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Subcommittee on Science, Technology, and Space

"Prenatal Genetic Testing Technology: Science, Policy, and Ethics"

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Mr. Chairman and members of the Subcommittee, thank you for inviting me to be with you today to discuss the science, ethics, and policy of prenatal genetic testing.

My name is Kathy Hudson and I am the Director of the Genetics and Public Policy Center and Associate Professor in the Berman Bioethics Institute and in the Institute of Genetic Medicine at Johns Hopkins University. Established with a grant from The Pew Charitable Trusts, the mission of the Genetics and Public Policy Center is to provide independent and objective information and analysis on genetic technologies and genetic policies. We hope our work provides useful tools for decision makers in both the private and public sectors as they consider and respond to the challenges and opportunities that arise from scientific advances in human genetics.

Genetic testing is undergoing tremendous changes. Scientists are identifying disease-causing mutations in humans at a remarkable pace and developing tests to detect them. There are over 1000 genetic tests available or in development, all of which could potentially be used in prenatal genetic testing. The growing availability and use of genetic testing in the reproductive context presents a host of complicated social, legal and ethical issues. I applaud this Committee for its foresight in taking up this issue and welcome the opportunity to share with you the results of the Center's work and experience in this arena.

The Genetics and Public Policy Center has spent the past two years investigating reproductive genetic testing, which includes prenatal genetic testing, the topic of today's hearing, as well as carrier testing and preimplantation genetic diagnosis. We are about to issue two reports on the topic. The first, *Reproductive Genetic Testing: Issues and Options for Policymakers*, aims to help focus and facilitate the discussion about reproductive genetic testing by outlining key scientific and medical facts, considering ethical and social implications, and

assessing both current and potential oversight for the development and use of reproductive genetic tests. It presents a range of policy options supported by expert analysis that consider the potential effects, good and bad, of distinctly different policy directions.

Our second report, *Reproductive Genetic Testing: What America Thinks,* presents the results from our in-depth effort to understand what the public knows, thinks and feels about genetic technologies. We undertook this effort so that policy leaders and other decision makers would have more nuanced and sophisticated information about public's attitudes towards these technologies than has previously been available to-date. This effort is the largest and most ambitious public opinion work to-date on this issue. We have surveyed over 6000 Americans, conducted focus groups, and interviewed hundreds of individuals who have had personal or professional experience with these technologies. Recognizing that one of the drawbacks to both qualitative and quantitative public opinion research is that individuals are asked to comment on complex scientific and ethical issues which they may have had little prior opportunity to consider, we conducted an extensive public engagement activity this summer to obtain more informed, reflective opinions from the general public. Over 500 citizens in six cities across the U.S. (Sacramento, CA; Seattle, WA; Kalamazoo, MI; Fort Worth, TX; New York City, NY; and Nashville, TN) and over 100 citizens on-line took part in *The Genetic Town Hall: Making Every Voice Count*. Participants were provided with background information about the technology and issues, heard contrasting viewpoints from "the experts", and engaged in discussion with their fellow citizens about the issues of concern to them.

The Center does not advocate for or against these technologies or for a particular policy outcome. Rather we believe that policy makers should have access to objective analysis, comprehensive information about what the public hopes for and fears from these technologies, and robust policy options to guide the development and use of reproductive genetic testing.

Scientific Background

Genetic testing is the laboratory analysis of DNA, RNA, or chromosomes. Testing can also involve analysis of proteins or metabolites that are the products of genes. Genetic testing is done to predict risk of disease, screen newborns for disease, identify carriers of genetic disease, establish prenatal or clinical diagnoses or prognoses and direct clinical care. Testing can be done using many different biological samples, including blood, amniotic fluid (from which fetal cells are obtained) or individual embryonic cells.

Two forms of analysis are possible. *Cytogenetic analysis* is used to detect abnormalities in chromosomal number and/or structure. *Molecular genetic testing* examines the DNA sequence of individual genes.

In general, *prenatal screening* includes those tests and procedures used to assess fetal risk for an abnormality, including genetic disorders. It does not provide a definitive diagnosis of a genetic abnormality but indicates whether diagnostic tests are warranted. The advantage of prenatal screening is that a normal result provides earlier reassurance and an abnormal result allows the option of further diagnostic tests.

