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United States General Accounting Office
Washington, DC 20548

October 4, 2000

The Honorable Arlen Specter
Chairman
The Honorable Tom Harkin
Ranking Minority Member
Subcommittee on Labor, Health and Human
Services, and Education
Committee on Appropriations
United States Senate

The Honorable Bob Smith
United States Senate

Subject: Human Fetal Tissue: Acquisition for Federally Funded Biomedical Research

Human fetal tissue is used in basic and preclinical biomedical research to advance knowledge of basic biological processes and improve research involving potential therapeutic approaches. It is also used in therapeutic transplantation or clinical research that involves the transplantation of human fetal tissue into patients for the cure or amelioration of diseases and disorders. The study, analysis, or use of human fetal tissue in biomedical research is considered by many medical researchers to offer promise for treatment of disorders and diseases such as Parkinson's disease, Alzheimer's disease, and diabetes.

You requested that we study the involvement of federal agencies under the jurisdiction of the Senate Committee on Appropriations, Subcommittee on Labor, Health and Human Services, and Education in the acquisition of human fetal tissue for biomedical research. You specifically asked us to provide information on (1) which federal agencies under the Subcommittee's jurisdiction sponsor biomedical research using human fetal tissue, (2) the number of human fetal tissue samples acquired annually, (3) the number of central human fetal tissue supply organizations receiving federal funds, (4) the costs associated with acquiring human fetal tissue, (5) how researchers select and monitor human fetal tissue suppliers, (6) the extent to which federal human fetal tissue acquisition policies adhere to federal law, and (7) how federal agencies ensure that federally funded researchers comply with human fetal tissue law.

To address these questions, we interviewed officials from the Department of Health and Human Services (HHS) and the National Institutes of Health (NIH), organizations that supply human fetal tissue for research, and selected institutional review boards that are responsible for the oversight of specific federally funded biomedical research

grants involving human fetal tissue. To gather information about the amount, sources, and costs of human fetal tissue used in biomedical research, we conducted a survey of NIH funded principal investigators for extramural and intramural research using human fetal tissue in fiscal years 1997, 1998, and 1999. Finally, we reviewed the laws, regulations, and policies relevant to human fetal tissue. We restricted our analysis to research projects that directly received human fetal tissue.[1] We carried out our work between July and September 2000 in accordance with generally accepted government auditing standards.

In brief, HHS officials reported that NIH is the only federal agency under the Labor, HHS, and Education Subcommittee's jurisdiction that sponsors research using human fetal tissue. On the basis of information supplied to us by NIH, we estimate that NIH awarded approximately $17.0 million for 103 research grants using human fetal tissue in fiscal year 1999. Principal investigators who responded to our survey acquired 12,116 human fetal tissue samples in fiscal years 1997 through 1999 for use in NIH-sponsored research. NIH funded three central human fetal tissue suppliers to provide human fetal tissue to biomedical researchers in fiscal year 1999. The costs of acquiring human fetal tissue were generally low. In fiscal year 1999, 49 percent of the principal investigators in our survey received human fetal tissue without paying an acquisition fee. Among those who did pay an acquisition fee, the average fee per sample was $80 in fiscal year 1999. The median number of tissue samples received by principal investigators in fiscal year 1999 was 26. In fiscal year 1999, 62 percent of principal investigators received human fetal tissue from central fetal tissue supply organizations, 31 percent from academic medical center hospitals, and 30 percent from health clinics or physicians' offices.[2] The principal investigators identified quality of the tissue supplier and a supplier's compliance with relevant regulations as the primary criteria for selecting their human fetal tissue suppliers. We found that federal human fetal tissue procurement policies and guidance are consistent with federal law. Review boards that are established at each institution performing HHS-funded biomedical research have the primary responsibility for ensuring that the procedures for acquiring human fetal tissue comply with federal, state, and local laws. The Office for Human Research Protections (OHRP) is the HHS entity that oversees the ongoing review practices of these institutional review boards.

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[1]This definition excludes (1) research involving human cord blood, placenta, amniotic fluid, and chorionic villi; (2) research involving derivatives of human fetal tissue such as human fetal cell cultures or human fetal cell lines; (3) studies involving a collection of existing human fetal tissue; and (4) pathology studies or autopsies.

[2]Sum of percentages is greater than 100 because some principal investigators had more than one supplier.

