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SUBJECT: HHS Proposed Testimony on advances in genetic technology.

DEADLINE: Tuesday, July 23, 1996

In accordance with OMB Circular A-19, OMB requests the views of your agency on the above subject before advising on its relationship to the program of the President.

Please advise us if this item will affect direct spending or receipts for purposes of the "Pay-As-You-Go" provisions of Title XIII of the Omnibus Budget Reconciliation Act of 1990.

COMMENTS: Hearing is before the Senate Committee on Labor and Human Resources on Thursday, July 25th. Dr. Francis Collins, Director of the National Center for Human Genome Research is the witness.

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Please include the LRM number shown above, and the subject shown below.

_____ Concur

_____ No Objection

_____ No Comment

_____ See proposed edits on pages _____

_____ Other: _____

_____ FAX RETURN of _____ pages, attached to this response sheet

**SENATE HEARING ON GENETIC TESTING
STATEMENT OF DR. FRANCIS COLLINS
DIRECTOR OF THE NATIONAL CENTER FOR HUMAN GENOME
RESEARCH
July 25, 1996**

Madame Chairman and members of the Committee, we are pleased to appear before you today to discuss advances in genetic technology and the resultant challenges for public policy. The Human Genome Project is an historic 15-year international research endeavor with the goal of producing detailed maps of the 23 pairs of human chromosomes and sequencing the 3 billion nucleotide bases that make up the human genome. Launched in 1990, the project is supported in the United States by the National Center for Human Genome Research (NCHGR) at the National Institutes of Health (NIH) and the Department of Energy (DOE). The primary mission of the project is to develop research tools--genetic and physical maps, DNA sequence information, and new technology--to allow researchers to find and analyze genes quickly and efficiently. The project thus far has been successful in meeting or exceeding the goals outlined in its original plan.

In October 1995 the Human Genome Project completed its fifth year with a record of excellent progress toward its goals. The first goal of the Human Genome Project, creating a detailed genetic map for the human genome, has been accomplished. Recently, a team of U.S. investigators published a physical map of the human genome composed of over 15,000 well-ordered markers; this represents a major milestone on the way to the next goal--a comprehensive physical map of the human genome. Though original projections were that this map would not be finished until the end of 1998, completion is now expected in 1997. These accomplishments have set the stage for the project's ultimate goal, sequencing all the DNA in the human genome by 2005.

In 1996, the NCHGR has increased its investment in two areas of DNA sequencing research. Pilot projects were initiated to address and resolve issues that will be confronted in large-scale sequencing of human DNA. These pilot projects are expected to generate between 50 and 100 million base pairs of human DNA sequence by 1998 and, in doing so, develop the methods that will be used in the determination of the complete human DNA sequence.

The NCHGR has also increased its investment in the development of new technology for DNA sequencing, concentrating on miniaturization and automation of current techniques. This approach has focused on improving speed and lowering cost. Progress in these projects has been remarkable as several laboratories have obtained at least 1 million base pairs of DNA sequence at a cost of about 50 cents per base pair. This represents a dramatic reduction in the cost of DNA sequencing from \$5-\$10 per base pair when the Human Genome Project began.

We do not have to wait for the first complete human genome sequence however, to begin to reap the benefits. New genetic information has already enormously increased the number and kind of disease genes being isolated. Not only are the so-called "single-gene" disorders giving up their secrets, but we are beginning to see the same discoveries for complex disorders, such as diabetes, schizophrenia, and breast cancer--disorders that are quite common in this country and in almost every corner of the globe.

