A Roadmap for the Integration of Genetics and Genomics into Health and Society

The Study Priorities of the Secretary's Advisory Committee on Genetics, Health, and Society

June 2004

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October 11, 2004

The Honorable Tommy G. Thompson
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Thompson:

As you know, the Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) was established in September 2002, and re-chartered in 2004, to serve as a public forum for deliberations on the broad range of human health and societal issues raised by the development and use, as well as potential misuse, of genetic technologies. Our Committee is also chartered to be a source of advice to the Department of Health and Human Services and, if requested, to other departments and agencies of the Executive Branch.

In light of its broad charter, the Committee decided to undertake a prioritization process to identify the most appropriate issues for our immediate attention. The results of that prioritization process, and rationale for the Committee's decisions, are presented in the enclosed report, *A Roadmap for the Integration of Genetics and Genomics into Health and Society: The Study Priorities of the Secretary's Advisory Committee on Genetics, Health, and Society*. The Committee hopes that the information and background materials on these issues will be useful to you and the HHS agencies. In addition, we hope that the report will help enhance public awareness of important issues raised by genetic and genomic technologies. We look forward to fulfilling the study plans laid out in this report, and stand ready to be of service to you and HHS on any other matters related to genetic and genomic technologies.

Sincerely,

Read V. Tuckson, M.D.
SACGHS Chair

ACKNOWLEDGEMENTS

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- For their participation as members of the SACGHS Intra-Meeting Task Force: Emily S. Winn-Deen, Ph.D. (chair), Debra G.B. Leonard, M.D., Ph.D., Reed V. Tuckson, M.D., Huntington F. Willard, Ph.D., Barbara Willis Harrison, M.S., and Cynthia E. Berry, J.D.

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EXECUTIVE SUMMARY

Advances in genetics and genomics promise to improve human health and, in addition, may have far-reaching implications for society in non-health arenas, including education, employment, and the law. The establishment of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) reflects the potential for genetics to improve public health as well as the potential for genetics to be misused. SACGHS has spent its first year exploring, analyzing, and deliberating on the broad range of human health and societal issues raised by the development and use of genetic technologies. In considering the depth and breadth of the issues before it, the Committee concluded that it would be more effective to assess them in a systematic and deliberative way. The Committee devised an iterative prioritization process to help identify areas designated in the SACGHS charter where policy recommendations are needed to enhance the integration of genetics into health care and barriers to progress that need to be lifted. In this report, SACGHS describes the issues that it identified and its reasons for selecting them as high priorities.

Specifically, the SACGHS iterative prioritization process resulted in the identification of 12 high-priority issues that can be roughly divided into opportunities for, and barriers to, the realization of the potential of genetics to advance the development of diagnostic, therapeutic, and preventive strategies to improve health. The opportunities include the following:

- Public discussion of the SACGHS vision for genetics;
- Public discussion of whether genetic information is different from other personal health information (conceptualized in the term *genetic exceptionalism*);
- Investigation of the health, ethical, legal, economic, and social implications of large population studies;
- Review of the potential of pharmacogenomics to improve public health;
- Assessment of the status of the quality and oversight of genetic technologies and services;
- Promotion of public awareness; and
- Assessment of the advantages and disadvantages of direct-to-consumer (DTC) marketing of genetic tests.

Barriers to the integration of genetics into health care can be identified within the following issues:

- Access to genetic technologies and services;
- Coverage and reimbursement of genetic technologies and services;
- Concerns about genetic discrimination;
- The education and training of health professionals in genetics and the adequacy of the health workforce; and
- Patents and licensing practices.

Although SACGHS considers all of these issues to be important, its goal was to identify priority issues for which the resulting recommendations would have the greatest impact on the integration of genetics into health care. To assist its prioritization process and to produce a work plan for the coming year, SACGHS devised a system that ultimately resulted in the classification of the issues into the following three categories: the highest priority issues that require in-depth study; high-priority issues that require only short-term action or monitoring; and overarching issues that

should be considered within the context of the other issues. Each issue was placed into a category, and the Committee members and *Ex Officios* ranked the issues within each category.

Although the Committee recognized the importance of all of the issues, it also believed that the public's interest would be served best if SACGHS focused on only a few of them over the coming year. The Committee ranked coverage and reimbursement of genetic technologies and services as the highest priority issue requiring in-depth study. Along with its immediate plan to develop recommendations on coverage and reimbursement, the Committee plans in the future to undertake in-depth exploration of the issues of large population studies, pharmacogenomics, and DTC marketing of genetic tests. The passage of Federal genetic non-discrimination legislation was ranked as the highest priority issue that could be best addressed by short-term action or monitoring. The Committee decided that short-term action also would adequately address genetics education and training and the issue of elaborating the Committee's vision for integrating genetics into health care and society. Within the short-term action category, SACGHS decided at this time to monitor patents and licensing practices and the oversight of genetic technologies and services. Finally, the Committee agreed that access, public awareness, and genetic exceptionalism are overarching issues that should be considered within the context of all of the other issues.

The Committee members hope that their exploration of these issues will lead to analyses and recommendations that will be of value to the Secretary, the Department of Health and Human Services, and the other departments and agencies represented on SACGHS.

A ROADMAP FOR THE INTEGRATION OF GENETICS AND GENOMICS INTO HEALTH AND SOCIETY

Introduction

Advances in genetics and genomics promise to improve human health and, in addition, may have far-reaching implications for society in many non-health arenas, including education, employment, and the law. The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) was chartered in September 2002 by the Secretary of Health and Human Services as a public forum for deliberation on the broad range of human health and societal issues raised by the development and use of genetic technologies, and, as warranted, to provide advice on these issues. The establishment of SACGHS reflects the potential to improve public health through genetics and genomics, as well as public concern about their use. In recognition of the importance of genetics and the potential for both positive and negative impacts on society, the SACGHS charter is a broad mandate to explore far-ranging issues and make recommendations on the uses of genetics in health and society.

During its first and second meetings, SACGHS explored, analyzed, and deliberated on the broad range of human health and societal issues raised by the development and use of genetic technologies. Through its initial deliberations, the Committee members realized that a systematic approach was needed to identify the issues on which they should focus their attention. Members embarked on a prioritization process in November 2003, considered all of the topics addressed throughout their deliberations, and narrowed the list of topics for further consideration. After the initial narrowing of the list of topics, the Committee developed issue briefs prior to the March 2004 meeting on the top 12 priority issues. The purpose of the issue briefs was to provide the Committee with background information, to describe previous and ongoing work by government agencies and committees, to outline policy options, and to facilitate the prioritization process. In considering all the current and potential applications of genetics, SACGHS believes its efforts are best spent focusing on issues that will improve public health and in areas where its attention will have the greatest impact. The Committee identified areas where action will enhance the integration of genetics into health care and lift barriers to progress. This report describes the Committee's rationale supporting its decisions and highlights its priorities.

Areas Considered by SACGHS During Its Initial Deliberations

During its deliberations of the past year, as specified in its charter, SACGHS has served as a public forum for the discussion of emerging scientific, ethical, legal, and social issues raised by genetic technologies. In addition to this charge, SACGHS' charter designated the following specific functional areas for consideration by the Committee:

- Assessing how genetic technologies are being integrated into health care and public health;
- Studying the clinical, ethical, legal, and societal implications of new medical applications and emerging technological approaches to clinical testing;
- Identifying opportunities and gaps in research and data collection efforts;
- Exploring the use of genetics in bioterrorism;
- Examining current patent policy and licensing practices for their impact on access to genetic technologies; and
- Analyzing the use of genetic information in education, employment, insurance (including health, disability, long-term care, and life), and law (including family, immigration, and forensics).

The first functional area---the assessment of how genetic technologies are being integrated into health care and public health—is the most extensive and inclusive of the categories. Topics discussed by the Committee within this category include: oversight of genetic testing, access issues, coverage and reimbursement, genetic exceptionalism, definition of genetic technologies, pharmacogenomics, education and workforce issues, and a statement of the Committee's vision.

The identification of gaps in research and data collection efforts is an important function that overlaps significantly with integration issues. Large population studies were considered within this category, as were data needs for coverage and reimbursement and the emerging field of pharmacogenomics.

Two additional topics discussed during SACGHS meetings are actually functional categories themselves: the effects of patents and licensing practices on the availability, clinical accessibility, and affordability of genetic technologies and the implications of the use of genetic technologies for bioterrorism.

To address the clinical, ethical, legal, and societal implications of new medical applications of genetics, the Committee considered public awareness of genetic technologies, informed consent issues, new health-related applications of genetic technologies, and the uses of these technologies for enhancement versus treatment.

Definitions

The term *genomics* is a relatively recent addition to the lexicon and represents a broad and comprehensive way of looking at the role and function of genes and their interactions. Though genomic tools are used to address similar questions asked in genetics, SACGHS believes that it is necessary and important to use the term in its deliberations and documents, given the growing role genomics is beginning to play in health and health care. Although *genomics* is new and distinct from *genetics*, the two fields overlap, and there is a lack of consensus regarding their definitions. In the Committee's view, the fields differ more in emphasis (i.e., single traits versus whole genomes) than in scope (what each encompasses).

Genetics is the study of inherited traits, of inherited variability, and of the mechanisms of transmission revealed by patterns of inheritance. Genetic diseases addressed by clinical practice (and specifically the specialty of medical genetics) include single gene disorders, chromosomal disorders (such as rearrangements or trisomy), and multifactorial disorders (such as heart disease or diabetes), in which the role of genes is apparent.

Genomics is the study of the structure and function of whole genomes and science related to genomes, including the expression patterns that result from the interaction of the whole genomic complement. *Genomic medicine* refers to the application of the principles of genomics to the prevention, diagnosis, and treatment of disease, as well as to determining the probability of future disease and, in general, deals with the combinatorial effect of many genes, rather than the effect of single genes.

The final category designated by the SACGHS charter was the analysis of the uses of genetic information in education, employment, insurance, and the law. Within this category, the Committee considered the need for Federal legislation to prohibit genetic discrimination in health insurance and employment, issues involving privacy and confidentiality, and forensic issues.

Key Issues Identified

As SACGHS considered the depth and breadth of the issues before it, Committee members determined that there was a need to assess all of the issues in a systematic and deliberative way. A Task Force appointed to narrow the list of topics for consideration initiated the prioritization process by asking each Committee member to choose his or her top five priorities from among all of the issues noted above. The systematic prioritization process was strengthened by the wide range of stakeholders and viewpoints in the field of genetics represented on the Committee. Although members may have had substantially different reasons for ranking an issue in the top five, the systematic process was fair, considered all viewpoints, and allowed the most critical issues to rise to the top. Through this process, the Task Force identified the top issues of greatest import and brought them to the full Committee for a second vote prior

to the March 2004 meeting. There were substantial differences between the rankings of members and *Ex Officios*. For example, the members ranked access as #1, while the *Ex Officios* ranked access as #10. As the Committee assessed each issue during the March meeting, the members discussed the source of these differences with the *Ex Officios*. The key issues can be divided roughly into the categories of opportunities for, and barriers to, the fulfillment of the potential of genetics to advance the development of diagnostic, therapeutic, and preventive strategies to improve health.

SACGHS believes it can have an impact by identifying opportunities to enhance and encourage the use of genetics to improve public health. The Committee's deliberations provide opportunities for articulating a vision of future uses for genetics and for increasing public awareness of genetics. The public's ability to understand genetics is key to its successful integration into health care. In addition, the Committee believes that understanding how genetic information differs from other personal health information, an issue on which consensus has not been reached, is important. Committee meetings also are opportunities for public discussion of genetic exceptionalism and its role in the development of public policy. SACGHS recognizes that genetic information can be inferred from many types of medical information and that it is exceedingly difficult to separate genetic information from other types of medical information. However, genetics may be perceived by the public to be unique. Arguments supporting this perception are that genetic information is a unique identifier, that it is relevant to family members, potentially predictive of future disease, passed on to our children, and may be associated with stigmas and have psychological impacts. Although other types of medical information also exhibit some of these characteristics, genetic information is unique in having all of them.

The Committee identified opportunities in research and data collection where the Federal government could contribute to the advancement of genetics. Although there may be specific gaps in research in other areas considered by the Committee, two issues arose that could be considered important data-gathering efforts. The Committee believes that large population studies, particularly those that will unravel of the genetic basis of multifactorial diseases, are key to putting the knowledge gained by the Human Genome Project into practice. Because the initiation of large population studies will require a significant investment, SACGHS' focus in this area could have a significant impact. SACGHS also might provide an important platform for discussion of the ethical, legal, and social implications of this research and ways to overcome the challenges of mounting projects of such scope and magnitude.

The field of pharmacogenomics also will provide tools for the further integration and transfer of human genome data into practical benefits. Pharmacogenomic (PG) tests will become an important tool in preventing the 100,000 deaths per year in the United States that currently are caused by adverse drug reactions. In particular, the Committee focused on physicians' need for relevant and practical advice on the application of PG data in the clinic today. Clinicians want and need specific guidance on how PG information should affect treatment options for their patients, for example, dosing regimes. Health providers will need cost data on pharmacogenomics to assist in coverage and reimbursement decisions. As with many of the issues under consideration, the success of pharmacogenomics is closely linked to other issues under consideration, including adequate reimbursement and data from large population studies. The Committee regarded both large population studies and pharmacogenomics as areas that require further study.