BACKGROUND AND METHODOLOGY

The NIH Revitalization Act of 1993 (P.L. 103-43) added two provisions to the Public Health Service Act regarding the acquisition and use of human fetal tissue.[3] The NIH Revitalization Act[4] prohibits a person from knowingly acquiring or transferring human fetal tissue for valuable consideration if the transfer affects interstate commerce. The statute defines "valuable consideration" as excluding reasonable payments associated with the transportation, implantation, processing, preservation, quality control, or storage of human fetal tissue. For therapeutic transplantation research, the NIH Revitalization Act requires written statements by the donor, the physician who obtained the tissue, and the researcher receiving the tissue to ensure that the provisions of the law are met. It further requires that all applicable state and local laws must be followed.[5]

Because we found no central source of information about the amount of human fetal tissue used for research or the number of human fetal tissue suppliers, we conducted a survey of principal investigators for all NIH-funded extramural and intramural research NIH reported to us as possibly using human fetal tissue for fiscal years 1997, 1998, and 1999. In the survey, we asked the principal investigators to identify (1) the number and type of entities they selected to be human fetal tissue suppliers, (2) the amount of tissue they received, (3) the number of shipments or acquisitions they received, and (4) the direct and indirect costs associated with human fetal tissue acquisition. We also asked principal investigators to identify the relevant oversight bodies at their institution, to describe the policies that exist at their institution regarding research using human fetal tissue, and to explain how their institution ensures compliance with federal, state, and local laws. We sent the survey instrument to all 160 of the investigators identified for us by NIH as having a research grant that may have involved the use of human fetal tissue for fiscal years 1997, 1998, and 1999. The survey was returned by 151 of the principal investigators, for a response rate of 94 percent. Of those respondents, 93 acquired fetal tissue for their research and completed the entire survey form, 47 told us that their research did not use human fetal tissue or that they did not acquire human fetal tissue in fiscal years 1997, 1998, and 1999, and 11 told us that they did not directly acquire human fetal tissue but used tissue acquired by another researcher included in our survey.[6]

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[3]Prior to the enactment of the NIH Revitalization Act, the National Organ and Transplantation Act of 1988 (P.L. 100-607) expanded the definition of "human organ" in the Public Health Service Act (42 U.S.C. section 274e) to include human fetal organs and tissue. This act thus prohibits the transfer of human organs, including human fetal tissue, for valuable consideration for use in human therapeutic transplantation.

[4]Section 112 of the NIH Revitalization Act, adding section 498B of the Public Health Service Act (42 U.S.C. section 289g-1).

[5]For a fuller description of this provision, see section 111 of the NIH Revitalization Act, adding section 498A of the Public Health Service Act, 42 U.S.C. section 298g-1.

[6]One hundred nineteen of the principal investigators received NIH grants in fiscal year 1999 (the remainder received funds only in fiscal years 1997 or 1998). For those with fiscal year 1999 grants the response rate was 97 percent; 68 acquired human fetal tissue in fiscal year 1999, 39 reported that they

FEDERALLY FUNDED BIOMEDICAL RESEARCH USING HUMAN FETAL TISSUE

HHS officials told us that NIH is the only federal agency under the Labor, HHS, and Education Appropriations bill that sponsors biomedical research using human fetal tissue. Separately, the Centers for Disease Control and Prevention told us that it does not conduct research using human fetal tissue. On the basis of information supplied to us by NIH, we estimate that NIH awarded to our survey respondents approximately $17.0 million for 103 research projects that used human fetal tissue in fiscal year 1999.[7] The researchers who responded to our survey collectively received $12.3 million in funding for extramural research at universities and research institutions, $3.2 million in funding for NIH intramural research, and $1.5 million for central human fetal tissue supply organizations.

NUMBER AND SOURCES OF TISSUE SAMPLES ACQUIRED

The NIH-sponsored biomedical researchers who responded to our survey acquired an average of roughly 4,000 samples of human fetal tissue in each year from fiscal years 1997 to 1999 (see table 1). We defined a tissue sample as a separate amount of tissue, or a single piece of tissue, in one vial. In fiscal year 1999, researchers received 4,147 samples in 1,878 shipments or acquisitions. The median number of tissue samples received by principal investigators in fiscal year 1999 was 26.

Table 1: Human Fetal Tissue Samples Acquired, by Fiscal Year

Fiscal year	Number of fetal tissue samples
1997	3,676
1998	4,293
1999	4,147
Total	**12,116**

The principal investigators we surveyed received human fetal tissue most often from central tissue suppliers. Among principal investigators who identified their sources for human fetal tissue in fiscal year 1999, 62 percent received human fetal tissue from central tissue suppliers, 31 percent from academic medical center hospitals, and 30

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did not use human fetal tissue in their research or that they did not receive human fetal tissue in fiscal year 1999, and 9 reported that they did not directly acquire human fetal tissue but used tissue acquired by another researcher we surveyed. In addition to data from the 68 researchers who acquired tissue in fiscal year 1999, our analyses for that year also included data from 10 researchers with NIH grants for only fiscal years 1997 and/or 1998 who told us that they also acquired human fetal tissue in fiscal year 1999.

