human abortion, that the use of ex utero fetal tissue for research (along with research involving fetuses generally) became controversial. In 1974, following the imposition a year earlier of a moratorium on federally-funded research on live fetuses, Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission recommended guidelines applicable to research conducted or funded by DHHS (then DHEW) and in 1975, the Department adopted regulations governing fetal tissue research while Congress passed similarly directed legislation.

Controversy erupted again in October 1987 when NIH scientists presented Director James B. Wyngaarden with a request to fund research on Parkinson's disease involving fetal brain tissue transplantation, already approved by an internal NIH review board. Director Wyngaarden sought an opinion from HHS Assistant Secretary Robert Windom, who responded

¹ <u>See e.g.</u> Gregory Gelfand & Toby R. Levin, "Fetal Tissue Research: Legal Regulation of Human Fetal Tissue Transplantation," <u>Washington & Lee Law Review</u> 50 (1993): 668; Cory Zion, "Comment, The Legal and Ethical Issues of Fetal Tissue Research and Transplantation," <u>Oregon Law Review</u> 75 (1996): 1282.

² <u>See</u> Gelfand & Levin, "Fetal Tissue Research," 668; Edgar Driscoll, Jr., "Nobel Recipient John Enders, 88; Virus Work Led to Polio Vaccine," Boston Globe, 10 September 1985: sec. Obituary.

³ <u>See</u> Gelfand & Levin, "Fetal <u>Tissue Research</u>," 668. In part as a result of that controversy, the National Institutes of Health (NIH) in 1973 imposed a temporary moratorium on federally funded research on live fetuses, <u>Id.</u>
⁴ Public Law 93-348 (Section 201 of the National Research Act).

⁵ National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Research on the Fetus: Report and Recommendations (Washington, D.C.: 1975); 45 C.F.R § 46.201-.211 (1997); 42 U.S.C. 274e (1997); 42 U.S.C. § 289g(a) (1997).

⁶ <u>See</u> James E. Goddard, "Comment, The NIH Revitalization Act of 1993 Washed Away Many Legal Problems with Fetal Tissue Transplantation Research But a Stain Remains," <u>SMU Law Review</u> 49 (1996): 383-84.

by declaring a temporary moratorium on federally funded transplantation research on fetal tissue from induced abortions. In March 1988, the Assistant Secretary asked NIH to establish an advisory committee to consider whether such research should be conducted and under what conditions.⁸ The twenty-one member Human Fetal Tissue Transplantation Research Panel (HFTTRP), composed of a cross-section of medical researchers, lawyers, ethicists, clergy, and politicians, deliberated until the Fall of 1988. The panel voted 19-2 to recommend continued funding for fetal tissue transplantation research, including guidelines to assure the ethical integrity of any experimental procedures. ⁹ In November 1989, HHS Secretary Louis Sullivan extended the moratorium indefinitely, adopting the position of minority panel-members who believed that such fetal tissue research would increase the incidence of elective abortion. 10 Two attempts by Congress to override the Secretary's decision were vetoed by President Bush and were not enacted into law.¹¹

In October 1992, a consortium of disease advocacy organizations filed suit against HHS Secretary Sullivan, alleging that the Hyde Amendment (banning federal funding for abortions) did not apply to research on and transplantation of fetal tissue, and moreover, that the fetal tissue transplantation research ban was beyond HHS's statutory authority under the law. 12 This suit

⁷ See Kenneth J. Ryan, "Symposium on Biomedical Technology and Health Care: Social and Conceptual Transformations: Technical Article: Tissue Transplantation from Aborted Fetuses, Organ Transplantation from Anencephalic Infants and Keeping Brain-Dead Pregnant Women Alive Until Fetal Viability," Southern California Law Review 65 (1991): 687 ("Although such approval [from the Assistant Secretary] was not required, the Assistant Secretary was consulted because of the scientific and ethical implications of the study").

⁸ Id. at 687 ("In the meantime the protocol was shelved and a moratorium placed on any use of NIH funding for such activities").