The Federal government clearly has a role in protecting the public's safety and ensuring that new technologies introduced into the health care system are safe and effective. SACGHS heard presentations at the October 2003 SACGHS meeting on the progress being made by Federal agencies and by professional organizations on the oversight of genetic testing.. However, despite these continued efforts independent analysis of the clinical validity of genetic tests offered as services does not always exist. Members thought that this gap was an important issue that warranted further consideration.

In keeping with this health-related focus, SACGHS identified the most significant barriers to the integration of genetics and genomics into health care. The Committee had previously designated protection from genetic discrimination as a top priority and, therefore, the Task Force considered it to be essential that this issue remain a top priority. The need for protection from genetic discrimination in employment and insurance is intimately linked to the integration of genetics into health care. Most Americans receive health insurance from their employers and may be reluctant to take advantage of new genetic technologies if they fear that the information may be used to limit their subsequent ability to get health insurance and employment. Whether or not genetic discrimination currently is a significant problem, the fear that it will occur appears to be acting as a barrier to the utilization of genetics to improve health.

The Committee believes that another significant barrier to the realization of the promise of genetics is the inadequate coverage and reimbursement for genetic technologies and services, particularly for those genetic technologies and services used for screening. Although the future of medicine increasingly will focus on the prevention of disease, rather than on its diagnosis, the current system does not adequately facilitate the use of or access to preventive technologies and services. In addition, the current system does not reimburse sufficiently for many genetic tests or for the genetic counseling that should accompany the receipt of genetic test results. Ultimately, reform of the current system of coverage and reimbursement may be needed. The identification of coverage and reimbursement as a top-priority issue was influenced by the great need in this area, by its relationship to access to genetic and genomic technologies, and by the potential role that can be taken in this area by the Department of Health and Human Services (HHS). Because HHS can be influential and its efforts in setting standards can be pathbreaking, recommendations regarding coverage and reimbursement could have an impact on health care and public health. In particular, the Centers for Medicare & Medicaid Services' (CMS') national coverage determinations often are adopted by private insurers. The Committee also identified unmet needs for data on cost analyses and for establishing principles and guidelines for decision-making on appropriate coverage and reimbursement for genetic technologies and services. To successfully integrate genetics into health care, guidance is needed on cost-effectiveness standards and on criteria for clinical validity and utility.

A well-trained and diverse workforce also is essential for access to and the proper use of genetics in health care. The Committee believes that the Federal government has a role to play in influencing support for genetics education, and the government has, in fact, for several years been committed to enhancing the education of health professionals in genetics, realizing that genetics has advanced well beyond the knowledge base of many health professionals and that an educated workforce will be essential for the appropriate use of these technologies. In particular, the Health Resources and Services Administration's (HRSA's) educational efforts have become an integral part of the larger goal of enhancing access to new genetic technologies. Professional organizations also are exerting considerable efforts to enhance the education of all health professionals in genetics. However, the Committee is concerned that all of these educational efforts cannot keep pace with the rapid expansion of the genetics knowledge base and believes that continuous efforts in genetics education will be required in order to avoid a lag time in the application of knowledge gained from genetic research. SACGHS considers the education of all health professionals in genetics to be a key component of the effective integration of these technologies into health care practice.

Committee members agreed that access to genetic technologies and services is essential for realizing the promise of genetics. Access to health care is one of the main health concerns in the United States and, as demonstrated by its inclusion in Healthy People 2010 and current HHS initiatives, it is already a high priority of the Federal government. Although many of the barriers to access are related to or encompassed by other issues, by highlighting access, SACGHS will shed light on this significant barrier to the integration of genetics into health care. In particular, the Committee is concerned that without

commitment to and action on issues of access, a legacy of the Human Genome Project could be an exacerbation of health disparities.

Patent and licensing practices may affect access to genetic technologies and services by limiting the number of providers and increasing the costs of these technologies and services. Committee members expressed concern that current patent and licensing practices are blocking or delaying research in biomedical sciences as well as the application of genetic information in clinical practice, i.e.; in genetic testing. Researchers may be limited or prevented from pursuing knowledge and cures for disease by patent holders exercising their intellectual property rights. Providers can be blocked by patents and licenses from performing genetic tests and single providers of a genetic test may limit or block access. For these reasons, the Committee chose to include this issue as a top priority warranting further consideration.

Direct-to-consumer (DTC) marketing of genetic tests was the final issue identified by the Task Force as requiring further consideration. Although DTC marketing plays an important role in increasing public awareness of the uses of genetic information, false or misleading advertisements may erode confidence in genetics and undermine the public's view of its benefits. In addition, DTC marketing of genetic tests may promote unrealistic expectations of genetic testing and further ideas of genetic determinism. Although this issue cannot easily be characterized as an opportunity, barrier, or gap in research and data collection efforts, the Committee nevertheless believed that because of the great promise of genetics, DTC marketing is an issue that requires further consideration. DTC marketing of genetic tests and services also has a role in facilitating the integration of genetics into health care and society. SACGHS believes that genetics will provide public benefit and therefore, it is important to understand the impact of DTC marketing of genetics.

Priority-Setting Process

During the March 2004 meeting, the Committee devised an issue classification system consisting of the following three categories: overarching issues that should be considered within the context of the other issues; high-priority issues that require only short-term action or monitoring; and highest priority issues requiring in-depth study. Members deliberated on each of the 12 issues separately and placed each one in the appropriate category. The categories were then considered separately, and the Committee members and Ex Officios ranked the issues within each category. The Committee used the following questions to help assess the relative priority of the issues. Members also were mindful of their overarching decision to focus on health-related issues and their pragmatic goal of having an impact.

- How urgent is the issue?
- Does the issue warrant the Committee's attention?
- Is there media attention to and/or public concern about the issue, and is there a need for public discussion and understanding of the issue?
- Does the government have jurisdiction/authority over the issue?
- Is federal guidance or regulation on the issue warranted, and is the government poised to act on the policy advice of the Committee?
- Does the issue raise concerns that only the government can address, or would government involvement be duplicative?
- Does the issue raise moral or ethical concerns that warrant government involvement/leadership?
- Will the Committee's policy advice on the issue significantly benefit society, or will the failure to address the issue prolong any negative impact it may be having?

- Do sufficient data about the issue exist for the Committee to develop informed policy advice; and is there another body already addressing the issue or that is better equipped to address the issue?
- Have the policy solutions to the issue already been worked out?

Priority-Setting Decisions

Overarching Issues

During the discussion on prioritization of the key issues, it became apparent that several issues were overarching and needed to be considered within the context of all of the Committee's discussions. The Committee regarded access and public awareness as inherent issues, encompassed within and important parts of all of the top-priority issues. The Committee agreed that access to genetic technologies and services is essential; however, because the barriers to access are defined by many of the other topics, this issue should be considered within the context of all of the Committee's deliberations. In this way, SACGHS will enhance understanding of the barriers to access throughout all of its work. The Committee also considered public awareness of genetics to be essential to the successful integration of genetic technologies into health care and society. Although identification of the appropriate means for promoting public awareness is a difficult task, members considered it to be so important that it will be addressed within the context of all the other topics. In addition, the Committee considered the issue of genetic exceptionalism to be a philosophical question that should be considered on a case-by-case basis during its deliberations.

High-Priority Issues That May Be Addressed by Short-Term Actions or Monitoring

Genetic discrimination protection remains a top priority for the Committee. The Committee thought that immediate action was required to encourage the passage of a genetic non-discrimination bill in the 108th Congress and agreed to send a second letter to the Secretary urging that continued pressure be applied to facilitate passage of the Senate bill 1053 in the House. Two additional priority issues were identified that could be addressed sufficiently by the Committee with short-term actions. First, the Committee planned to continue fact-finding between the third and fourth meetings on genetics education and workforce training efforts and drafted a resolution regarding those efforts for consideration at the June 2004 meeting. Second, although the Committee considered its charter to be an effective vision statement, it agreed to prepare this report describing its priority-setting process, deliberations, and decisions. In conjunction with this report, the Committee also hopes to make the 12 attached issue briefs that were prepared earlier this year to advance the priority-setting process available to the public in order to broaden public awareness of these issues.

Two issues were designated as requiring "monitoring only" for the near future. The Committee believes that significant progress is being made by Federal agencies on improving oversight of genetic testing; however, SACGHS still has a role in the continued monitoring of their work. In addition, the Committee decided to defer in-depth consideration of patents and access issues until after a recently established National Academy of Sciences committee studying this subject completes its work.

Highest Priority Issues Requiring In-Depth Study

The highest priority issues requiring further in-depth study will be the main focus of the Committee's efforts during the next year. A vote by Committee members established the following order for the highest priority issues: coverage and reimbursement, large population studies, pharmacogenomics, and DTC marketing. The Committee ranked coverage and reimbursement as its highest priority issue because

of its importance in facilitating the integration of genetics into health care, and it plans to carry out additional data and information gathering on this issue and to prepare a report with recommendations. Large population studies and pharmacogenomics will be considered at the February 2005 meeting. DTC marketing will be addressed at a future date; however, the Committee thought that the topic warranted an immediate response in the form of a letter expressing its concerns.

Conclusion

SACGHS has focused for the past year on the identification of priority issues for which recommendations by the Committee will have the greatest impact on the integration of genetics and genomics into health care. Through a systematic process, the Committee identified 12 key issues and developed a work plan to address each one. The Committee's highest priorities for 2004 are the passage of Federal genetic non-discrimination legislation and the development of recommendations on coverage and reimbursement of genetic technologies and services. The Committee plans to begin addressing the other top-priority issues later this year. Committee members hope that their exploration of these issues will lead to analyses and recommendations that will be of value to the Secretary, HHS, and the other departments and agencies represented on SACGHS.

APPENDIX

Issue Briefs

The following issue briefs were developed by staff prior to the March 2004 SACGHS meeting to provide the Committee with background information on the top 12 priority issues, to describe previous and ongoing work by government agencies and committees in these areas, to outline policy options, and to facilitate the prioritization process. These briefs do not represent the official views of SACGHS or of the United States Government.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Access to Genetic Technologies
Issue Brief

Issue Statement

Barriers to access to genetic technologies can prevent patients and consumers from fully benefiting advances in genetics and resulting genetic services. Access can be impeded at several points along the genetic technology development and use continuum. Are there specific areas in which intervention by the Federal government might minimize barriers to access to these services?

Relevance to the SACGHS Charter

This issue relates to two of the seven functional categories identified in the SACGHS charter—assessing how genetic technologies are being integrated into health care and public health and examining current patent policy and licensing practices for their impact on access to genetic technologies.

Background

Healthy People 2010 identified access to health care as one of the major health concerns in the United States. Because many factors have an impact on the delivery of health care, there are numerous points at which access can be impeded. Figure 1 illustrates the different factors and how they interact and can create barriers for patients seeking care. Genetics is only one of the many health disciplines that are affected by these factors.

Although many of the factors that affect access to genetic technologies also affect access to other health services, some factors may be of special concern for or uniquely impede access to genetic technologies.

During the research and development phase, it is important for studies to include data from diverse populations. Diverse representation of the population in clinical trials has particular importance in genetic research, because genetic variation among populations may account for differences in disease prevalence, drug reactions, and susceptibility to environmental triggers, among others. Broad inclusion of populations in the research and development phase will ensure that sufficient evidence exists to demonstrate the safety and effectiveness of

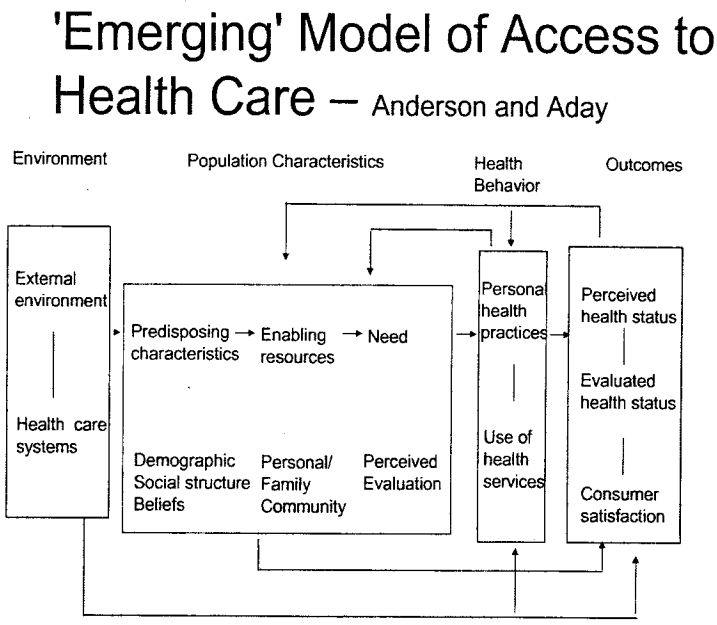

Figure 1. Anderson, A; Aday, LA. Access to medical care in the U.S.: realized and potential. *Med Care* 1978; 16(7):533-546.

genetic technologies for all and thereby enhance access for all groups. The National Institutes of Health and the Food and Drug Administration both have adopted policies promoting the inclusion of women and minorities in clinical research.