Prenatal genetic testing (or prenatal genetic diagnosis) is genetic testing of fetal cells obtained through procedures such as amniocentesis and CVS. Prenatal genetic testing of a fetus requires two steps: an invasive procedure (amniocentesis or CVS) to obtain fetal genetic material

and an analysis of the material to identify genetic abnormalities or characteristics. Fetuses may be at increased risk for genetic abnormalities because of the mother's age (35 or greater at delivery), because the parents already have a child or other family member with a genetic condition, because one parent has a balanced chromosome rearrangement or because prenatal screening or carrier testing indicates an increased risk.

Amniocentesis is usually performed in the second trimester of pregnancy, at approximately 15-20 weeks gestation. A small amount of amniotic fluid is removed from the sac that holds the developing fetus. The fluid contains fetal cells that provide the material for genetic analysis. Amniocentesis is generally considered a relatively simple and safe procedure when performed by an experienced physician. Although miscarriage after amniocentesis is infrequent (one in 200-400 cases), it is a major reason the procedure is not routinely offered to all women. Infection and leakage of amniotic fluid are other rare complications of amniocentesis.

Chorionic villus sampling (CVS) is an alternative to amniocentesis, and can be performed during the first trimester of pregnancy. Fetal cells are obtained through biopsy of the chorionic villi — the cells that will become the placenta. CVS is generally done at 10-13 weeks gestation. Fewer physicians do CVS than amniocentesis, and as a result, it is not available in all areas. The risk of miscarriage after CVS is approximately 1 in 100, as compared with the 1/200-400 risk following amniocentesis. CVS can be used to determine all disorders that can be diagnosed by amniocentesis except the presence of neural tube defects, since CVS does not include analysis of amniotic fluid alpha-fetoprotein.

Prenatal Genetic Testing: Points to Consider

With that background in mind, I would like to make five main points about prenatal genetic testing.

1. Information and its use.

Genetic tests give information - information that, in the reproductive context, can provide great reassurance or precipitate a decision. Before pregnancy, prospective parents may learn through carrier testing whether or not they are at risk of having a child with a genetic disease and may have to decide whether or not to try to have a baby. During pregnancy, prenatal genetic testing can rule out or diagnose a genetic disease in utero. When a genetic anomaly is identified, prospective parents make the difficult decision of whether to continue a pregnancy, or not. There are a host of issues related to prenatal genetic testing. Some of the issues relate to the information obtained from the testing, others relate to the profound decisions that prospective parents make based on the results. But I want to emphasize that the decision to have a genetic test - to get information - and the decision about what to do with the information, are two separate, but interrelated issues.

People differ in their desire to obtain information about the future. Since most genetic tests show no genetic problems, many find the information reassuring. Others want the information in order to have the opportunity to prepare emotionally, financially, and medically for the birth of an affected child. For these individuals, knowing as much as possible about the health of the fetus, as early in the pregnancy as possible, is of primary interest. Others, however, prefer to decline testing and welcome the child first, and then address any health problems the child may have. For them, prenatal testing may seem intrusive and unnecessarily worrisome. For couples who would consider abortion in case of a serious genetic condition,

information about the condition and the prognosis helps them make the decision whether or not to terminate the pregnancy.

There are probably as many reasons to undergo prenatal testing — or to refuse it — as there are parents. Whether someone will ultimately accept or decline testing, and what course of action they will take based on the information testing provides, is impossible to predict. But as this Committee considers whether prenatal genetic testing is in need of Congressional attention, I would urge you to treat the information and the decision about what to do with the information as separate matters.

2. Preserving the right to know – and not to know

The philosophy of those providing reproductive genetic testing is "non-directive" genetic counseling. Simply put, this means that, because the implications of these decisions are so profound and so personal, the decision whether or not to have prenatal genetic testing, and what to do with the test results, must reside with the prospective parents. Indeed there is strong support among Americans for this approach. A majority of Americans (64%) agree with the statement[1] "We ought to let people decide for themselves when it is appropriate to use reproductive genetic technologies because the consequences are so personal." Although most health care providers practice non-directive counseling in providing information about the risks and benefits of testing and the choices that may be faced depending on results, some observers have raised the concern that prospective parents may feel pressured to agree to prenatal genetic testing – pressure from their health care provider or from society at large.