⁹ See Pedro F. Silva-Ruiz, "SECTION II: The Protection of Persons in Medical Research and Cloning of Human Beings," American Journal of Comparative Law 46 (1998): 278-279; Kimberly Fox Duguay, "Fetal Tissue Transplantation: Ethical and Legal Considerations," Buffalo Women's Journal of Law and Social Policy 1 (1992):

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10</sup> See Goddard, "NIH Revitalization Act," 384.

11 Id.; Also during this period, in an apparent attempt to find an alternative to fetal tissue derived from elective derived from established (without success) a tissue bank to collect fetal tissue for research from a contain pathological defects, the ectopic pregnancies and miscarriages. Because spontaneously aborted tissue may contain pathological defects, the use of ectopic and miscarried abortuses is disfavored for transplantation and most other research.

¹² Nikki Constantine Bell, "Regulating Transfer and Use of Fetal Tissue in Transplantation Procedures: The Ethical Dimensions," American Journal of Law & Medicine 20 (1994): 280.

was mooted on January 22, 1993 when the new administration shifted national biomedical policy and directed HHS Secretary Donna Shalala to remove the ban on federal funding for human fetal tissue research.¹³ On February 5, 1993, Secretary Shalala officially rescinded the moratorium, and in March 1993, NIH published interim guidelines for research involving human fetal tissue transplantation.¹⁴ Governing legislation was quickly proposed in Congress, and President Clinton signed the NIH Revitalization Act of 1993 into law on June 10, 1993.¹⁵

It is important to note that, throughout the period of controversy over the use of fetal tissue from induced abortions in transplantation, other areas of fetal tissue research continued to receive governmental funding and attention. One journalist has observed that "during the period of the moratorium, NIH—except for studies involving fetal material obtained from elective abortions—continued to support human fetal tissue research. In 1992, this support totaled some \$12.4 million, more than 90 percent of which went toward extramural projects."¹⁶

B. FEDERAL STATUES

(1) NIH Revitalization Act of 1993

Codified at 42 U.S.C. § 289g-1 & g-2, the NIH Revitalization Act of 1993 includes most prior statutory and regulatory provisions on research involving fetal tissue transplantation. In substance, any tissue from any type or form of abortion may be used for research on transplantation, but only for "therapeutic purposes." Note, however, that such research is not unfettered. First, it must be conducted in accordance with applicable State and local law (see

¹³ 58 F.Reg. 7457 (22 January 1993).

¹⁴ DHHS. OPRR Reports, <u>Human Subjects Protections: Fetal Tissue Transplantation—Ban on Research Replaced by New Statutory Requirements</u>, by Gary B. Ellis, Director, OPRR (Bethesda, MD: 1994), 1-2. The NIH guidelines were withdrawn upon passage of Public Law 103-43 ("NIH Revitalization Act of 1993"), codified at <u>NIH Revitalization Act of 1993</u>, U.S. Code, vol. 42, secs. 289g-1 & 289g-2 (1997) as Section 498A of the Public Health Service Act.

¹⁵ Id.

¹⁶ Myrna E. Watanabe, "Research: With Five-Year Ban on Fetal Tissue Studies Lifted, Scientists are Striving to Make Up for Lost Time," The Scientist 7 (4 October 1993): 1.

¹⁷ 42 U.S.C. § 289g-1(a)(1) (1997). <u>See</u> Goddard, "NIH Revitalization Act," 390, 394 ("a huge problem... Congress neglected to define the term 'therapeutic purposes' ...").

discussion, infra). ¹⁸ Second, a written statement must be obtained from the mother/donor verifying that (a) she is donating fetal tissue for therapeutic purposes; (b) no restrictions have been placed on the identity of the recipient; and (c) she has not been informed of the identity of the recipient. ¹⁹ Third, the attending physician must sign a written statement affirming five additional requirements about the abortion, effectively placing a "fire wall" between the decision to abort and the decision to donate tissue for fetal research. ²⁰ Finally, the person principally responsible for the experiment must affirm his or her own knowledge of the source of the tissue, that others involved in the research are also aware of this fact, and that he or she had no part in the decision or timing of the abortion.²¹ The drafters included no specific penalties in 42 U.S.C. § 289g-1.