[7]This total was calculated by summing the grant funding amounts we received from NIH for survey respondents who told us that their research used human fetal tissue in fiscal year 1999. This total probably is slightly understated, however, because some of the researchers who did not respond to our survey may have used human fetal tissue.

percent from health clinics.[8] Fifty four percent of all of the human fetal tissue samples received by the NIH-sponsored researchers we surveyed came from central tissue suppliers in fiscal year 1999. Likewise, 34 percent of the tissue samples came from health clinics and 10 percent from academic medical centers.

CENTRAL TISSUE SUPPLY ORGANIZATIONS

NIH sponsors three central human fetal tissue supply organizations. The Birth Defects Laboratory at the University of Washington is funded by NIH for the sole purpose of providing human fetal tissue to federally funded biomedical researchers. While most of the laboratory's funds are provided by NIH, it also charges researchers a small fee for the human fetal tissue samples it collects, prepares, and distributes. The laboratory distributed 2,869 human fetal tissue samples and collected $52,035 in fees directly from researchers in fiscal year 1999. NIH provided a grant award of $346,743 to maintain the laboratory's capabilities in fiscal year 1999. NIH also funds 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 primarily to serve as suppliers of human nonfetal tissue for the study of developmental disorders, but both banks also supply a relatively small amount of human fetal tissue to biomedical researchers. In fiscal year 1999, NIH funds totaled $563,823 for the University of Maryland Bank and $574,643 for the University of Miami Bank. The University of Maryland Bank provided 195 human fetal tissue samples to investigators in fiscal year 1999, and the University of Miami Bank provided approximately 40 samples between March 1 and August 31, 1999.

In addition, some researchers obtained human fetal tissue from private, nonprofit central tissue supply organizations that did not directly receive federal funds. In their responses to our survey, the principal investigators who received tissue from these sources most frequently obtained tissue from Advanced Bioscience Resources, Incorporated (Alameda, California), and the Albert Einstein College of Medicine Human Fetal Tissue Repository (New York, New York).

COSTS OF ACQUIRING HUMAN FETAL TISSUE

The direct acquisition fees for human fetal tissue were low. In fiscal year 1999, 49 percent of the respondents to our survey did not pay any acquisition fees for the human fetal tissue they received. Among those who paid acquisition fees in fiscal year 1999, investigators reported an average fee of $80 per human fetal tissue sample, with a minimum fee of $2 and a maximum fee of $214. In addition, tissue acquisition fees varied substantially among the different sources identified in our survey. Only one of the researchers who received human fetal tissue from academic medical centers paid an acquisition fee ($12). More than four-fifths of the researchers who received tissue from health clinics paid no fee. The fees per sample of human fetal tissue from health clinics ranged from $2 to $75, with an average of $22. In contrast,

[8]Sum of percentages is greater than 100 because some principal investigators had more than one supplier. Three percent of these respondents did not categorize their tissue source.

78 percent of the researchers receiving human fetal tissue from a central tissue supplier paid an acquisition fee—those fees ranged from $5 to $214 per sample, with investigators paying an average fee of $96.[9]

Second, some of the principal investigators who completed our survey had additional expenses for transporting, processing, preserving, storing, and ensuring the quality of human fetal tissue specimens, even if they paid nothing to acquire the tissue. For all of the principal investigators who responded to our survey, total expenditures for acquiring human fetal tissue in fiscal year 1999 totaled approximately $359,000, including both tissue acquisition fees and these other expenses (see table 2). This total includes about $142,000 in acquisition fees, $80,000 in shipping and transportation costs, and $135,000 in other internal laboratory costs for processing, preserving, storing, and ensuring quality.[10]

Table 2: Total Costs Related to Acquiring Human Fetal Tissue, Fiscal Year 1999

Cost category	Number of investigators incurring cost	Average annual cost per investigator	Total for all investigators
Acquisition fee	40 (51%)	$3,554	$142,144
Shipping and transportation costs	42 (54%)	$1,914	$80,405
Other direct costs	9 (11%)[a]	$176	$1,580
Internal costs	13 (17%)[b]	$10,350	$134,550
Total			**$358,679**

[a]Two respondents who said that they had other direct costs but did not provide a cost figure are not included.
[b]Seven respondents who said that they had internal costs but did not provide a cost figure are not included.

CRITERIA FOR SELECTING HUMAN FETAL TISSUE SUPPLIERS

In response to an open-ended question on our survey, principal investigators reported that quality of tissue and compliance with federal regulations were their primary criteria for choosing a human fetal tissue supplier. Overall, 55 percent of the respondents who received human fetal tissue in fiscal year 1999 told us that they

[9]Twelve percent of researchers who obtained human fetal tissue from central supply organizations paid no fee. Ten percent of researchers who identified central supply organizations as the entity that supplied their tissue did not tell us whether or not they paid an acquisition fee.