Some fear that as testing becomes available for an increasing array of inherited diseases and conditions, couples will face growing medical and societal pressure to use all available

[1] From Genetics & Public Policy Center 2004 Survey of 4,834 Americans

technology—on the theory, perhaps, that if it is knowable, it should be known. Fear of liability – that they could be charged with failing to consider all potential genetic problems – could drive providers to seek as much information as genetic testing can provide. And as screening and testing become earlier and capable of detecting a broader range of conditions, the concern is that society will see reproductive testing as the "right" and "responsible" thing to do. Some believe that individuals will face growing medical and societal pressure to avoid the birth of a child that has not "passed" all the requisite genetic tests. On the other hand, some have argued that the more widespread genetic testing becomes, and the more each individual knows about his or her unique genetic makeup, the more society will be tolerant of human differences. Rather than expecting each fetus to meet some definition of genetically "normal," the knowledge that no individual is a "perfect specimen" may lead to greater acceptance of every individual and less pressure to use all available technology to have a "perfect" child.

Our policy report addresses these issues. Clearly, attention should be paid to preserving the rights of prospective parents *not* to use prenatal genetic testing. This can be accomplished by improving the counseling and access to information couples receive. Currently, information about prenatal testing is conveyed in a variety of settings and contexts. Sometimes it is a physician who discusses prenatal testing with the patient, sometimes a nurse or midwife and sometimes a patient is referred to a genetic counselor. Providers have varying levels of knowledge and comfort discussing these issues, and often very little time in which to cover all of the information adequately. Thus, patients may end up making decisions based on incomplete or inaccurate information. Some may proceed with testing without fully considering the decisions they may have to make depending on the results of the tests. Health care providers may present these tests as routine, just like all the other tests one gets during pregnancy, which may explain

why patients sometimes report feeling pressured to agree to testing. Enhancing the genetic literacy of providers or providing better access to genetic counseling could help alleviate these concerns.

If a genetic condition is found during prenatal genetic testing, careful attention to how test results are conveyed and ensuring parents have access to the complete clinical picture can assist families in making informed decisions. Some disability advocates say that providers who discuss prenatal screening and testing describe conditions in the most extreme clinical terms and assume that parents will want to terminate an affected fetus. They believe that providers are predisposed to counsel in favor of that decision, without giving sufficient context to the prospective parents about what it would actually be like to raise a child with the particular disorder. One direct approach is to enhance the counseling available to parents by making sure that genetic counseling includes access to information from people living with genetic diseases and their families so that prospective parents may better understand the reality of having a child with the disease. Patient advocacy organizations working on behalf of people with the condition could work with providers to facilitate such interactions.

Importantly, a more direct or holistic approach would be to ensure that society continues to support *all* prospective parents, including those who make the decision not to test, or not to end a pregnancy and that there continues to be a range of legal protections and support for people with disabilities and their families.

3. Ensuring test accuracy and quality care

The decisions made on the basis of prenatal genetic tests are weighty – if a prospective parent is going to decide whether or not to continue a pregnancy on the basis of a test result, the

accuracy and reliability of the test is of utmost importance. The prenatal genetic tests routinely used have low false positive and false negative rates and are of generally high quality. But, right now government oversight of genetic testing is patchy at best. There are at least two issues here. The first is to make sure that a test is clinically valid before it goes to market. The second is to ensure that laboratories are performing the tests correctly so that the results are reliable. More attention needs to be paid to the role of federal agencies in making sure that genetic tests being used by laboratories are accurate and reliable.

In our policy report we provide a detailed analysis of the current regulatory environment for reproductive genetic testing. Government oversight in this area is limited and fragmented. There is no government review of tests by the Food and Drug Administration (FDA) or any other federal agency before they are marketed. In addition, although laboratories performing prenatal genetic testing are regulated by the Centers for Medicare and Medicaid Services (CMS) through the Clinical Laboratory Improvement Amendments of 1988 (CLIA), there are no specific requirements under CLIA to show proficiency in molecular genetic testing, making it difficult to evaluate laboratory performance of genetic tests. Interestingly, in our 2002 survey, we found that only 30 % of respondents knew that the federal government does not review or approve reproductive genetic tests before they go on the market.