By contrast, 42 U.S.C. § 289g-2 provides significant criminal and civil penalties for violation of four prohibited acts (relating to interstate commerce, for purposes of jurisdiction): (1) purchase or sale of fetal tissue "for valuable consideration" beyond "reasonable payments [for] transportation, implantation, processing, preservation, quality control, or storage ..."; (2) soliciting or acquiring fetal tissue through the promise that a mother/donor can designate a donee; (3) soliciting or acquiring fetal tissue through the promise that the transplant will be made into a relative of the mother/donor; or (4) soliciting or acquiring fetal tissue after providing "valuable consideration" for the costs associated with the abortion itself. 22

Human Research Extension Act of 1985 (2)

Codified at 42 U.S.C. § 289g, this statute provides guidance on fetal research generally, directing that no Federal research or support may be conducted on a nonviable living human

¹⁸ 42 U.S.C. § 289g-1(e) (1997).

¹⁹ 42 U.S.C. § 289g-1(b)(1) (1997). ²⁰ 42 U.S.C. § 289g-1(b)(2) (1997).

²¹ 42 U.S.C. § 289g-1(c) (1997).

²² 42 U.S.C. § 289g-2(a)-(c) (1997). But see Goddard, "NIH Revitalization Act," 393-94 (criticizing vague terms; questioning constitutionality of ban on recipient designation).

fetus ex utero or a living human fetus ex utero for whom viability has not been determined, unless (a) the research or experimentation may enhance the health, well-being, or probability of survival of the fetus itself; or (b) will pose no added risk of suffering, injury, or death to the fetus where the research or experimentation is for "the development of important biomedical knowledge which cannot be obtained by other means." In either instance, the risk standard must be the same for fetuses carried to term as for those intended to be aborted.²⁴

(3) National Organ Transplant Act

The National Organ Transplant Act (NOTA), 42 U.S.C. § 274e, prohibits the sale of any human organ for "valuable consideration" if the sale involves interstate commerce. ²⁵ In 1988, the Congress amended NOTA to include fetal organs within the definition of "human organ," effectively prohibiting the sale of fetal tissue within interstate commerce. ²⁶

C. FEDERAL REGULATIONS²⁷

(1) 45 C.F.R. § 46.201-211

Located within the general protections for biomedical research subjects provided by federal regulation, 45 C.F.R. § 46.201-211 speaks directly to research involving human fetal

²³ Human Research Extension Act of 1985, U.S. Code, vol. 42, sec. 289g (1997).

²⁴ 42 U.S.C. § 289g(b) (1997).

²⁵ National Organ Transplant Act, U.S. Code, vol. 42, sec. 274e (1997). "Valuable consideration" is defined at 42 U.S.C. § 274e(c)(2) (1997) by its negation: "valuable consideration' does not include the reasonable payments associated with the removal, transportation, implantation, processing, preservation, quality control, and storage of a human organ or the expenses of travel, housing, and lost wages incurred by the donor of a human organ in connection with the donation of the organ." A similar definition (excluding donor costs) is provided at 42 U.S.C. § 289g-2(d)(3) (1997).

²⁶ 42 U.S.C. § 274e(c)(1) (1997).

²⁷ Note: federal regulations are applicable only to federal agencies and the expenditure of federal research funds. <u>Cf.</u> 45 C.F.R. § 46.123(b) (regulation permitting HHS Secretary to terminate all federal funding to any institution if the Secretary determines that researchers have "materially failed [their] responsibility for the protection of the rights and welfare of human subjects").

tissue.²⁸ First promulgated in 1975, this regulation covers research on "(1) the fetus, (2) pregnant women, and (3) human in vitro fertilization" and applies to all DHHS "grants and contracts supporting research, development, and related activities directed towards those subjects.²⁹ The regulation states explicitly that "the purpose of this subpart [is] to ... assure that [applicable research] conform[s] to appropriate ethical standards and relate[s] to important societal needs."³⁰ Like its statutory counterpart at 42 U.S.C. §§ 289g, 289g-1 & g-2, 45 C.F.R. § 46.201-211 attempts to address the particular concerns inherent in fetal tissue research and to reduce attendant risks. These protections include (1) provision for stringent IRB review;³¹ (2) prestudies on animals and non-pregnant individuals;³² (3) an assessment of minimal risk to the fetus (except where the research purpose is intended "to meet the health needs" of the mother or the fetus);³³ (4) separation of researchers from the decision to terminate or any assessment of fetus viability;³⁴ (5) prohibition on inducements to terminate for purposes of the research.³⁵ Specific restrictions are imposed on the inclusion of pregnant women or fetuses in utero in research activities.³⁶