During the test development and marketing process, patent holders may legally enforce their patent rights in a manner that impedes genetic research and the development of genetic technologies. Also, exclusive licensing practices may limit the number of tests that can be performed or restrict who can perform a test, and royalty fees can increase a test's cost. As a result, individuals who could benefit from genetic testing may not be able to obtain or pay for a test. In cases of rare disease testing, laboratories and test manufacturers holding a patent may not have a financial incentive to develop or market a genetic test because there may be only a small number of people interested in testing. These issues are described in greater detail in the *Patents and Access Issue Brief.*

Regulatory requirements also can affect access to rare disease tests. Tests for some rare conditions are available only through research laboratories; however, research laboratories may not return test results that are to be used for clinical purposes unless the laboratory is certified according to the Clinical Laboratory Improvement Amendments (CLIA). Although the Centers for Medicare & Medicaid Services, the Federal agency responsible for administering CLIA and for providing technical assistance to laboratories seeking certification, takes a flexible approach in certifying small academic research laboratories, if the requirement for CLIA certification is seen as too onerous or costly to obtain, academic laboratories may forego offering the tests.

The cost of genetic testing also creates difficulties in accessing genetic technologies. Insurance companies may not always reimburse for genetic testing services, especially if the insurer does not consider genetic services to be medically necessary or cost-effective. For example, the Medicare program does not cover screening tests, including predictive genetic tests, for people who do not have specific signs or symptoms or a personal history of disease. For those who must pay for genetic testing out-of-pocket or for those who choose to pay to prevent their insurer from knowing they are getting tested, genetic tests and counseling can be quite expensive (for example, the BRCA1/2 test costs $2,760; genetic counseling adds approximately another $200 to $300). This is particularly problematic for individuals who already have high medical bills or who cannot afford health insurance. These issues are described in greater detail in the *Coverage and Reimbursement Issue Brief.*

Lack of knowledge about genetic technologies and their indications for use also may limit access to appropriate genetic technologies. Individuals will not know to seek genetic services if they and their providers are unaware that a genetic technology is available and appropriate. This may be particularly problematic given that genetic specialists primarily practice at academic health centers in specialty departments and that many primary health care providers are not sufficiently trained in genetics. It is important for health professionals to be educated about genetic tests and trained to be sensitive to and meet the diverse needs of their patients, especially because certain populations may be at increased risk for a genetic disease or may have unique traditions and beliefs that influence their decisions about whether to seek and utilize genetic services. The status of genetics education efforts is described in more detail in the *Genetics Education and Training Issue Brief.*

Fear of stigmatization and genetic discrimination in employment and health and life insurance also can discourage individuals from seeking genetic testing. The absence of federal legislation and gaps in state protections may make some individuals believe that they are at risk for being denied health or life insurance or employment or that they may be charged higher premiums as a result of a genetic predisposition to disease. Also, misinterpretation and misuse of genetic information by insurers can lead to wrongful denial of coverage. This issue is described in greater detail in the *Genetic Discrimination Issue Brief.*

SACGT Efforts

Through an Access Work Group, SACGT explored financial barriers to access as well as disparities in access to genetic testing services, the inclusion of broad populations in the test development process, the availability of culturally appropriate genetic services, the importance of understanding the relevance and significance of human genetic variation to health status, and health promotion and disease prevention issues. The Work Group's efforts regarding genetic testing and genetic education and counseling are described in the *Coverage and Reimbursement Issue Brief.* The Work Group also held a town meeting on disparities in access to genetic testing as part of the Office of Minority Health's National Leadership Summit on Eliminating Racial and Ethnic Disparities in Health. The expiration of SACGT's charter precluded further progress in these areas.

Policy Considerations

Access to health care is a high priority of the Federal government, as demonstrated by its inclusion in Healthy People 2010 and current initiatives of the Department of Health and Human Services. Examination of the issue from a genetics perspective may be useful to these efforts. Furthermore, because genetics is an underlying contributor to a range of health problems, improving access to genetic services has the potential to have a positive impact on other areas of medicine, health care and prevention, and public health.

Because many of the issues in genetics have an access component (e.g., patents, genetic discrimination, coverage and reimbursement), access might provide a broad context within which to consider these issues. On the other hand, its breadth can make the development of concrete recommendations more challenging. Furthermore, because barriers to access and disparities in access are issues endemic to the entire health care system, and because genetics is integrated into numerous medical disciplines, efforts to address specific aspects of the access issue that are applicable throughout the health care system may be difficult and may be better addressed by another body with a broader mandate.

OUTCOME

The Committee regarded access as an inherent issue, encompassed within all of the top-priority issues and significant to each one. The Committee agreed that access to genetic technologies and services is essential; however, the barriers to access are defined by many of the other topics. Therefore, this issue should be considered within the context of all of the Committee's deliberations.

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Public Awareness and Understanding of Genetic Technologies Issue Brief

Issue Statement

Public understanding of genetic technologies may play a role in facilitating their appropriate integration into health care and society. However, genetic technologies are highly complex, and many may require some understanding of basic genetic and biological principles in order to be fully understood. Moreover, when media coverage of genetic advances is incomplete or misleading, public understanding can be undermined. How essential is public awareness and understanding to the appropriate integration of genetic technologies into health care and society? Is assuring the genetic literacy of the public an appropriate role for the Federal government? In general, should the Federal government be doing more in this area and, if so, what additional efforts should be undertaken?

Relevance to the SACGHS Charter

This issue relates to a number of the seven functional categories identified in the SACGHS charter, including assessing how genetic technologies are being integrated into health care and public health and serving as a public forum for the discussion of emerging issues raised by genetic technologies.

Background

Ideally, increased public understanding of genetic technologies may enhance individual doctor/patient interactions, help ensure the appropriate use of these technologies, improve health outcomes and health status, and provide a wider forum for the discussion of genetics policy within society. Conversely, lack of public understanding may lead to inappropriate treatment. As research advances knowledge of the genetic basis of common diseases, genetic information is likely to become a part of healthcare interactions for more and more people. Although most patients will not need to have full knowledge of the mechanics of genetics testing, a basic understanding of the implications of genetic test results will be beneficial, especially as genetics moves beyond traditional specialty settings. Additionally, the application of genetic technologies has expanded to areas that are not related to health, such as forensics, determination of paternity, and even trait selection (for example, sex selection for the purpose of family balancing).

Media coverage plays an important role in educating the public about genetic advances and communicating their relevance to health and health care in a manner that is understandable to laypersons. However, because advances in genetics are not always easily packaged into sound bites, media coverage can be problematic, as it tends to oversimplify and sometimes mislead. The consequences can be serious if the coverage causes false hope or hopelessness or other adverse outcomes for individuals and families. Some of the common genetics themes covered by the media include cautionary tales highlighting the risks and unintended consequences of genetic engineering.

Basic genetics education at the K-12 level may be important in providing a foundation for genetic literacy and public understanding. As such, many efforts are under way to enhance K-12 science education. There are many sources of educational materials related to genetics for students and teachers. The National Institutes of Health provides teaching supplements, including a supplement on human genetic variation, for grades 9-12 (science.education.nih.gov/customers.nsf/ highschool.htm). The Biological Sciences Curriculum Study, a non-profit organization that develops science curricula for elementary grades through college, makes genetics curricula available for K-12 teachers and provides professional development opportunities for science teachers at all levels.

Current Status

Currently, not a great deal is known about the level of public awareness regarding genetics and genetic technologies, because it is generally difficult to measure. Most of the surveys conducted to gauge public awareness of genetics have focused on specific issues, such as cloning. From an analysis of surveys taken between 1987 and 2003 involving public opinion on the use of certain genetic technologies (www.genetics-and-society.org/analysis/opinion/ summary.html), it appears that along with general support for the health-related use of genetics, concerns remain regarding other applications of genetic technologies. Many of these surveys asked normative questions about genetic technologies, although few have addressed the public's actual knowledge of the processes involved or the implications of the technologies.

A 2002 national survey by the Genetics and Public Policy Center addressed the issue of public awareness of genetic issues. This survey, one of few to address actual knowledge, concluded that public awareness of genetic technologies was high, but that accurate knowledge about them was significantly lower. The survey showed that although most of the respondents (80 to 90 percent) were aware of genetic technologies such as reproductive cloning, genetic testing, and genetic engineering, their understanding of the applications themselves was limited. For example, 48 percent thought that prenatal genetic tests were currently available for intelligence, and 79 percent thought that tests were available to determine predisposition to mental illness.

Currently, many efforts are under way to enhance public understanding of genetics and genetic technologies. Federal agencies are funding efforts in this area, as is the private sector. The Department of Energy has funded many projects focused on genetics education, such as "Delivering the Human Genome to the Public," an interactive Internet-based educational tool. Through its Ethical, Legal, Social Implications program, the National Human Genome Research Institute (NHGRI) has funded studies measuring the knowledge and understanding of particular issues in genetics, such as the genetics of a specific disease (www.genome.gov/10001798). In 2002, NHGRI held a workshop as part of a long-range planning effort to review its activities in education and public outreach. Workshop participants noted, among other things, that print and broadcast news play an important role in science literacy and trust in science, but that public outreach efforts are the hardest to implement and the least effective. The Health Resources and Services Administration and the March of Dimes jointly are supporting public education programs such as the Genetic Literacy Project. Through a grant to the Hastings Center, the project is preparing a report addressing public knowledge and attitudes surrounding genetics. The American Association for the Advancement of Science has launched several projects that address public awareness issues. The Behavioral Genetics Project, for example, aims to provide tools for an open discussion between lay groups and the genetics professions surrounding gene/environment interaction and their roles in human behavior.

SACGT Efforts

SACGT made plans to develop a report to the Secretary on the importance of public understanding of genetic tests. This report was to be based on the deliberations of a working group that had developed and gathered public comments on a draft information brochure on genetic testing. The Committee's report would have highlighted the importance of public understanding of genetic testing; recommended the development and dissemination of information about genetic tests to the general public and to patients/consumers considering genetic testing; called attention to the need for information materials tailored to particular communities, including groups linked by ethnicity, culture, or language; and transmitted a copy of the brochure as a model of the type of information needed to enhance public

understanding and as an example that could be used for the preparation of additional brochures on specific tests and categories of tests.

Policy Considerations

The issue of public awareness and understanding lacks clear definition, which complicates efforts to address it in a thorough and effective manner. There is debate about what public awareness and understanding are and how these qualities should be measured and tracked. No comprehensive studies have been conducted to gauge the public's awareness and knowledge level of genetics, and no baseline data exist to assess the need for additional educational campaigns or to measure the success of any new educational campaigns. Although some suggest that current efforts to measure public opinion on the potential applications of genetic technologies are sufficient, others believe that these assessments will fall short unless basic levels of knowledge with respect to the technology in question also are taken into account.

Debate continues about the role public awareness and understanding play in the integration of genetic technologies into health care and regarding whether the current level of public awareness and understanding of genetic technologies is adequate. It is not clear how much effort is being devoted to enhancing public understanding in the private and public sectors. It also is not clear whether current efforts are insufficient and whether more sources of reliable information on genetics and genetic technologies are needed.

In addition, questions remain about roles and responsibilities for enhancing public awareness and understanding of genetics. Is this a federal responsibility? Should the Federal government be doing more to create public awareness campaigns, information brochures, and websites as sources of reliable information on a range of genetic issues or as forums for the discussion of the possible impact of genetics? How would sensitive topics such as prenatal and preimplantation genetic diagnosis be addressed? Could federal information materials be misconstrued as advocating a particular course of action? Could liability become an issue?

There also are questions about the extent to which genetics education at the K-12 and undergraduate levels are important for public awareness and understanding of genetics. What efforts are being made to enhance basic science courses? Are there gaps in the genetics content of these courses that, if addressed, could help increase public awareness of genetic technologies? What is the federal role in this area?

OUTCOME

The Committee regarded public awareness as an inherent issue, encompassed within all of the top-priority issues and significant to each one. Public awareness of genetics is essential to the successful integration of genetic technologies into health care and society.

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Genetic Exceptionalism Issue Brief

Issue Statement

The term *genetic exceptionalism* refers to the concept that genetic information is inherently unique, should receive special consideration, and should be treated differently from other medical information. According to this perspective, genetic information is unique or special for a number of reasons: it is a unique identifier; it is heritable and shared through generations; it has relevance to family members; it can be predictive of future disease; it can be and has been used to stigmatize and discriminate; and it can be sensitive and have psychological impacts. Others hold that these characteristics also are shared by other types of medical information (e.g., HIV status can be sensitive, stigmatizing, and relevant to family members), and, as such, genetic information should not be treated differently from other medical information. The questions that surround this debate include the following: Is genetic information inherently unique? If genetic information is inherently unique, do its qualities warrant special attention? Should our public policies be premised on genetic exceptionalism? Does the idea of genetic exceptionalism serve a social good that should be advanced through laws and institutions? Is there an alternative concept that would allow the special features of genetic information to be acknowledged without necessitating a genetic exceptionalist approach?

Relevance to the SACGHS Charter

This issue relates to at least two of the functional areas identified in the SACGHS charter—assessing how genetic technologies are being integrated into health care and public health and analyzing uses of genetic information in education, employment, insurance (including health, disability, long-term care, and life), and law (including family, immigration, and forensics). In some respects, however, the issue bears on all of the Committee's functions and could help define how it approaches its deliberations on many issues.