In NCHGR's Division of Intramural Research (DIR) and in many institutions around the country, scientists are already using large-scale genome-based approaches to study human genetic diseases. DIR investigators utilize cutting-edge genome science to develop streamlined techniques to rapidly isolate and analyze disease-linked genes, generate improved methods to diagnose inherited and acquired genetic disease, and investigate treatment strategies. Animal models with disease that mimic genetic human disorders are being developed to aid in understanding causes and possible treatments of several diseases. For example, earlier this month researchers at NCHGR and their collaborators reported the development of a laboratory mouse with a disease which has virtually all the characteristics of Ataxia-Telangiectasia (A-T) observed in people, including neurologic problems, cancers of the immune system, slow growth, radiation sensitivity, and abnormal development of sperm and eggs. A-T is of particular importance since carriers are estimated to represent 1% of the population, and are apparently at increased risk of a variety of cancers, including breast cancer. Although scientists have gleaned clues about the function of the human A-T gene from similar genes in single-celled yeast, the new mouse model gives them the first opportunity to study the disease in a controlled way in multi-celled animals other than humans.

THE ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS PROGRAM

As an integral part of the Human Genome Project, the NCHGR and the DOE have each set aside a portion of their funding to anticipate, analyze, and address the ethical, legal, and social implications (ELSI) of the new advances in human genetics that have resulted from the HGP. The current goals of the ELSI program are to improve the understanding of these issues through research and education, to stimulate informed public discussion, and to develop policy options intended to ensure that genetic information is used for the benefit of individuals and society. The NCHGR ELSI program is focusing on several high-priority areas raised by the most immediate potential applications of new genetic technologies: privacy and fair use of genetic information; responsible clinical integration of new genetic technologies; ethical issues surrounding the conduct of genetics research; and, professional and public education about these issues. The ELSI program is now positioning itself to address the issues which will arise once the complete sequence is known.

Privacy and fair use of genetic information:

As our knowledge grows about the genetic basis of disease, so too does the potential for discrimination and stigmatization based on the information contained in our genes. Of particular

concern is the fear of losing jobs or health insurance because of a genetic predisposition to a particular disease. A woman with a positive family history who tests positive for BRCA1 has an estimated 85 percent likelihood of developing breast cancer, and a 50% risk of ovarian cancer. Fighting those risks with intensive surveillance or surgery, without health insurance, would for many individuals result in economic ruin and probable tragedy.

Last year, the NIH-DOE Joint Working Group on Ethical, Legal, and Social Implications of Human Genome Research (ELSI Working Group) and the National Action Plan on Breast Cancer (NAPBC) developed and published recommendations for state and federal policy makers to protect against genetic discrimination:

Definitions

"Genetic information" is information about genes, gene products or inherited characteristics, that may derive from the individual or a family member.

"Insurance provider" means an insurance company, employer, or any other entity providing a plan of health insurance or health benefits including group and individual health plans whether fully insured or self-funded.

1) Health Insurance Access, Renewability, and Portability

Insurance providers should be prohibited from using genetic information, or an individual's request for genetic services, to deny or limit any coverage or establish eligibility, continuation, enrollment or contribution requirements.

2) Health Insurance Affordability

Insurance providers should be prohibited from establishing differential rates or premium payments based on genetic information, or an individual's request for genetic services.

3) Genetic Privacy

Insurance providers should be prohibited from requesting or requiring collection or disclosure of genetic information. Insurance providers and other holders of genetic information should be prohibited from releasing genetic information without prior written authorization of the individual. Written authorization should be required for each disclosure and include to whom the disclosure would be made.

In order to assure that the nation benefits from the fruits of genetic research, safeguards must be in place to protect individual privacy and prevent insurance and employment discrimination. Despite the initiatives of various states including New Hampshire, Ohio,

Minnesota, Maryland and most recently New Jersey to pass legislation aimed at protecting individuals from being denied health insurance based on their genetic status, we have at best a patchwork of privacy and anti-discrimination proposals. In addition, state laws do not provide protection for the many Americans who obtain their health insurance coverage through employer-based plans, because the federal Employee Retirement Income Security Act (ERISA) exempts self-funded plans from state oversight. Therefore, to provide minimum protection nationwide, these issues must be addressed at the federal level.