One possibility is to increase federal oversight of genetic testing to ensure it is accurate and safe. FDA and CMS may have the authority currently to expand their role. In addition, Congress could pass legislation delegating additional authority to these agencies to ensure that prenatal genetic testing is done right.

Although professional groups have issued guidelines for providers for the appropriate use of some genetic tests, there are currently only a handful of guidelines for a genetic testing

compared to the large number of genetic tests available. The number of genetic tests available is rapidly increasing, and there is no technological barrier to using them in prenatal genetic testing.

In the absence of government regulation, professional self-regulation is often a valuable tool. But the sheer number of tests and the speed with which they are developing, means that professional societies such as American College of Obstetricians and Gynecologists and the American College of Medical Genetics are hard pressed to keep up. In our policy report, we propose several options to address the need for more professional guidelines in the absence of more robust federal oversight. One possibility would be that federal funding could be made available through the agencies of the Department of Health and Human Services to help facilitate guideline development.

As mentioned previously, another approach to improving care is to improve the information that patients have. The quality of patient care would be enhanced if health providers were more knowledgeable about testing and prospective parents had all the information and counseling they needed to understand the choices they are making and the implications of those choices. Perhaps most importantly, counseling, screening and testing needs to be offered when parents are able to make the best use of the information. Most experts agree that genetic risk information and reproductive genetic testing options should be discussed with prospective parents *before* pregnancy during routine visits. The health care provider should take a family history and assess genetic risk based on family history, maternal age and ethnic background and discuss carrier testing options. Carrier testing done before pregnancy allows prospective parents to know their risks without having to make a decision to terminate a pregnancy.

4. For what purpose

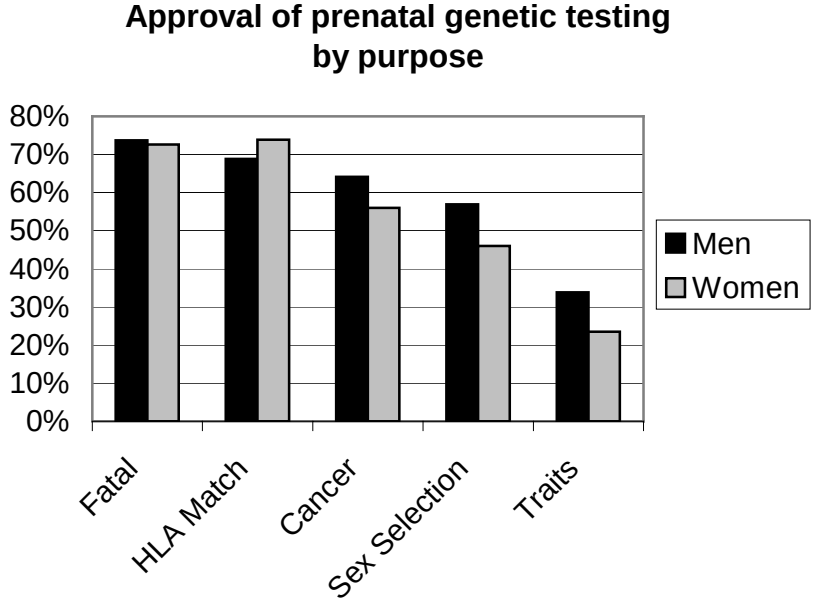
There are many different genetic tests available, and questions abound as to whether, and how to regulate what people are testing for. There are tests for fatal childhood conditions such as Trisomy 13 or Tay Sachs disease. There are tests for serious disorders including Down syndrome, cystic fibrosis, and sickle cell anemia. Tests are also available for adult-onset disorders, such as Huntington disease, that would not affect the individual for many years, during which time a treatment may be discovered. There are also genetic tests that identify predisposition to, or increased risk of, developing a disease such as breast cancer as an adult. There is considerable debate about which of these tests are ethically appropriate for use in the reproductive context.

Many observers are concerned that the use of prenatal genetic testing will escalate to the point where it is used to test for what some call "designer traits" – characteristics unrelated to health such as intelligence or athletic ability. These most controversial tests, however, are not yet, and may never be, available in any context because these complex attributes result from the interaction of a host of environmental and genetic factors.