Background

The sequencing of the human genome precipitated many questions about the nature of genetic information, and many attendant concerns have been raised about the potential use and misuse of this information. The term *genetic exceptionalism*, borrowing from the previously coined term *HIV exceptionalism*, was first used during the deliberations of the Task Force on Genetic Information and Insurance, formed in 1991 by the Joint National Institutes of Health (NIH)-Department of Energy Working Group on the Ethical, Legal, and Social Implications of Human Genome Research. The task force considered the issue of treating genetic information separately, but concluded that this approach was not workable. Its 1993 report argued that other medical information, such as HIV status, is equally sensitive and that if strict safeguards on genetic information are necessary, they must extend to all health-related information. The report's findings stimulated much debate in the bioethics literature around the idea that genetic information is "exceptional" and thus should be treated differently from other health-related information.

Proponents of genetic exceptionalism argue that genetic information is inherently different from other medical information because it is uniquely private. Specifically, they point out that genetic information bears on three spheres of privacy—information, relationships, and decisions. For example, genetic information is information most people expect to keep private; genetic information often bears on family and other relationships; and genetic information is used in making medical and life-altering decisions, for

example, reproductive decision-making. Furthermore, at times in the past, genetics and genetic information have been egregiously misused, misunderstood, and misapplied.

An important context for the debate about special treatment for genetic information in health care is the history of special treatment that has been accorded to information about HIV status, alcohol or drug abuse, sexually transmitted diseases, and psychiatric records. Proponents of genetic exceptionalism note that genetic information deserves the same special treatment as these other types of medical information. They contend that genetic information embodies several unique characteristics: it can be predictive of future disease; it is a unique identifier; it can reveal information relevant to family members; it is transmitted from parent to child; it can affect groups and communities; it can be used to discriminate and stigmatize; and it can cause serious psychological harm. Proponents of the concept argue that because genetic information has special effects and potential harms, it is exceptional and must be regulated accordingly by special privacy and non-discrimination laws.

However, the concept of genetic exceptionalism also has been widely critiqued. First, critics point out that it is illogical and infeasible to meaningfully define or separate genetic information and non-genetic information. They also argue that there is nothing truly unique about genetic information and suggest that there are other types of medical information that share some of the unique characteristics of genetic information (e.g., HIV status, hepatitis C status). Others suggest that the protection of genetic information inadvertently leads to unequal protection for people with non-hereditary diseases (e.g., a cancer caused by a spontaneous somatic mutation as opposed to one caused by a germline mutation such as that found in BRCA1/2). Policies that accord genetic information special protections could give the public a false sense of security and, ironically, come at the expense of efforts to protect other potentially sensitive medical information.

Finally, there is general agreement that some genetic technologies, for example, recombinant DNA technology, present special risks, including the potential to cause human germline modification. Since 1976, NIH, through the NIH *Guidelines for Research Involving Recombinant DNA Molecules* and the role of the Recombinant DNA Advisory Committee, has provided special oversight of basic and clinical research involving recombinant DNA.

Current Status

There is evidence that some in the medical community may be taking an exceptionalist approach to genetics in an attempt to protect the privacy and best interests of patients. Providers sometimes counsel patients to pay out of pocket for genetic testing to avoid potential future discrimination by insurers or employers, and they agree not to enter test results into the patient's medical record. In other respects, providers may not be taking special precautions simply because an intervention utilizes genetic technology and information. For example, from the standpoint of informed consent practices in clinical care, genetic tests appear to be handled like other diagnostic tests; special informed consent practices do not appear to be in widespread use. In general, the medical community tends to be wary of applying genetic exceptionalism to public policy, citing concerns about the potential negative impact of overly burdensome, unclear, and complicated regulations.

From a public policy perspective, genetic exceptionalism approaches appear to be in favor. At the state level, the majority of state legislatures have taken a genetic exceptionalist approach in their laws pertaining to genetic privacy and genetic discrimination in health insurance and employment. Currently, 29 states have genetic privacy laws; 48 states have genetic non-discrimination in health insurance laws; and 31 states have genetic non-discrimination in employment laws. These state laws vary widely in the protections they offer, definitions of relevant terms (such as genetic information and genetic test), and enforcement options. Furthermore, because state laws that relate to employment-based group health plans

are generally preempted by the Employee Retirement Income Security Act (except for those laws that regulate only insurance and insurance products), these state law protections do not apply to self-insured group health plan coverage, significantly limiting the reach of state non-discrimination in health insurance laws. A few states have adopted a "blended" perspective (providing special treatment for genetic information in certain situations only) or an integrated perspective (viewing genetics as so integral to health that genetic information cannot be separated from health information) regarding their public policies in these areas.[1] For example, Minnesota and Washington take an integrated approach by amending existing employment discrimination and privacy statutes to include genetic information, while Michigan takes the blended or balanced approach by having special consent requirements for genetic tests, but considering genetic information to be no more or less special than other medical information.

Some actions at the federal level might be seen as taking a genetic exceptionalist approach. Although the Health Insurance Portability and Accountability Act of 1996 (HIPAA) is not genetic-specific legislation and, therefore, is not considered an exceptionalist statute, it does prohibit rating individuals differently from the group or denying coverage to an individual on the basis of genetic information in the group health insurance market only. Executive Order 13145, issued by President Clinton in 2000, prohibits discrimination in federal employment based on genetic information. In October 2003, the U.S. Senate passed the Genetic Information Nondiscrimination Act of 2003, a bill that would broadly prohibit rate setting, denial of coverage, and employment decisions based on genetic information. The HIPAA privacy rule, which took effect in April 2003, affords genetic information the same protections as other protected health information.

SACGT Efforts

SACGT was mindful of the concerns about policy development based on genetic exceptionalism, but it did not carry out a formal study of its conceptual underpinnings, advantages and disadvantages, or societal and public policy implications.

Policy Considerations

The concept and application of genetic exceptionalism raise a number of policy considerations. The challenge of effectively defining genetic versus non-genetic information for public policy purposes would need to be met. Nearly all diseases are now thought to have a genetic component; hence, the term *genetic disease* is slowly growing more obsolete. Almost all medical information could arguably be defined as genetic in nature, thus obviating the need for the distinction in the first place. If genetic information were categorized as either highly sensitive or not sensitive, there would be debate about what information should be placed into each category and who should make these decisions.

Physically separating genetic from non-genetic information in medical records would pose an enormous practical challenge. Adding requirements regarding the physical separation of different types of information may be so complicated and costly as to actually interfere with the delivery of effective and high-quality care. That is, these requirements may further frustrate attempts by health care practitioners to provide optimal care to their patients and may impede the sharing of relevant medical information.

Other concerns include the effect of genetic exceptionalism on medical research and on the sensitive and private nature of other medical information. In addition, adopting a genetic exceptionalist approach in law and policy may serve to reinforce the flawed perception of genetic determinism, a concept that inappropriately endows genetics with absolute power.

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[1] Partnership for Prevention. *Harnessing Genomics to Prevent Disease and Improve Health: A State Policy Guide*; Spring 2003.

On the other hand, rejecting the genetic exceptionalist approach also raises policy considerations. Concerns about inadequate protections of genetic information may cause people to withhold information from health care providers or forgo genetic services altogether. Given that genetic information is widely perceived to be special or unique by the public, a non-exceptionalist approach may be in conflict with prevailing social values. Finally, as a pluralistic society, the United States favors policymaking using an incrementalist approach. For this reason, a possible advantage of the genetic exceptionalist approach might be the ability to make incremental progress on systemic issues such as access to health care.

With regard to the development of genetic technologies for treating disease or conditions or products based on genomic knowledge, some argue that special review and regulation may be warranted. On the other hand, although the need for special scrutiny for human gene therapy research has been accepted, some raise concerns that special oversight for other genetic technologies would impede progress.

If a broad social consensus about the appropriate treatment and status of genetics is lacking, recommendations about genetic exceptionalism might be premature. On the other hand, the many public policy debates occurring in the public and private sectors around genetics might benefit from a clear and reasoned discourse on the subject. SACGHS recommendations might help sort out the meaning of genetics for society, the status it should be accorded, and the public policies most likely to reflect that status and, thereby, may help avoid unintended consequences with respect to policymaking on genetic issues.

OUTCOME

The Committee regarded genetic exceptionalism as an inherent issue that should be considered on a case-by-case basis during its deliberations on each issue.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Genetic Discrimination
Issue Brief

Issue Statement

As genetic technologies move from discovery into mainstream clinical medicine, they have the potential to greatly improve human health and the health status of the population. However, there are concerns that patients are not taking advantage of genetic services or participating in genetic research studies because of fears that they may be discriminated against based on genetic information. Although very few actual cases of genetic discrimination in health insurance and employment have been documented, perceptions persist that such discrimination is occurring or will occur in the future. The recognition that these fears, whether based on reality or perception, may stand in the way of the realization of the benefits of these new technologies has led to the passage of anti-genetic discrimination laws at the state level and pending legislation at the federal level. Although SACGHS has taken a position in support of federal legislation to prohibit genetic discrimination in health insurance and employment, there may be related policy issues that the Committee might wish to consider. For example, will a federal law be effective in preventing discrimination in these areas? Are there other areas beyond health insurance and employment—disability insurance, life insurance, education, adoption, immigration policy—where the potential for the misuse of genetic information warrants concern and attention? What further steps, if any, should SACGHS take with regard to the genetic discrimination issue?

Relevance to the SACGHS Charter

This issue is relevant to two of the functional areas outlined in the SACGHS charter—assessing how genetic technologies are being integrated into health care and public health and analyzing the use of genetic information in education, employment, insurance (including health, disability, long-term care, and life), and law (including family, immigration, and forensics).

Background

In defining the problem of genetic discrimination, it is useful to recognize that certain discriminatory practices are legal and are widely practiced. For example, private health insurers are legally permitted to classify individuals and groups differently based on many health conditions and personal characteristics for the purpose of making coverage and premium decisions, provided that they do not rate members within the same group (with the same health condition) differently. Under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), it is permissible for a group insurer to raise premiums for the entire group, but not for a single individual within that group. However, discrimination based on race, color, national origin, disability, religion, gender, and age is generally prohibited under the U.S. Constitution or federal civil rights laws. Relevant federal laws and rules include Title VII of the Civil Rights Act of 1964, the Americans with Disabilities Act (ADA), and Executive Order 13145 (protecting federal employees against genetic discrimination in employment). State laws also may offer additional protections against discrimination based on other personal qualities, such as sexual orientation.

Proponents of genetic non-discrimination legislation wish in particular to limit insurers' use of genetic information in rate setting and coverage decisions and employers' use of genetic information in employment decisions. In essence, they want to make it illegal to treat individuals differently based on genetic information (in certain proscribed situations within the health insurance and employment arenas). They argue that even if an insurer were to treat all similarly situated individuals the same (e.g., all women with a BRCA1/2 mutation) with respect to rate setting or coverage, this is still discrimination, because

genetic information, like disability and age, is not a fair basis upon which to treat a group differently. It may be particularly unfair in cases where the presence of a certain gene mutation does not necessarily indicate the presence of disease or accurately predict future disease occurrence. Traditionally, only a limited number of qualities have been accorded discrimination protection under the law, and many of these successes have been hard won. The threshold for civil rights protection is high, and it has not yet been established that genetic status meets this threshold. Some have argued that the approach taken by certain existing laws, such as HIPAA, which allows differential treatment of a group based on genetic information but prohibits differential treatment of any individual within that group, is adequate and represents an appropriate public policy paradigm for the genetic discrimination issue.

The sequencing of the human genome has generated an unprecedented amount of information that is likely to be beneficial to the health and well-being of many Americans. However, fears of genetic discrimination have the potential to stymie the realization of this promise. In particular, concerns have been documented with respect to a reluctance to participate in genetic research and to seek genetic testing. Several polls on the topic of genetic privacy and discrimination reveal that the public strongly prefers that its genetic information be kept private and that there is considerable concern that employers or insurers, or other third parties, may gain access to this information. However, at this point in time, there has been little documentation of genetic discrimination by health insurers. This may be due to the fact that most predictive genetic tests are in their infancy and do not definitively predict a health outcome or clear financial risk to insurers. It also might result from difficulties in documenting cases or barriers to reporting.

Although genetic discrimination in employment also seems to be rare, two recent cases demonstrate how genetic information can be misused in the workplace. According to a 2001 lawsuit brought by the Employment Opportunity Commission under the ADA, Burlington Northern Santa Fe Railway conducted genetic testing of employees without their knowledge or consent in order to assess claims for work-related injuries based on carpal tunnel syndrome. Since the case was settled before going to trial, it did not set any legal precedent on the issue of genetic discrimination in employment. A 1998 case, *Norman-Bloodsaw* v. *Lawrence Berkeley Laboratory*, found that testing employees for sickle cell status, among other things, without their knowledge amounted to an unreasonable search and seizure, constituting a violation of the Fourth Amendment. Legally, this case was precedent-setting only with respect to unconsented, surreptitious genetic and other diagnostic testing. Moreover, social misuse of genetic information occurred on an even wider basis in the 1970s, when many African Americans who were screened for sickle cell disease and found to be carriers were denied employment as well as educational opportunities as a result.

Despite the lack of actual documented cases of genetic discrimination in either health insurance or employment, many believe that anticipatory federal legislation is needed in this area to prevent the problem before it begins, to encourage the utilization of medically useful genetic tests and services, and to secure the realization of the promise of the Human Genome Project through continued genetic research.