I am extremely gratified at the Congressional response to the development of these recommendations. Several bills have been introduced to address the potential misuse of genetic information in health insurance. It is quite remarkable that a year ago there were no bills that addressed these critical issues and today there are nearly a dozen legislative proposals. The Senate Labor and Human Resources Committee is to be commended for its efforts on S. 1028, The Health Insurance Reform Act of 1995, and the inclusion of genetic information among the factors an insurer may not use to deny or limit coverage. While this is a significant step forward, it would not prohibit insurers from using genetic information to set exorbitant rates and thereby make insurance coverage essentially inaccessible for many Americans.

Currently, the NAPBC and the ELSI Working Group are collaborating on the next area of potential discriminatory use of genetic information: the employment arena. A workshop on the use of genetic information in the workplace will be held this fall to delineate potential policy options.

Responsible clinical integration of new genetic technologies:

As a result of the Human Genome Project, new disease genes are discovered almost weekly. Once a disease gene is identified it is virtually only a matter of months before a diagnostic test can be made available. Developing effective treatment and preventive measures is a much more prolonged endeavor. These new diagnostic technologies are moving quickly from research into clinical practice, which raises concerns about the impact of these findings on people's lives and health.

This year, tests became available in the research arena for identifying mutations in the BRCA1 gene that predisposes individuals to breast cancer, the HNPCC genes that predispose individuals to colon cancer, and the apolipoprotein E gene that plays a role in the inherited form of Alzheimer's disease. Predictive genetic testing in the face of poor or uncertain preventative or therapeutic interventions raises many concerns regarding benefits and risks. The safety and effectiveness of these new predictive tests must be addressed to ensure a level of quality and reliability.

Three key initiatives are underway to address crucial questions surrounding genetic testing, especially for cancer susceptibility. NCHGR and several other NIH Institutes are co-sponsoring a Cancer Genetics Studies Consortium, focusing on the psychological and social

impact of cancer testing on individuals and their family members. Recommendations for approaches to genetic testing and counseling for cancer risk are being developed. The studies are well underway, and the investigators have developed draft recommendations for the optimal medical management of patients and families who carry mutations in the major gene for heritable breast cancer, BRCA1, and the HNPCC colon cancer genes.

A second initiative is the National Cancer Genetics Network, sponsored by the National Cancer Institute (NCI). It is currently suggested that the 28 NCI cancer centers would act as a hub for the network. Individuals interested in undergoing testing will be enrolled by physicians who are participating in the Network. Those physicians would receive educational materials to facilitate their ability to deliver these complex genetic services, which is essential because most physicians have not received this type of training. Patients would follow a uniform informed consent process and would be provided with up-to-date and validated educational information about the benefits and risks of testing. This would enable them to make an informed decision about whether or not to proceed. All patients, regardless of mutation status, would be enrolled in a confidential registry, so that the consequences of deciding whether or not to be tested and the effectiveness of various follow-up interventions can be evaluated. The network is critical because the premature introduction of cancer susceptibility testing into general clinical practice in the absence of large-scale follow-up studies may prevent our ability to answer crucial management questions.

The final NCHGR initiative on testing, the Task Force on Genetic Testing (TFGT), was established by the ELSI Working Group to examine the development and delivery of safe and effective genetic tests and the quality of the laboratories providing the tests. The Task Force includes representatives from the biotechnology industry, professional medical and genetics societies, the insurance industry, consumers, and federal agencies. In light of the rapid pace of disease-gene discovery and genetic test development, the findings of the TFGT will be crucial to the development of sound policies and practices for the introduction of new genetic tests. The group has now issued draft principles and expects to complete its work in early 1997.

Ethical issues surrounding the conduct of genetic research:

Genetic research may result in the discovery of information that is powerful and potentially predictive. In addition, such information may have familial implications. While in some cases such information may be beneficial to research subjects and their families, there is also potential for misinterpretation or misuse. Special concerns have arisen about the process of informed consent, particularly when the risks and benefits of research participation may not be fully known. Concerns have also arisen about how best to prevent the preliminary or premature release of research results and to protect individual privacy rights for genetic research participants. Examination of existing research guidelines and recommendations over the past five years has revealed that current guidance and protections need to be enhanced in order to deal with the special considerations related to genetics research.