[10]Shipping and transportation costs include any costs associated with transporting tissue samples from the supplier to the researcher by any means, including by personal delivery or commercial shipping company, and shipping supplies such as sample containers or sterile media provided by the researcher. Other direct costs include renting space at a supplier's facility, in-kind services or donations of staff time or supplies to the tissue supplier, and any other financial considerations to the tissue supplier. Internal costs are any costs researchers may have incurred as a result of acquiring fetal tissue that they would not have otherwise, such as equipment for storing the tissue.

selected a tissue supplier on the basis of the qualifications and reliability of its staff, its reputation for high-quality work, or other reasons indicating a preference for a high-quality supplier. Forty-four percent of these 1999 respondents told us that the supplier's compliance with federal and state laws, or its nonprofit status, was an important reason for their selection. Thirty-seven percent told us that the location of the tissue supplier was important (21 percent told us that the tissue supplier was part of their institution). Fewer respondents (29 percent) selected a tissue supplier simply because appropriate human fetal tissue was available there. Finally, 9 percent of those who received human fetal tissue in fiscal year 1999 told us that the low cost of the tissue was a factor in their selection of a supplier.

HUMAN FETAL TISSUE POLICIES AND GUIDANCE

The NIH Revitalization Act of 1993 places limits on the procurement of human fetal tissue. The statute bars anyone from knowingly acquiring, receiving, or transferring human fetal tissue for valuable consideration if the transfer affects interstate commerce. For therapeutic transplantation research, it further bars directed donations of human fetal tissue and payment of valuable consideration for costs associated with terminating a pregnancy. Each of these prohibitions carries criminal penalties, including fines and imprisonment. Because these provisions do not require implementing regulations,[11] NIH addresses the importance it attaches to these statutory requirements and the criminal penalties that the prohibitions carry through guidance to its grantee researchers. In its forthcoming policy statement on "Research on Human Fetal Tissue," NIH emphasizes that "the scientific and ethical challenges associated with research utilizing human fetal tissues make it imperative that researchers and their institutions be clearly aware of and in compliance with federal requirements," especially those that carry criminal penalties.

INSTITUTIONAL REVIEW BOARDS

Except for research conducted at its own facilities, NIH does not directly oversee the conduct of research using human fetal tissue. Instead, under the regulations regarding the protection of human subjects, institutional review boards oversee HHS-funded research using human fetal tissue.[12] These review boards are required at all institutions conducting HHS-supported research. The boards are responsible for approving research proposals before studies begin and for periodically reviewing studies after they are under way to ensure compliance with relevant regulations for the protection of human subjects. OHRP is the HHS entity responsible for ensuring that the institutional review boards are conducting the appropriate reviews of HHS-funded research using human fetal tissue. Before grant funds are distributed, the grantee institution submits an "assurance" to OHRP. The assurance is a written

[11]In addition, although not directly addressing the procurement of human fetal tissue, NIH regulations specifically require that "activities" involving these materials must be in accordance with any applicable state or local laws (45 C.F.R. section 46.210).

[12]Almost all of our survey respondents identified the institutional review board at their institution as the body responsible for oversight of their research.

statement of an institution's requirements for its institutional review board and human-subject protections. If the institution receives only one grant from HHS, a single project assurance is submitted to OHRP. If the institution receives many HHS grants, a multiple project assurance is submitted. In the assurance, the institution states that the research will be conducted in compliance with applicable federal, state, and local laws. Institutions are required to renew multiple project assurances every 5 years after an initial period of 3 years. Continuing reviews of the HHS-funded projects are conducted annually by the institutional review boards.[13]

NIH's Office of Intramural Research periodically reviews each intramural investigator using fetal tissue to confirm that they are complying with the relevant requirements.

AGENCY COMMENTS

NIH and OHRP officials reviewed a draft this report. They provided technical comments, which we incorporated where appropriate.

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We will make copies of this letter available to those who are interested on request.

Major contributors to this report were Martin T. Gahart, Emily J. Rowe, Jenny C. Chen, Lisanne Bradley, and Stefanie Weldon. Please contact me at (202) 512-7119 if you have any questions.

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[13]Our review did not evaluate the effectiveness of institutional review board oversight. We previously reported that NIH-sponsored investigators conducting therapeutic human fetal tissue transplantation research were in compliance with federal laws and regulations. See *NIH-Funded Research: Therapeutic Human Fetal Tissue Transplantation Projects Meet Federal Requirements* (GAO/HEHS-97-61, Mar. 10, 1997).