Currently, 48 state laws address the issue of genetic non-discrimination in health insurance, 31 state laws address the issue of genetic non-discrimination in employment, and 18 state laws address genetic non-discrimination in life, long-term, and disability insurance. In developing state protections against genetic discrimination in health insurance and employment, debate has occurred regarding the appropriate definitions of *genetic information* and *genetic test,* and there has been concern about limiting the scope of the definitions while simultaneously addressing the concerns of all stakeholders. Some concern has been expressed that individuals who undergo testing in one state may at some point move to another state with less stringent (or no) protections. However, the variation that legislating at the state level allows, although a potential concern in this case, also permits states to make their laws responsive and relevant to their citizens. Finally, because state laws that relate to employment-based group health plans generally

are preempted by the Employee Retirement Income Security Act (with the exception of laws that regulate only insurance or insurance products), these state law protections do not apply to self-insured group health plan coverage, significantly limit the reach of state non-discrimination in health insurance laws. This creates barriers to the states' ability to comprehensively regulate insurance practices.

Because existing state and federal law and regulation collectively does not provide comprehensive protection against genetic discrimination in employment or health insurance, federal legislation has been introduced on this issue in both the House and Senate in every Congress since and including the 103rd Congress.

Current Status

In October 2003, the Senate unanimously passed S.1053, the Genetic Information Nondiscrimination Act of 2003. This legislation prohibits the use of genetic information by group (self-funded and otherwise) and individual insurers in the setting of premiums or the denial of coverage. It also prohibits employers' use of genetic information in the making of certain employment decisions, such as hiring, firing, compensation, and promotions. In May 2003, Representative Louise Slaughter introduced H.R. 1910, the Genetic Information Nondiscrimination Act of 2003. H.R.1910 is similar to S.1053, except in its definitions of *genetic test* and *protected genetic information* and in its enforcement and penalty provisions, which grant broader remedies. In November 2003, Representative Cliff Stearns introduced H.R.3636, the Genetic Privacy and Nondiscrimination Act of 2003, which differs from S.1053 and H.R.1910 in a number of ways, including the absence of an employment title. In a briefing of SACGHS in October 2003, a staff member of the House Committee on Education and the Workforce pointed out that because three House Committees have jurisdiction over this issue, the process of considering and acting on legislation in this area is expected to be lengthy. The House's intentions with respect to considering these bills this session are not clear.

SACGT/SACGHS Efforts

SACGT wrote two letters on the subject of genetic discrimination, one to Secretary Shalala in April 2000 and one to Secretary Thompson in May 2001. The 2000 letter to Secretary Shalala expressed SACGT's concern regarding public misgivings about the potential for the misuse of genetic information and pointed out that these worries could lead to underutilization of beneficial genetic tests. Recognizing the potential for harm stemming from the use of genetic testing technologies, the Committee expressed support for federal legislation to prohibit discrimination on the basis of genetic information in both employment and health insurance. The letter to Secretary Thompson highlighted the Committee's continued support of Federal legislation in the area of genetic non-discrimination and outlined several principles that the Committee believed were critical to effective legislation. SACGT believed that the incorporation of these key points would ensure that legislation would simultaneously prevent the misuse of genetic information and ease fears about genetic discrimination.

After being briefed on S.1053 at its first meeting in June 2003, SACGHS, in its first action as a Committee, sent a letter to Secretary Thompson citing similar concerns and expressing support for S.1053. The Committee agreed at its June 2003 meeting that this issue requires continued monitoring.

Policy Considerations

Since SACGHS has agreed that this issue requires continued monitoring, are additional committee actions warranted? At this time, additional recommendations are likely to have limited impact on the content of and need for Federal legislation, because the issue and various policy options already have been

considered and are included in the language of pending bills. Furthermore, the Committee already has made recommendations on the need for federal protections and has expressed support for S.1053. The need for further recommendations in this area could be premised upon developments with respect to the passage of genetic non-discrimination legislation or, failing passage, other policy approaches.

If federal legislation were to be enacted in this area, several policy considerations would arise. Some have raised questions about how a federal genetic non-discrimination law might interact with existing law in the areas of health insurance, employment, and discrimination. Although S.1053 endeavors to address this concern through careful consideration of possible interactions, statutes in these areas, including the ADA, HIPAA, and the Employee Retirement Income Security Act, are complex and their interrelatedness has not been tested. Further, state law may interact in unexpected ways with federal non-discrimination legislation.

Methods for assessing the law's impact on the utilization of genetic services and participation in genetic research may be useful for providers, payers, and researchers. However, ascertaining whether a federal law is providing adequate or improved protection against genetic discrimination may be challenging, because to date no impact analysis has been conducted that provides the baseline data. Enactment of federal legislation also might clarify whether adverse selection will increase and become a major problem for insurers. A concern when legislating in this area is the comprehensiveness of the law. Currently, existing state and federal laws provide a patchwork of protections, and a federal law should effectively fill any gaps. However, the situation may need to be monitored for obvious gaps or regulatory loopholes that could allow discrimination to occur.

Finally, because implementing a federal law in this area could be construed as taking a genetic exceptionalist approach, its enactment may be informative about whether exceptionalism has effects on public perceptions about genetic determinism, the utilization of genetic services, and participation in genetic research. In a society that tends to embrace genetic determinism, a law that is exceptionalist in nature may serve to solidify that belief. Conversely, such a law may assuage the fears stemming from this belief by protecting against the possibility of harm. However, no research has been done on specific state or federal laws to assess their impact on beliefs about genetic determinism.

Genetic information plays an important role in many other areas, including disability insurance, life insurance, education, adoption, and immigration policy. Genetic discrimination in other areas (e.g., life insurance) has received little attention by legislators. Evaluation of the need, if any, for protection against misuse of genetic information in these settings may be useful, as would evaluation of the appropriate level of protection required in each setting. Passage of federal legislation prohibiting discrimination in employment and health insurance settings may settle the issue. Conversely, it may have the effect of drawing attention more generally to the problems associated with the misuse of genetic information and encouraging the prompt evaluation or greater scrutiny of potential problems in all settings.

OUTCOME

The Committee decided to address the issue of genetic discrimination with short-term action and monitoring. Further action will be considered in the event that Federal genetic non-discrimination legislation does not pass in the 108th Congress.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Genetics Education and Training of Health Professionals Issue Brief

Issue Statement

Our increasing understanding of the role of genetics in human health and disease is expected to yield more targeted approaches to health care and public health. Because of the interdisciplinary nature of genetics, a wide range of health professionals will require training in genetics in order to achieve optimal use of genetic technologies and ensure the appropriate integration of genetic knowledge into the health care and public health systems. Currently, health professionals are not sufficiently trained and educated in genetics to meet these goals, and efforts are lacking both in professional education and training and throughout clinical practice (continuing education). Questions that need to be explored include the following: What are the existing gaps in the education and continuing education of health professionals? Are current efforts to address these gaps sufficient, or are additional efforts needed? Should the primary locus of responsibility for closing these gaps be educational institutions, professional societies, foundations, government, or some combination of these organizations? What is the appropriate role of the Federal government in addressing this issue?

Relevance to the SACGHS Charter

This issue is relevant to one of the seven functional areas identified in the SACGHS charter—the integration of genetic technologies into health care and public health.

Background

To promote the effective translation of new genetic knowledge into practice, to enhance access to genetic technologies, and to help ensure that they are utilized appropriately, health professionals must be adequately educated and trained in genetics. Several studies have documented health professionals' level of knowledge and understanding of genetics. For example, a survey of non-geneticist physicians reported that 25 percent rated their knowledge of genetics as excellent to good and 72 percent rated their knowledge as fair to poor.[2] Another survey on physician knowledge of genetic testing reported an overall correct response rate of 37 percent.[3] Giardello et al. reported that physicians misinterpreted genetic test results in 31 percent of colon cancer cases (1997).[4] These studies suggest that genetic knowledge amongst many health professionals is inadequate.

Medical School Curricula. In 1974, a report of the National Academy of Sciences (NAS) found that only about 25 percent of physicians had courses in genetics available to them during their medical training.[5] An article published in 1998 reported that 69 percent of physicians had taken one or more genetics courses in medical school.[6] Although the data suggest an increased presence of genetics in current

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[2] Menasha, JD; Schecter, C; Williams, J. Genetic testing: a physician's perspective. *Mt. Sinai J of Medicine* 2000; 67(2):144-151.

[3] Hunter, A; Wright, P; Cappelli, M; Kasaboski, A; Surh, L. Physician knowledge and attitudes toward molecular genetic (DNA) testing of their patients. *Clin Genet* 1998;53:447-455.

[4] Giardello, FM; Brensinger, JD; Peterson, GM; et al. The use and interpretation of commercial APC gene testing for familial adenomatous polyposis. *NEJM* 1997;336:823-827.

[5] Committee for the Study of Inborn Errors of Metabolism, Division of Medical Sciences, Assembly of Life Sciences, National Research Council. Washington, DC: National Academy of Sciences; 1975.

[6] See note 2.

medical school curricula, deficiencies still remain. Several studies have shown an association between recency of graduation and whether the health professional had taken a genetics course and the level of knowledge of genetics.

Nursing School Curricula. In 1995, a survey of 1,000 nurses found that only 15 percent of them were offered genetics courses during their basic education.[7] Sixty-three percent stated that information on genetics was covered inadequately or not at all. Surprisingly, the amount of time devoted to genetics in nursing school curricula actually declined in the last decade. In 1984, the average number of instructional hours devoted to genetics in Bachelor of Science in Nursing programs was 10.5 hours. In 1996, the average was six hours. In 1984, nearly all (99 percent) of the surveyed nursing programs included genetics content in their curricula. A decade later, a similar survey found that 66 percent of programs taught genetics content.[8,9] A 2003 review article on the issue of educating nurses in genetics cited these three studies as evidence for "major gaps in genetic knowledge among practicing nurses and deficiencies in the type and amount of genetic content in nursing curricula."[10]

Licensure and Board Specialty Examinations. The United States Medical Licensing Examination (USMLE), a three-part test, fulfills the examination requirements for medical licensure in the United States. In the content outline for the Step 1 examination, human development and genetics are included under the general principles, and genetic disorders are included under each of the individual organ systems. Recently, several new questions on genetics were integrated into the USMLE, representing an acknowledgement of the increasing importance of genetic knowledge to the practice of medicine.

Continuing Education. Continuing education is an important way for practicing health professionals to learn about current genetic advances. Hunter et al. reported that 49 percent of non-geneticist physicians surveyed attended educational conferences or workshops that included genetics as a significant part of the program.[11] A survey of physicians from the Pacific Northwest reported that fewer than 20 percent of family practitioners and internists had participated in continuing medical education (CME) programs with genetics content, compared to more than one-third of obstetricians/gynecologists and pediatricians.[12] A survey of the leading medical specialty societies by the American Medical Association found that only 36 percent currently offer CME materials in medical genetics, although 32 percent currently are developing such materials. Sixty-five percent of the medical societies reported including a clinically relevant genetics program at their annual meetings. In a 1998 survey, 70 percent of nursing organizations reported that they were not planning any programs in genetics.[13]

Recommendations of Previous Advisory Bodies. Several national committees and task forces, professional organizations, and community leaders have highlighted the need for enhanced education in genetics. More than 25 years ago, an NAS committee recommended that genetics should be included in

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[7] Scanlon, C; Fibson, W. Managing genetic information: implications for nursing practice. Washington, DC: American Nurses Association; 1995.

[8] Hetteberg, CG; Prows, CA; Deets, C; et al. National survey of genetics content in basic nursing preparatory programs in the United States. *Nurs Outlook* 1999;47:168-174.

[9] Monsen, RB. Genetics in basic nursing program curricula: a national survey. *J Matern Child Nurs* 1984;13:177-185.

[10] Lessick, M; Wong, P. Providing genetics education: meeting the needs of maternal-child health nurses and others in this fast-evolving field. *AWHONN Lifelines* 2003;7(3):251-256.

[11] See note 2.

[12] Hayflick, SJ; Eiff, MP; Carpenter, L; Steinberger, J. Primary care physicians' utilization and perceptions of genetics services. *Genet Med* 1997;1:13-18.

[13] Monsen, RB; Anderson, G. Continuing education for nurses that incorporates genetics. *J Continuing Ed in Nursing* 1999;30(1):20-24.

medical school courses in order to raise the level of genetic knowledge of physicians.[14] In 1994, an Institute of Medicine (IOM) committee reiterated the importance of genetics education of health professionals, particularly for primary care physicians who offer and interpret tests.[15] In addition to an increased focus on basic genetics, the IOM report recommended an expansion of education on genetic counseling and on the ethical, social, and legal issues related to genetic testing. In 1997, a National Institutes of Health-Department of Energy Task Force on Genetic Testing encouraged the development of genetics curricula in medical schools and suggested that genetics questions should be on general licensure and board specialty examinations.[16] All three groups also emphasized the importance of continuing education programs in genetics.