Stored tissue samples are valuable resources for genetics research. Due to increasing concerns about the adequacy of informed consent and privacy protections when stored tissue samples are used in genetics research, the Centers for Disease Control and Prevention (CDC) and the ELSI program supported a meeting to explore these issues. After intensive deliberations, recommendations were developed and published in December, 1995 in the Journal of the American Medical Association. As a direct result of these deliberations, a number of other groups have now taken up this issue including the American Society of Human Genetics and the American College of Medical Genetics, the College of American Pathologists and numerous other organizations which represent the pathology community.

Professional and public education:

As more genetic tests become available to the public, the use and interpretation of those tests and the information they generate will no longer be managed by genetic specialists alone. There will be too few professionals with the advanced training in genetics to meet the expected demand for genetic testing and services. As patients ask more questions about genetic tests and disease risk, responsibility for the use and interpretation of tests and genetic information will increasingly fall to primary care physicians, nurses, physician assistants, and public health professionals who are not specialized or trained in genetics.

Therefore, it is imperative that all of our nation's health care professionals have the knowledge, attitudes, skills and resources they need to effectively integrate genetics into the diagnosis, prevention, and treatment of disease, and to address the related ethical, legal, and social issues. In 1995, NCHGR held a meeting of health professional and education experts to define education priorities for the ELSI grant program. These experts concluded that while public education is important, professional education is of the highest priority, because most individuals will seek genetic information from medical professionals. To this end, NCHGR is now working with professional organizations and consumer groups on a proposal to establish a National Coalition for Health Professional Education in Genetics. Yesterday, we concluded the first planning meeting of the Coalition and I believe these successful discussions will provide the necessary direction for our health professionals in this important area.

The Future of genetic research

As we begin to look beyond the completion of the DNA sequence, it becomes evident that genetic information will affect not only how we perform biomedical research but how we treat and prevent disease. In this regard, the decision of the Committee to confer Institute status on the NCHGR is most welcome. In fundamental ways, the creation of the National Human Genome Research Institute (NHGRI) will recognize NCHGR as the national leader in this medical and research revolution. The new NHGRI will be critically positioned to exploit several important scientific opportunities that might otherwise be neglected:

• **Functional genomics.**

New technologies and methodologies will facilitate the study of gene function, not gene by gene, but thousands at a time. This will allow us to begin to unravel the complex networks of interactions between genes in health and disease.

• **Technology development.**

Sequencing technology, like computer technology, is open ended. Improved engineering techniques will continue to drive down costs and increase productivity as we expand our sequencing efforts.

• **Comparative genome analysis.**

The genomes of several mammalian species will be sequenced and compared to identify key regulatory and control sequences. The regulation of when and where a gene is expressed is critical to understanding the role of genes in disease.

• **ELSI research and policy development.**

The NHGRI will continue to support research and policy development on key ethical, legal, and social implications of human genome research.

The establishment of a National Institute to lead and support the Human Genome Project and its promising new approach to biomedical science is imperative if the United States is to maintain its global leadership in biomedicine. As this new technology wave spreads throughout the world, international competitors will quickly adapt this trend to their own national research programs.

Conclusion

Congress, and particularly this Committee, has long been the leader in supporting genetic research and the Human Genome Project. Therefore, it is fitting that this Committee is now taking the lead in addressing the important policy issues raised by this research. Protecting privacy and preventing the misuse of genetic information is essential not only for us to reap the benefits of this research but indeed, in order to carry on the research at all. Increasingly we hear of people unwilling to participate in genetic research out of fear that information about their genes might be used against them by insurers or employers. Genetic discrimination has been hailed as the "civil rights" issue of this decade. We have the unique opportunity to address genetic privacy and discrimination issues now as the scientific information unfolds, before we find ourselves in a full-fledged crisis. I look forward to continuing to work closely with the Congress to develop sound policies to ensure that the Human Genome Project and new genetic information is used to benefit, not harm, the American people.

This concludes my remarks. I would be pleased to answer any questions you may have.