Of special relevance to fetal tissue research, 45 C.F.R. §§ 46.209 and 210 address requirements for federal funding of activities directed towards fetuses ex utero, including nonviable fetuses.³⁷ Section 46.209 focuses on viable and nonviable (but still living) fetuses.³⁸

²⁸ <u>Subpart B—Additional Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women, and Human In Vitro Fertilization, Code of Federal Regulations, Title 45, Vol. 1, Part 46.201-211 (1997).</u>

²⁹ 45 C.F.R. § 46.201(a) (1997).

³⁰ 45 C.F.R. § 46.202 (a) (1997).

³¹ 45 C.F.R. § 46.205(a) (1997).

³² 45 C.F.R. § 46.206(a)(1) (1997).

³³ 45 C.F.R. § 46.207(a) (1997).

³⁴ 45 C.F.R. § 46.206(a)(3) (1997).

³⁵ 45 C.F.R. § 46.206(a)(4) (1997).

³⁶ 45 C.F.R. § 46.208 (1997).

³⁷ 45 C.F.R. § 46.209-210 (1997).

³⁸ 45 C.F.R. § 46.209 (1997). According to 45 C.F.R. § 46.203(d) (1997), "viable as it pertains to the fetus means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration ... If a fetus is viable after delivery, it is a premature infant." At 45 C.F.R. § 46.203(e) (1997) "nonviable fetus means a fetus ex utero which, although living, is not viable," and at 45 C.F.R. § 46.203(f) (1997) "dead fetus means a fetus ex utero which exhibits neither heart

Until a determination has been made of fetal viability, no research may occur unless (1) there is no additional risk to the fetus and the purpose is the development of important biomedical knowledge that cannot be obtained elsewhere; or (2) the purpose is to enhance the viability of the particular fetus to the point of survival. Once viability is determined, the regulation specifies that research on a nonviable fetus may only occur where (1) vital functions of the fetus are not artificially maintained; (2) experimental activities that would themselves terminate heartbeat or respiration are not employed; and (3) the underlying purpose of the research is the development of important biomedical knowledge that cannot be obtained elsewhere. Where a fetus ex utero is determined to be viable, its status is protected under 45 C.F.R. § 46.101 et seq. as a human subject. Note finally that research on fetuses for which viability has not been determined, or fetuses that have been deemed nonviable, may occur only where the mother and father are legally competent and have given their informed consent, or where only the mother consents if the father's identity or whereabouts cannot be ascertained; he is not reasonably available; or the pregnancy resulted from rape.

45 C.F.R. § 46.210 provides fewer limitations and deals exclusively with research involving the dead fetus, fetal material derived from dead fetuses, or the placenta. The regulation states that "activities involving the dead fetus, macerated fetal material, or cells, tissue, or organs excised from a dead fetus shall be conducted only in accordance with any applicable State or local laws regarding such activities."

(2) 45 C.F.R. § 63.31

beat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached)."

³⁹ 45 C.F.R. § 46.209(a)(1)-(2) (1997); this language is essentially equivalent to 42 U.S.C. § 289g(a)(1)-(2) (1997).

⁴⁰ 45 C.F.R. § 46.209(b)(1)-(3) (1997).

⁴¹ 45 C.F.R. § 46.209(c) (1997).

⁴² 45 C.F.R. § 46.209(d) (1997).

⁴³ 45 C.F.R. § 46.210 (1997). <u>See</u> note 38 <u>supra</u> for definitions.

⁴⁴ Id.