Current Status

A number of studies and projects are under way to enhance the genetics education of health professionals in both the private and public sectors. Some projects are focused on education about specific diseases and conditions, while others cover a broader spectrum of genetics education. Over the last decade, public and private organizations (e.g., the National Coalition for Health Professional Education in Genetics) have developed and provided genetics educational materials and programs for health professionals and have prepared more than 35 guidance documents. Professional sector efforts to educate physicians have focused on curricular changes, CME, combined residencies, and licensing exam changes. The Federal government also has funded a number of studies and projects on genetics education of health professionals, such as the Genetics in Primary Care Project. In a recent survey of the SACGHS *Ex Officio* agencies, 7 agencies reported spending $102 million to support 180 projects related to genetics education, training, and workforce. The survey also found that during the years covered by the survey (2000-2003), there has been a steady increase in the funding of programs addressing genetics education and training within these seven agencies.

SACGT/SACGHS Efforts

At its August 2000 meeting, SACGT formed a work group to identify gaps or areas in need of improvement regarding genetics education of health professionals. SACGT staff serving on the Education Work Group also undertook extensive fact finding and analysis in the area of genetics education and training of health professionals, and the work group presented its findings to the Committee in August 2001. Over the next two years, the work group convened a roundtable and organized a policy conference to gather the perspectives of the public and leaders in health education and practice. Topics included the challenges of incorporating genetics into the education of health professionals and ways to address problem areas and gaps. The work group had been in the process of developing a report when SACGT's charter expired. At its October 2003 meeting, SACGHS heard extensive presentations on issues surrounding genetics education, training, and workforce.

Policy Considerations

As genetic technologies advance at an increasingly rapid pace, assuring the adequacy of the education of health professionals becomes paramount. Several considerations in this area may need to be addressed. Although the level of ongoing activities in genetics education and training in the private and professional

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[14] See note 4.

[15] Assessing Genetic Risks: Implications for Health and Social Policy, Andrews, LB; Fullarton, JE; Holtzman, NA; Motulsky, AG (eds.). Washington DC: National Academy Press; 1994.

[16] NIH-DOE Task Force on Genetic Testing. Holtzman, NA; Watson, MS (eds). *Promoting the Safe and Effective Use of Genetic Testing in the United States*; 1997.

sectors may prove to be sufficient, various findings of the reported published literature demonstrate inadequacies remain in provider knowledge about genetics and in providers' ability to implement this knowledge in clinical practice.

Views differ about the appropriate federal role in genetics education and training. Although some say that the level of Federal government activity in this area is appropriate and adequate, others suggest that it needs to be better documented and may not be sufficient. For example, the Federal government may have a role in facilitating the translation of genetics into practice, but not necessarily in developing guidelines, curricula, or educational tools, a role that might more appropriately be under the purview of professional societies. However, the Federal government may be in a unique position to leverage changes in the education of health professionals through funding and leadership, and it already takes a lead role in the funding of the education of health care professionals through programs authorized under Title VII and Title VIII of the Public Health Service Act, which can serve as mechanisms for encouraging change.

Presenters at the October 2003 SACGHS meeting identified a number of barriers to enhancing genetics education and training of health professionals. At the most global level, the health care system's complexity and fragmentation present a major challenge, and the level of coordination that would be required to achieve systemic change is significant. Furthermore, genetics is not the only area in which health care providers need more knowledge and skill, which means that there is competition for the time and attention of trainees and providers in curricula, training programs, and continuing education. Other more discrete barriers include the inherent complexity of the subject matter and a lack of appreciation of the importance or broad relevance of genetics to medicine and health care. Heterogeneity of state professional practice laws and the diversity of the audience for educational programs also pose practical barriers to improving genetics education and training for health professionals.

Although there is consensus that all health care providers need more information about genetics because they will ultimately be utilizing it in their practices, broad agreement is lacking about how much or exactly what type of information is needed by the various types of health professionals. The issue of what non-geneticist health care providers should know bears directly upon the question of when they should refer patients and to whom, and it is an important factor in the proper integration of genetic technologies into the health care system. Questions also remain about the adequacy of the genetics workforce. For example, are there sufficient numbers of genetics specialists and well-trained generalists, and what is the appropriate ratio of specialists to generalists? Also, how might these numbers need to change as genetic technologies become more fully integrated into health care and public health?

Recommendations defining the appropriate roles of the federal, state, and local governments, professional societies and organizations, and the academic community in genetics education and training could potentially be a useful guide to these various stakeholders. SACGHS recommendations in this area also could serve to clarify the extent to which this problem currently is being adequately addressed. If genetics education of health professionals is being addressed adequately by the efforts of the Federal government, the private sector, and the academic community, a statement to this effect may be clarifying and informative for future discussions of this question. Along these lines, a summary of the survey information SACGHS has collected on current federal efforts in genetics education, training, and workforce may be helpful. Similarly, if SACGHS determines that more effort is needed in this area, recommendations addressing current gaps and areas for improvement could be useful. SACGHS observations and recommendations will lend visibility to this issue and may precipitate needed action and change.

OUTCOME

The Committee decided that education and workforce training issues are best addressed with short-term action in the form of a resolution to be forwarded to the Secretary.

Patents and Access
Issue Brief

Issue Statement

Patents promote innovation by creating an incentive to disclose inventions publicly through the granting of exclusive rights for a limited period of time. Typically, disclosure of an invention spurs competitors to further develop the underlying art and ideas or to find a better means to the same end. This is true of DNA-based inventions as well as any other form of innovation. However, according exclusive rights to an invention limits future use of that invention, and licensing fees add costs to biomedical research and to the health care system. In recent years, concerns have emerged that gene patents and/or licensing practices may be inhibiting basic and clinical research and blocking the development and performance of genetic testing services by clinical laboratories. Some key policy questions concern whether patent and licensing policies affect research in genetics and access to clinical genetic technologies in unique ways and, if so, whether the public good derived from basic research and access to health care can be improved without compromising the intent of patent protection.

Relevance to the SACGHS Charter

The impact of patent policy and licensing practices on access to genetic technologies is one of seven functional categories identified in the SACGHS charter.

Background/Current Status

Article 1 of the U.S. Constitution states that "Congress shall have the power...to promote the progress of science and useful arts, by securing for limited times to Authors and Inventors the exclusive right to their writings and discoveries." Federal law (35 USC §101) defines patentable subject matter and outlines conditions for patentability. Specifically, an invention must be non-obvious, novel, and useful to be considered patentable subject matter. The patent application must be "enabling" as well, that is, it must define the process by which the invention was created in such a way that another person in the same field could create it. In January 2001, the United States Patent and Trademark Office (USPTO) expanded upon the utility criterion with respect to patents involving DNA, stating that in these cases, the utility of the invention must be specific, substantial, and credible.

A patent does not necessarily allow owners to use their invention, rather it grants the patent holders the right to exclude others from making, using, selling, or importing the invention. Inventors may be precluded from using or developing their invention because of pre-existing patents held by others. A license is the legal instrument and technology transfer tool that a patent owner may use to grant another person/entity the right to use the patented invention. Licenses may be exclusive or non-exclusive and may include any number of terms and conditions (e.g., financial arrangements for or restrictions on its use). Technology transfer is the term used to describe the movement of inventions and ideas, whether patented or not, from research to practical application. Patent law does not address licensing practices, and USPTO does not regulate them.

Many have argued that because the Federal government supports a significant amount of biomedical research with public funds, the results of those studies belong to the public. Prior to 1980, the Federal government retained ownership of all inventions created with federal funding, and very few of them were successfully developed into useful products. In 1980, the Bayh-Dole Act was enacted to promote the transfer of technology to the private sector. The act allows Federal contractors and grantees to patent

their inventions and encourages their commercial development, but the government retains the right to use these licensed inventions, royalty free, for the public good. Two other laws, the 1980 Stevenson-Wydler Act and 1986 Federal Technology Transfer Act, extended the rights and responsibilities of the Bayh-Dole Act to government employees. The Technology Transfer Commercialization Act of 2000 added provisions to the law to prevent technology transfer of federally funded inventions from unduly encumbering future research and discovery. In 1996, patent law was amended to exempt medical practitioners from infringement suits when using patented medical or surgical techniques in medical practice. Laboratory physicians and biotechnology patents, however, were specifically excluded from the exemption. In 2002, bills were introduced in Congress proposing to allow researchers and medical practitioners to use patented genes sequences for non-commercial research purposes and for medical practice, including the practice of laboratory medicine. The bills were not acted upon, and the sponsor of the legislation is no longer in Congress.

Department of Health and Human Services (HHS) patent policy promotes the use of patents for biomedical technologies only when a patent facilitates the availability of the technology to the public for preventive, diagnostic, therapeutic, or research or other commercial uses. HHS licensing policy seeks to ensure development of each technology for the broadest possible application and requires that commercial partners expeditiously develop the licensed technology. HHS uses exclusive licensing only when necessary for the further development of the technology. In addition, National Institutes of Health (NIH) policy on research tools encourages the sharing of tools developed by NIH-funded grant recipients.

Different aspects of patents and licensing can affect the conduct of research. The patent process can hinder research if publication of scientific results is delayed for patent filing. In addition, researchers may fear restrictive patent enforcement and have limited resources and experience for comprehensive patent searches on their research subject. Since most patent conflicts are handled by the courts, researchers running small laboratories and small companies are at a disadvantage because they do not have the resources to mount an expensive legal defense against infringement charges regardless of the patent's validity. Although academic research rarely has been restricted from using patented inventions purely for research purposes, a recent court case may affect this longstanding practice. In a 2002 case (*Madey* v. *Duke*), the U.S. Court of Appeals for the Federal Circuit held that academic research is an activity that furthers a university's business and does not fit within the narrow scope of the research exemption. According to the Court, the research exemption applies to "activities solely for amusement, to satisfy idle curiosity or for strictly philosophical inquiry." The ruling in effect restricts the research exemption for unlicensed use of a patent. Although a researcher can still seek a license for the use of patented inventions for purely research purposes, the time needed to negotiate licenses may cause delays in research, and there is no guarantee that a license will be granted.

Aspects of patents and licensing also affect the conduct of clinical genetic testing. Many laboratories have been prevented from or have chosen not to offer clinical tests because of actual or anticipated patent or license enforcement. In addition, in the future the development and use of genetic technologies for clinical testing may involve multiple patents and may require multiple licensing agreements with different patent holders. Overly restrictive licensing terms could limit the progress of research and translation into valuable health care products or diagnostics, including genetic technologies. Furthermore, multiple patents may apply to a single gene (e.g., patents on specific mutations identified as causes of disease or polymorphisms), requiring multiple licensing agreements that result in high costs for the diagnostic or screening panel analyzing mutations in a single gene. This problem is amplified for tests screening numerous different genes in a single assay. In some cases, royalties may be so expensive that it is not economically viable for a clinical laboratory to offer a particular genetic test. Licensing fees can be particularly onerous for clinical genetic laboratories because they operate within the current health care economic environment. Moreover, even if such costs are passed on to patients, current reimbursement levels for genetic tests do not cover the cost of testing even before the licensing fees are considered. A

study by Mildred Cho, et al. found that many clinical laboratories ceased offering a genetic test because of licensing restrictions. Of 132 laboratory directors interviewed, 25 percent reported that they stopped performing a clinical genetic test because of a patent or license. Fifty-three percent of respondents reported that they decided not to develop a new clinical genetic test because of a patent or license.[17]

The commercialization of a genetic test for Canavan's disease has been noted as an example of how licensing practices can affect the cost and accessibility of genetic tests. Miami Children's Hospital (MCH) holds the patent on the gene responsible for Canavan's disease and any methods for screening mutations in this gene. When MCH initially sought to license the patent, it issued licenses that imposed limits on the number of tests that a laboratory could perform, penalties for any academic laboratory that exceeded the set capitation, and a royalty fee of $12.50 per test performed. Families affected by Canavan's disease sued MCH over what they considered to be a restrictive licensing agreement and excessive royalties for the use of a genetic test for the disease that would limit accessibility of genetic testing for Canavan's disease. The families had participated in the research effort to identify the gene involved in the disease for the public good. In their lawsuit, they also argued that the informed consent was flawed because they were not told about MCH's intent to patent its findings. In May 2003, the U.S. District Court for the Northern District of Illinois dismissed all counts, with one exception for unjust enrichment.

Another controversy surrounding restrictive licensing involves BRCA-1 and BRCA-2, two genes important in the etiology of hereditary breast cancer. Myriad Genetics, Inc., holds several patents covering the tests for these genes. Myriad offers diagnostic testing for samples from around the world and has licensed only a few other laboratories to perform the test. The complexity of the test is cited as one reason for restricting the number of laboratories performing the study to highly specialized reference laboratories such as Myriad. However, there are concerns that the cost of the licenses is keeping the cost of the test high and reducing access both in the United States and abroad. There also are some concerns about interference with research on breast cancer outcomes as they relate to BRCA status. In addition, some experts suggest that there may be alternative approaches to the analysis of the genes that may improve on Myriad's approach, but that cannot be explored because of the patent. The patents on the BRCA 1 and 2 genes illustrate the international elements of the issue, because the controversy has crossed U.S. borders as Myriad attempts to enforce its patents in Europe and Canada.

As part of a long-range planning process, the National Human Genome Research Institute (NHGRI) sponsored a roundtable discussion in December 2002 to explore patenting and licensing issues. Participants discussed a number of issues, including the possibility of crafting a research exemption; mechanisms for resolving patent infringement cases that would avoid expensive lawsuits; and the use of patent pools to bring licensing costs down. Workshop participants identified a need for the development of licensing guidelines, possibly modeled after guidelines that were developed to enhance and facilitate the sharing of research tools. They also suggested that legislative proposals to address gene patent concerns are unlikely to pass without significant involvement of consumer groups and demonstrated effects on health care costs and accessibility.