Americans' support for the use of reproductive genetic testing depends heavily on the circumstances under which it is being used. In a 2004 survey conducted by the Genetics & Public Policy Center, respondents were asked a set of questions about the appropriateness of using prenatal testing to find out whether a fetus will:

- develop a fatal childhood disease;
- be a good match to donate his or her blood or tissue to a brother or sister who is sick and needs a transplant;
- have a tendency to develop a disease like adult-onset cancer;
- be a certain sex; and
- have desirable characteristics like high intelligence or strength (hypothetically).

About two-thirds of the general public approved of the use of prenatal genetic testing for a fatal childhood disease and for tissue matching. A slight majority of survey participants approved of using reproductive genetic testing technologies to identify alterations associated with a tendency to develop an adult-onset disease like cancer. There was less support for using testing to identify or select sex and a majority disapproved of using hypothetical prenatal genetic testing to identify characteristics like intelligence or strength. Thus, a majority of Americans approve of prenatal genetic testing to identify health-related genetic characteristics and a similar majority disapprove of its use to identify traits. Attitudes towards prenatal genetic testing vary somewhat by race, education, religion, income and, as shown, by sex but follow the same general pattern with a majority of all groups supporting prenatal genetic testing for health-related uses.



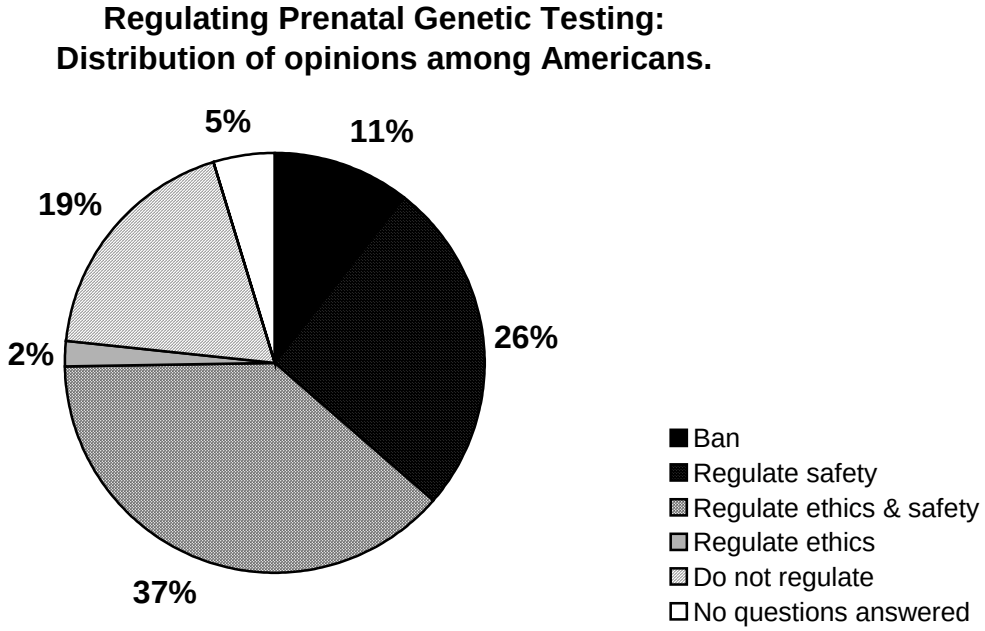
2004 Survey of 4,834 Americans

5. Diverse Views on Government Oversight of Prenatal Testing

Lastly, I would like to share with you some insights into what the American public thinks is the appropriate role of government in overseeing the development and use of reproductive genetic testing. In our April 2004 survey we asked 4,834 individuals whether the government:

- should regulate prenatal genetic testing based on quality and safety
- should regulate prenatal genetic testing based on ethics and morality
- should regulate prenatal genetic testing based on both quality and safety AND ethics and morality
- should not allow prenatal genetic testing at all
- should not regulate prenatal genetic testing at all.

Their responses are shown in the graph below and reveal the remarkable diversity of views present among Americans.



In conclusion, genetic tests provide information. There are a number of steps that could be taken to ensure that people have the right to know and the right not to know genetic information, to ensure that the information is accurate, and that society continues to support *all* prospective parents and their children. The Genetics and Public Policy Center would be happy to provide additional information and analysis as you consider prenatal genetic testing or other issues raised by advances in human genetics. Thank you.