This regulation affirms that provisions governing the protection of human research subjects at 45 C.F.R. § 46.101 <u>et seq.</u> are controlling on all Federal grants relating to fetal tissue transplantation research.⁴⁵

D. UNIFORM ACTS

Uniform Anatomical Gift Act (UAGA)⁴⁶

Originally promulgated to encourage organ availability for transplantation, the Uniform Anatomical Gift Act (UAGA) has been widely enacted into law by the States. First proposed in 1968 in a version enacted by all fifty states and the District of Columbia, a 1987 revision has been enacted by twenty-two states. The uniform Act is relevant not only because Federal fetal tissue statutes and regulations explicitly condition funding and authority on compliance with State and local laws, but also because private researchers are bound by State statute even absent Federal authority. In its 1987 definition, UAGA defines a "decedent" as a "deceased individual [that] includes a stillborn infant or fetus." The law permits the use of human tissue for the purposes of education, research, or the advancement of science. It requires that an attending physician determine the time of death, and like 42 U.S.C. § 289g-1(b), the Act provides that

⁴⁵ Subpart C—Special Provisions, Code of Federal Regulations, Title 45, Vol. 1, Part 63.31 (1997).

⁴⁶ Uniform Anatomical Gift Act 1-17, 8A U.L.A. 29 (1994).

⁴⁷ See NCCUSL fact sheet, 1; Zion, "Legal and Ethical Issues," 1292.

According to the National Conference of Commissioners on Uniform State Laws, "A Few Facts About THE REVISED UNIFORM ANATOMICAL GIFT ACT (1987)," Fact Sheet (1998) the following states have enacted the 1987 revision: Arizona, Arkansas, California, Connecticut, Hawaii, Idaho, Indiana, Iowa, Minnesota, Montana, Nevada, New Hampshire, New Mexico, North Dakota, Oregon, Pennsylvania, Rhode Island, Utah, Vermont, Virginia, Washington, Wisconsin. The two important new sections in the 1987 revision are Section 10 (criminal prohibition on the purchase or sale of body parts, discussed infra) and Section 4 (presumption of willingness to donate tissue or organs in the absence of known objection after reasonable efforts to discern patient/next-of-kin intent, not applicable in the context of fetal tissue derived from elective abortion). Gelfand & Levin, "Fetal Tissue Research," 671-75.

⁴⁹ Unif. Anatomical Gift Act 3. <u>But note</u> Zion, "Legal and Ethical Issues," 1293 ("UAGA ... does not differentiate between a fetus donated from a miscarriage or one given through an elective abortion. Presumably, either type of donation is included, but a certain determination is difficult").

⁵⁰ Unif. Anatomical Gift Act 6(a)(1)-(2).

informed consent must be obtained prior to the donation of any tissue.⁵¹ Like 45 C.F.R. § 46.209(d), the parents of the fetus have the ultimate authority to decide whether to make a donation.⁵²

Several sections of UAGA may be materially different from existing Federal law and regulation. For example, an entire body or parts of a body may be donated as an "anatomical gift" to a recipient, including individual donees.⁵³ This section is consistent with 42 U.S.C. §§ 289g-1(b)(1)(B)-(C) and 289g-2(b)(1) only where designation by the mother/donor of a donee/recipient for aborted fetal tissue means a designated researcher or research facility (since designation or even knowledge of an individual recipient is prohibited), or where fetal tissue is donated for research not involving transplantation.⁵⁴ In addition, the Act provides that "neither the physician or surgeon who attends the donor at death nor the physician or surgeon who determines the time of death may participate in the procedures for ... transplanting a part."⁵⁵ This section, although waivable, appears slightly more stringent than statutory and regulatory restrictions at 42 U.S.C. § 289g-1(c)(4) and 45 C.F.R. § 46.206(3) on researcher involvement in the decision or act of abortion, prohibiting researchers' physical presence or assistance at the clinical procedure from which fetal tissue for research is derived.⁵⁶ Finally, commentators have

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⁵¹ Unif. Anatomical Gift Act 8(b); 5.

⁵² <u>See</u> Gelfand & Levin, "Fetal Tissue Research," 679 ("UAGA makes the mother's consent determinative unless the father objects, and ... does not provide for notice to the father. The federal regulations [at 45 C.F.R. § 46.209(d)] require the father's consent, unless he is 'unavailable' to consent').