In October 2003, the Federal Trade Commission (FTC) issued the report, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, which suggested that broad patents may be having anti-competitive effects and may be blocking innovation in certain high-technology industries, such as computers and biotechnology. The report makes a number of recommendations aimed at restoring the balance between competition and patent policy and improving patent quality (e.g., by reducing the number of obvious patents). The report also recommends new mechanisms to make it less

[17] Cho, MK, et al. Effects of patents and licenses on the provision of clinical genetic testing services. *J Mol Diagn* 2003;5(1):3-8.

onerous to challenge invalid patents and new procedures to allow increased access to pending patents for the purposes of avoiding infringement and business planning. The report also urges an increase in funding and resources for USPTO.

NHGRI and the Department of Energy (DOE) currently are supporting a project to assess the licensing policies and practices of institutions regarding DNA-based patents. The project will include a categorization of subtypes of DNA-based patents according to how they were commercialized and may help to identify specific problems that need to be addressed. The study is funded through August 2004.

In addition, a joint committee of the National Academies' Science, Technology and Economic Policy Board and Science, Technology, and Law Program will review the patenting and licensing of human genetic material and proteins in order to evaluate the evolution to date of patents on DNA sequences and the emerging direction of patenting protein structures and functions. The implications for the conduct of research, the development of commercial products, and clinical practice to diagnose and treat a variety of human diseases will be evaluated. The first meeting of the National Academy of Science committee occurred on February 27-28, 2004.

SACGT Efforts

SACGT explored the issue of gene patenting and licensing through a roundtable discussion with diverse experts in June 2000. At a subsequent meeting, the Committee decided that further study by appropriate experts might be needed to determine whether certain licensing practices are adversely affecting access to beneficial genetic tests. In a letter to the HHS Assistant Secretary for Health (ASH), SACGT suggested that although there was broad agreement—including agreement among patient groups—that gene patents and licenses are essential to the development and commercialization of high-quality diagnostic and therapeutic products, concerns had been raised among some academic laboratories, professional societies, and patient groups that certain commercialization approaches may be a) having adverse effects on access to and the cost and quality of gene tests; b) deterring laboratories from offering tests beneficial to patients by the use of certain licensing practices; and c) affecting the training of specialists who offer genetic testing services and the development of quality assurance programs. In a reply to the letter, ASH concurred with the need for additional data and reported, as noted earlier, that the NHGRI Ethical, Legal, and Social Issues program would be initiating a study to gather data on this issue.

Policy Considerations

Although the role of patents in spurring innovation and investment in biomedical research is widely recognized and supported, and U.S. courts have made it clear that inventions involving genes and genetic technologies are patentable subject matter, there has been some controversy over what types of inventions in the biomedical sciences should be patented and how broad those patents should be. The main concerns about patents and licensing of genetic technologies arise from a tension between two important needs: 1) protection of the rights to intellectual property in order to encourage investment of time and dollars in research and 2) access to scientific discovery that may be used for improvements in health care. The two sides of this conflict are interdependent. The biotechnology and pharmaceutical industries rely heavily on research from the public sector to advance science that leads to product development, and researchers and clinicians benefit greatly from products and services produced by industry. The public also benefits when better diagnostics and therapeutics are available sooner. Conflict occurs when either side believes the balance is tilted away from it.

Research Issues. Public funds support a great deal of biomedical research, and the public expects that its investments will be translated into improvements in health care. With the Bayh-Dole Act, Congress sought to promote the translation of research findings into commercial products by providing incentives

for innovation and invention and mandating that efforts be made to transfer new technologies funded with federal money into practical applications.

Views within the research community differ about the extent to which the costs of patents and licenses are balanced by the benefits. If patents on DNA-based inventions are too broad, research on the genes involved can be inhibited. Some contend that this already is the case. Scientific knowledge increases rapidly when different investigators can apply multiple approaches to the same scientific problem. Patent holders who are unwilling to allow use of their inventions with reasonable terms could block this process and inhibit the process of scientific discovery. In addition, patent stacking (many patents on a single gene or multiple genes relevant to a single disease) may inhibit scientific discovery and technology development by making it difficult for a researcher to obtain all of the necessary licenses. Patent holders also may choose to block access to their technology for certain uses that conflict with their social values or business plans. On the other hand, many assert that patent protection for genetic technologies does not and will not retard research or impede access and that patent protection provides the necessary environment to stimulate both innovation and investment in all technologies. Will the change in the technology transfer laws in 2000 prohibiting technology transfer of federally funded inventions from unduly restricting future research and discovery have an effect? Is the impact of the law being monitored and analyzed?

Clinical Issues. There are concerns about the effect of gene patenting on the practice of medicine. Patents and licensing policies may increase the cost and affect access to medical products, including genetic tests and treatments based on genetic technology. Patenting of therapeutics may raise fewer concerns because the significant investment required for Food and Drug Administration (FDA) approval warrants the protection patents afford. In contrast, genetic tests offered by a laboratory do not require FDA approval, can be developed under Clinical Laboratories Improvement Act regulations, and benefit from the incremental improvements that occur when the larger medical community continues to work on them. In addition, concern also has been raised, and has been expressed in testimony to SACGT, that in the current system the training of laboratory clinicians is suffering. This is because the future directors of academic and private sector clinical diagnostic laboratories are trained in the academic laboratories, and as these laboratories reduce the type and number of tests performed, they may be less able to provide the next generation of clinicians the experience required to develop the knowledge and skills necessary to provide excellent diagnostic services to the public. Question in this area include the following: How do patent and licensing policies affect the availability of and equitable access to genetic testing services? Should access to basic health care be a priority over access to new technologies (genetic or other)? Do gene patents require special consideration because of their potential ability to improve public health? Are the effects of patents in the field of genetics significantly different from those other areas, and, if so, should they be afforded differential treatment? Is having a single provider of a genetic test in the best interest of the public health? Is there a mechanism for balancing the protection of the discoverer with the broad utilization of gene discoveries for health care? Could legislation serve as such a mechanism, or could other policy instruments be used to effect change?

Patent Issues. Changes in patent policy can have economic ramifications. In the view of USPTO, concerns that patent protection of genetic technologies will inhibit research and impede access are unfounded; in fact, USPTO asserts that patent protection provides the necessary environment to stimulate both innovation and investment in all technologies. Because the patent system is considered to be a critical factor in the success of the biotechnology and pharmaceutical industries, there is considerable resistance to any changes to patent law or policy. Comments made by President Clinton and United Kingdom Prime Minister Tony Blair in March 2000 about keeping the human genome sequence public precipitated a drop in biotechnology stocks and capital losses for the industry. On the other hand, legislative proposals have been introduced and amendments to patent law enacted in the past, so modifying the law would not be unprecedented. Questions include the following: How would new

alterations in patent law affect the biotechnology industry and its performance in the stock market? Could any changes in current law undermine support and thus innovation, potentially doing more harm than good?

Despite general agreement regarding the importance of patents for innovation in the development of new technologies, concern remains that some DNA-based patents may be too broad or obvious to a person practiced in the art. Some questions have been raised in Congress about whether research should be restricted by patents. However, attempts to create research exemptions pose difficult issues of scope; defining research and separating it from commercial interests can be challenging. What specific issues involving patents seem to be most problematic? Have the utility guidelines been effective in reducing gene patent submissions whose utility is in question? Given the medical community's interest in using patented genes with known clinical significance (and patent utility), what effect has raising the utility bar had on the clinical use of gene patents? Should SACGHS review the FTC report to assess whether it might address some of the problems with current patent policy? In considering whether to address patent policy, should SACGHS consider whether any recommendations in this area might have limited influence, given that the Committee does not directly advise USPTO?

Licensing Issues. Exclusive licenses can be necessary and beneficial if they are the only way a discovery will be commercialized. On the other hand, even broad licensing can affect access when royalty fees are high and conditions are placed on the duration of the license, the field of use, sublicensing, and reach-through rights. In terms of genetic tests specifically, exclusive licenses can affect the development of method validation and proficiency testing by peers, create a lack of diversity in analytical methods and test interpretation, thwart the development of confirmatory testing in a second laboratory for unusual cases, and possibly restrict access to testing for indigent patients. Do licensing practices affect access to genetic technologies? Are they of greater concern than patent policies? What are the licensing terms that are creating the majority of problems for genetic test providers? In particular, do exclusive licenses raise particular concerns for genetic testing providers? How prevalent are exclusive licenses?

Key Questions. What exactly are the impacts of gene patents on basic research, translational research, and access to health care? Overall, are they beneficial or are they causing adverse effects? To what extent does the patenting of genetic information and technology pose unique problems for research and clinical care? If there are unique problems, can they be adequately addressed by current strategies for management of patents and licensing, or are new strategies needed? Is there currently enough data to identify the most problematic issues and answer questions posed by the Committee? To what extent can we expect the findings of the DOE/NHGRI-funded studies to assist with these questions? To what extent can we expect the NAS study to assist with these questions? Is SACGHS an appropriate body to consider these issues and to make recommendations, and to whom?

OUTCOME

The Committee will continue to monitor this high-priority issue and will reconsider patents and access after the NAS committee has issued its report, expected in August 2005.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Oversight of Genetic Technologies
Issue Brief

Issue Statement

Genetic technologies are evolving with great speed, and new genetic tests are being introduced into clinical care at a rapid pace. In March 2004, 684 genetic tests were clinically available, and 347 were in development. However, the clinical validity and utility of many of these tests has not been independently established. The Food and Drug Administration (FDA), Centers for Medicare & Medicaid Services (CMS), Centers for Disease Control and Prevention (CDC), and Federal Trade Commission (FTC) all have roles in the oversight of the development, use, and marketing of genetic technologies. In 2000, the Secretary's Advisory Committee on Genetic Testing (SACGT) issued a report recommending that steps be taken by these agencies to augment the current oversight of genetic tests, including the initiation of premarket review of laboratory-developed genetic tests. SACGHS was briefed in October 2003 about the current efforts of the agencies to strengthen their oversight programs. Does SACGHS consider these efforts sufficient? If so, is any further attention needed? If not, what steps, if any, should be taken?

Relevance to the SACGHS Charter

The oversight issue is relevant to integration of genetic technologies into health care and public health, one of the seven functional areas in the charter.

Background

Currently, genetic tests and gene-based products are regulated at the federal level through three overarching mechanisms: 1) the Clinical Laboratory Improvement Amendments (CLIA) (42 CFR Part 493); 2) the Federal Food, Drug, and Cosmetic Act (FDCA) (21 USC § 301 et seq.); and 3) the Federal Policy for the Protection of Human Subjects (45 CFR Part 46, or the Common Rule) during investigational phases and FDA human subject protections (21 CFR Parts 50 and 56). In addition, FTC plays a more limited role through the authority granted by the Federal Trade Commission Act (15 USC §§ 41-51) to regulate unfair and deceptive advertising.

Four Department of Health and Human Services (HHS) agencies have roles in the oversight of the development and use of genetic tests and products—CDC, CMS, FDA, and the Office for Human Research Protections (OHRP). Although they do not have regulatory functions, the National Institutes of Health, the Health Resources and Services Administration, and the Agency for Healthcare Research and Quality support research activities and demonstration projects that generate knowledge about and experience with genetics and genetic technologies. In addition, some states regulate genetic technologies, and some professional organizations have issued practice guidelines.

CLIA Program. All laboratory tests in which results are provided to the patient must be conducted in laboratories certified under CLIA. The CLIA program provides oversight of laboratory practices through comprehensive evaluations of the operating environment, personnel, proficiency testing, quality control, and quality assurance. The regulatory requirements applied to these laboratories increase in stringency with the complexity of the tests performed. CMS administers CLIA through its own inspection program and with the assistance of state programs and deemed professional organization accreditation programs. CLIA focuses on good laboratory practices rather than on clinical practice, within the limits of the authority for the program outlined in the CLIA statute (Section 353, PHSA). Its ability to assess the

clinical validity[18] and utility of a test is limited, and CLIA certification does not constitute clinical validation of a test.

CMS and CDC develop and update CLIA certification standards with advice from the Clinical Laboratory Improvement Advisory Committee (CLIAC). CLIAC has recommended that laboratory directors take greater responsibility for documenting clinical validity, that CLIA should be modified to provide greater assurance of accurate and reliable testing, and that specific requirements for genetic testing should be added. In May 2000, CDC published a notice of intent and gathered public comments on a proposal to add standards specific to genetic testing laboratories. CDC and CMS are working on a Notice of Proposed Rule Making that would add a genetic specialty to the CLIA certification process.

FDA. FDCA requires all kits for laboratory tests that are packaged and sold to multiple laboratories, including genetic tests, to be approved for safety and effectiveness by FDA before they can be marketed. FDA classifies these test kits as in vitro diagnostic devices (IVDs). Most new genetic tests, however, are provided as clinical laboratory services (laboratory-developed tests or so-called homebrews) and do not use commercial test kits. As such, they are not currently reviewed by FDA.