⁵³ Unif. Anatomical Gift Act 6.

⁵⁴ <u>See</u> Zion, "Legal and Ethical Issues," 1293 ("The act may need an amendment that prohibits specification of a donee ..."); <u>accord</u> Gelfand & Levin, "Fetal Tissue Research," 673.

⁵⁵ Unif. Anatomical Gift Act 7(b).

⁵⁶ See e.g. 45 C.F.R. § 46.206(3) ("Individuals engaged in the activity [of research] will have no part in: (i) Any decisions as to the timing, method, and procedures used to terminate the pregnancy, and (ii) determining the viability of the fetus at the termination of the pregnancy"); see also Zion, "Legal and Ethical Issues," 1294 ("These provisions create a 'Chinese Wall' between the individuals effecting the abortion and those conducting fetal tissue research and transplantation ... While this language standing alone would likely preclude most undue influence, the UAGA also provides for the waiver of the 'Chinese Wall' [R]evision may be necessary").

noted that, unlike 45 C.F.R. § 46.209(b) which covers tissue from living but nonviable fetuses, UAGA apparently does not. "UAGA does not apply to tissue donations from live persons, such as blood donations, skin donations, bone marrow, or kidney donations, so there may be no applicable law for fetal donation in such cases." The authors suggest that "UAGA is probably

best applied by analogy until an amendment can resolve this point."58

In other areas, UAGA closely tracks federal statutory provisions and, as a result, may share similar difficulties. Sections 10(a)-(b) of the uniform Act, included in the 1987 revisions, prohibit the actual sale or purchase of any human body parts for any consideration beyond that amount necessary to pay for expenses incurred in removal, processing, and transportation of the tissue. This is essentially the same proscription included at 42 U.S.C. § 289g-2(a) barring the acquisition or transferal of fetal tissue for "valuable consideration," with the same exceptions. One commentator has argued that the Federal provision (and by extension UAGA) is unenforceably vague in its definition of reasonable processing fees, "leav[ing] ... room for unscrupulous tissue processors to abuse the law" Drafters on the Federal level and in the states that have enacted UAGA's 1987 no-sale provision have attempted to address this concern by making violation of the section a felony with substantial penalties. Some states have added

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⁵⁷ <u>See</u> Gelfand & Levin, "Fetal Tissue Research," 671. At least one commentator has suggested that UAGA may not govern *any* fetal tissue donation, Jonathan Hersey, "Comment, Enigma of the Unborn Mother: Legal and Ethical Considerations of Aborted Fetal Ovarian Tissue and Ova Transplantations," <u>UCLA Law Review</u> 43 (1995): 174 ("[I]n the vast majority of abortion procedures, the woman is alive. Therefore, if one believes that a fetus maintains few or no rights independent of the woman, the UAGA statutes are inapplicable to fetal tissue donations").

⁵⁹ Unif. Anatomical Gift Act 10(a)-(b).

⁶⁰ 42 U.S.C. § 289g-2(a) (1997).

⁶¹ See Goddard, "NIH Revitalization Act," 394.

⁶² 42 U.S.C. § 289g-2(c) (1997); discussion of state laws, <u>infra</u>. <u>But see</u> Hersey, "Enigma," 113 ("Only the 1987 version of the UAGA explicitly prohibits sales of procured organs. Thus, unless the states still enforcing the 1968 version have supplementary statutes banning the purchase and/or sale of fetal tissue and organs, the specter of a cottage industry of fetal reproductive organs looms ...").

a further clarification in their enactment to indicate that the donation of human tissue for

transplantation is to be understood as a service and not a sale. 63

⁶³ Defining the transaction as a service rather than a sale may assist regulators and the courts in better distinguishing between reasonable overhead (permitted under 42 U.S.C. § 289g-2(d)(3) and Unif. Anatomical Gift Act 10) and profit (not permitted). It would certainly still be the case under UAGA that the mother/donor could not be compensated beyond reasonable expenses for donation of fetal tissue, although such payments may be permissible under Federal law for research activities not involving transplantation.