Although FDA does not currently regulate laboratory-developed genetic tests, it does regulate the analyte specific reagents (ASRs) used by laboratories as the active ingredient in some genetic tests. The ASR Rule subjects reagent manufacturers to certain general controls, such as good manufacturing practices and labeling restrictions. ASRs to be used for human testing may be sold only to laboratories that are certified by CLIA as high-complexity laboratories (i.e., the laboratory must meet the most stringent CLIA programmatic standards). Laboratories conducting ASR-based tests must meet CLIA requirements and must include a disclaimer that the test has been validated by the laboratory and has not been cleared by FDA. Although the ASR rule does give FDA some regulatory authority over a subset of laboratory reagents used for clinical testing, according to some estimates the vast majority of genetic tests do not use ASRs.

Assessment of the clinical validity or utility of genetic tests provided as services, with or without ASRs, is not required prior to their clinical use. Laboratories are required to take responsibility for the analytical validity of tests using ASRs that they provide. However, homebrews that do not use ASRs are not subject to any restrictions or labeling requirements.

OHRP. Additional federal oversight is provided during the research phase of genetic testing or gene-based drug development if the research involves human subjects or identifiable samples of their DNA.

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[18] The terms *analytical validity*, *clinical validity*, and *clinical utility* are important to understand in the context of the oversight topic. The term *analytical validity* refers to how well a test performs in the laboratory—that is, how well it measures the property or characteristic it is intended to measure (in the case of a genetic test, the property can be DNA, proteins, or metabolites). In other words, does the test do what its makers claim it does? If so, it must produce the same results repeatedly and in different laboratories (given the same set of procedures). *Clinical validity* refers to the accuracy with which a test predicts the presence or absence of a clinical condition or predisposition. Thus, a test would be clinically valid if it successfully detects the disease or predisposition. Initially, the test has to be conducted on individuals who are known to have the condition (as well as those who do not) to determine its success rate. Clinical utility refers to the usefulness of the test and the value of the information from a medical standpoint. If a test has clinical utility, it means that the results, positive or negative, provide information that is useful for the clinical management of a patient's care, because the information can be used to predict an effective treatment or preventive strategy. The term *utility* also has been used to recognize the value of information in other non-health arenas, such as estate planning for an individual facing a terminal condition for which no prevention or treatment is yet available.

OHRP and FDA administer regulations (45 CFR 56, or the Common Rule, and 21 CFR 50 and 56) governing the protection of human research subjects. OHRP oversees the protection of human research subjects in HHS-funded research. FDA oversees the protection of human research subjects in trials of investigational devices, drugs, or biologics being developed for eventual commercial use. Fundamental requirements of these regulations are that experimental protocols involving human subjects must be reviewed by an Institutional Review Board to assure the safety of the subjects, to review and approve the informed consent process, and to evaluate whether risks outweigh potential benefits.

FTC. The Federal Trade Commission Act gives FTC broad jurisdiction over unfair or deceptive acts or practices and false advertisements for foods, drugs, devices, and services. This jurisdiction includes advertising claims by marketers of genetic tests. A 1954 liaison agreement between FTC and FDA established agency roles and responsibilities. Accordingly, FTC has primary jurisdiction for the advertising of foods (including supplements), over-the-counter drugs, devices, and cosmetics, and FDA has primary jurisdiction for the labeling of medical products and for both the advertising and labeling of prescription drugs by manufacturers.

Professional Organizations. Recognized professional organizations provide oversight in voluntary partnership with CMS and CDC. The College of American Pathologists (CAP) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) are two such organizations. CAP, which has a long history of providing accreditation services to laboratories, requires them to meet standards that are considered to be more stringent than those of CLIA. CAP and JCAHO also develop laboratory and clinical guidelines and standards. CAP also is actively working to improve its accreditation processes, specifically to add to the inspection process the review of the validation data for laboratory-developed tests. Professional organizations, such as the American Association of Blood Banks and the American Society of Crime Laboratory Directors, also offer accreditation programs for laboratories offering DNA testing (e.g., identity testing).

Current Status

Currently, no regulatory or professional body assures the clinical validity and utility of genetic tests offered as laboratory-developed genetic testing services. FDA currently is reviewing whether it has authority under FDCA to regulate laboratory-developed genetic tests. In addition, FDA is considering modifying the ASR rule to provide additional safeguards. These will be based on the risk associated with the test and not simply on whether the analyte is used for a genetic test, and will, for example, also apply to analytes such as antibodies used to determine exposure to infectious disease.

Although genetic tests that are offered as services are not subject to FDA review or required to demonstrate clinical validity, manufacturers of IVD kits, including genetic test kits, must provide proof of clinical validity for FDA approval. The current expense and delay of approval of IVDs is believed to be a major reason for the paucity of commercially manufactured IVD genetic test kits, resulting in the extensive reliance on laboratory-developed tests. Members of the IVD manufacturing community have proposed a new regulatory category of IVDs, referred to as "in vitro analyte tests" (IVAT), that could expedite time to market for IVDs by requiring that a test demonstrate only analytical validity, not clinical validity or utility. The proposal was submitted to FDA for consideration in 2003.

SACGT Efforts

In response to a June 1999 request from the HHS Assistant Secretary for Health, SACGT assessed, in consultation with the public, the adequacy of the oversight of genetic tests. Following a multifaceted, broad-based public consultation effort, SACGT concluded that additional oversight was warranted for all

genetic tests because of the current limits of federal oversight, the rapidly evolving nature of genetic tests, their anticipated widespread use, and the extensive concerns expressed by the public about the potential for misuse or misinterpretation. In a July 2000 report, *Enhancing the Oversight of Genetic Tests*, SACGT made the following key recommendations:

- FDA should begin to regulate genetic tests provided as laboratory services using an innovative, flexible approach that will not limit the development of new tests or inordinately delay their availability;
- CLIA regulations should be augmented to incorporate specific provisions for genetic testing laboratories;
- Public-private collaborations should be supported to ensure the continued analysis of postmarket data, and CDC should have lead responsibility; and
- HHS agencies should be provided with sufficient resources to carry out expanded oversight of genetic tests, including test review, enhanced CLIA oversight of testing laboratories, coordinated data collection, and information dissemination.

SACGT also endeavored to develop a categorization scheme that could be used by FDA to classify genetics tests according to the level of risk and therefore the level of review needed. The Committee discovered that one of the key challenges in formulating such a scheme was accounting for the multiple uses (e.g., diagnostic, presymptomatic, predictive) of a single genetic test. After extensive deliberations and the development of several draft genetic test classifications schemes, the Committee ultimately decided that no methodology would be able to distinguish high-risk tests that warranted a stringent level of review from lower risk tests that warranted a lower level of review. SACGT's efforts to identify data elements critical to the evaluation of genetic tests were found to be most useful to FDA; a template that includes these elements was modified and is being used by FDA for current device reviews.

Policy Considerations

The public may have a false sense of assurance that the Federal government has established that genetic technologies are safe and effective. Although CMS certifies laboratories providing health-related genetic testing to patients through the CLIA program, CLIA certification assures the analytical validity of health-related laboratory tests — but not their clinical validity. Oversight of genetic testing in areas that are not related to health is largely a private sector/professional organization endeavor; the Federal government does not have a role in regulating the availability of non-health-related genetic tests. As a result, laboratories also may offer unvalidated genetic testing in areas not related to health. FTC could take action against laboratories that make false advertising claims about genetic tests; however, it has not yet used its authority for reasons reviewed in the direct-to-consumer marketing issue brief. Another concern involves clinical laboratories that are conducting genetic tests without any oversight through CLIA and the need for mechanisms to identify these laboratories and bring them into CLIA compliance.

Although there seems to be a consensus about the need for enhanced oversight of genetic tests, debate continues regarding the most appropriate mechanism for effecting change. With regard to proposals for the greater involvement of FDA, opponents argue that laboratory development of genetic tests is a part of the medical practice of laboratory physicians and that although FDA has a role in assuring the safety of medical devices, the agency is prohibited from interfering with the practice of medicine. It can take time for the accumulation of clinical data regarding the clinical validity of new genetic tests, and there are concerns that premarket review of genetic tests would slow the development of new genetic tests or cause laboratories to stop offering them. Some believe that augmenting the CLIA regulations might be a more appropriate way to achieve enhanced oversight, although others believe that current CLIA regulations are sufficient and that additional regulatory burdens to these laboratories would become quite onerous. In

addition, although CMS takes a flexible approach in certifying small academic research laboratories and provides technical assistance to laboratories seeking certification, many laboratories conducting rare disease testing still believe that CLIA regulations are difficult and/or costly to meet. Some laboratories also may be affected by state requirements.

Has a balance between protecting the public and ensuring access to new and cutting edge technologies already been achieved? Do current regulatory mechanisms strike an adequate balance between access, safety, competition, and the independence of medical practice? Does the current system of oversight take into account the conflicting interests among the many stakeholders? Are there non-regulatory ways that the objectives of enhanced oversight might be achieved? For example, CDC's Office of Genomics and Disease Prevention is working on a database with the latest information on clinical experience with genetic tests. This database could become a valuable resource if coupled with a more effective mechanism for the dissemination of the accumulated information through real-time computer access by health care practitioners. Is there a role for SACGHS in balancing the legitimate interests of these parties? Does SACGHS consider current efforts to enhance oversight to be sufficient? If not, what steps, if any, should be taken? SACGT has already looked at the issue and made recommendations to HHS. Does SACGHS agree with the assessment and recommendations of SACGT, and can SACGHS add more value or insight to the process? Given the significant amount of information presented to the Committee on this topic in October, should SACGHS consider providing a status report to the Secretary?

OUTCOME

The Committee will continue to monitor the progress of the Federal agencies involved in the oversight of genetic technologies, but it does not believe further action is warranted at this time.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Vision Statement
Issue Brief

Issue Statement

One of the priority issues under consideration by the Committee is the development of a vision statement that would serve as a framework for future SACGHS recommendations. The vision statement would describe how a future with fully integrated genetics should and should not look, would highlight activities that should be encouraged, and would identify the gaps, barriers, and potential hazards that need to be addressed. Would the development of such a vision statement be of value to the Secretary of the Department of Health and Human Services (HHS)? Would it be of broader value to the Federal government and the public?

Relevance to the SACGHS Charter and Function

SACGHS was established to 1) provide a forum for expert discussion and deliberation and the formulation of advice and recommendations on the range of complex and sensitive medical, ethical, legal, and social issues raised by new technological developments in human genetics; 2) assist HHS and, at its request, other Federal agencies in exploring issues raised by the development and application of genetic technologies; and 3) make recommendations to the Secretary HHS concerning how such issues should be addressed. A vision statement relates well to the Committee's function to explore, analyze, and deliberate on the broad range of human health and societal issues raised by the development and use, as well as potential misuse, of genetic technologies and make recommendations to the Secretary and other entities as appropriate. A vision statement could encompass all seven of the functional areas spelled out in the SACGHS charter—assessing how genetic technologies are being integrated into health care and public health; studying the clinical, ethical, legal, and societal implications of new medical applications, such as preimplantation genetic diagnosis and emerging technological approaches to clinical testing; identifying opportunities and gaps in research and data collection efforts; exploring the potential misuse of genetics in bioterrorism; examining current patent policy and licensing practices for their impact on access to genetic technologies; analyzing uses of genetic information in education, employment, insurance (including health, disability, long-term care, and life), and law (including family, immigration, and forensics); and serving as a public forum for discussion of the emerging scientific, ethical, legal, and social issues raised by genetic technologies.

In light of its broad mandate, SACGHS is composed of experts in a broad range of scientific, medical, legal, and ethical disciplines and non-voting *Ex Officio* representatives of 19 governmental agencies and offices. The HHS agencies are the Administration on Children and Families; the Office of the Assistant Secretary for Health; the Agency for Healthcare Research and Quality; the Centers for Disease Control and Prevention; the Centers for Medicare & Medicaid Services; the Food and Drug Administration; the Health Resources and Services Administration; the National Institutes of Health; the Office for Civil Rights; and the Office for Human Research Protections. Beyond HHS are the Departments of Justice, Commerce, Defense, Education, Energy, Labor, and Veterans Affairs, as well as the Equal Employment Opportunity Commission and the Federal Trade Commission.

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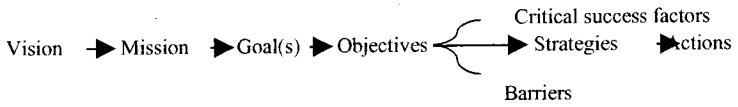
Background

Vision statements are commonly used to guide an organization toward an idealized unifying end product and to provide a portrait of the future. They define and identify an organization's goals and explicate specific steps and targeted actions that need to be taken to bring the vision to fruition. Figure 1 is a standard graphic used to illustrate the process of fulfilling a vision.

Figure 1. The Process of Fulfilling a Vision



Definitions:

Vision: A vision defines the desired future state. It identifies where the organization intends to be in the future or where it should be to best meet the needs of its constituents, incorporates a shared understanding of the nature and purpose of the organization, and uses this understanding to move the organization toward a greater purpose.
Mission: A statement of the overall purpose of an organization. It describes what you do, for whom it is done, and the benefits.
Goals: Broad, long-term aims that define accomplishment of the mission.
Objectives: Specific, quantifiable, realistic targets that measure the accomplishment of a goal over a specific period of time.
Critical success factors: Major items or issues that must be controlled to achieve one or more objectives.
Barriers: Existing or potential challenges that hinder the achievement of one or more objectives.
Strategies: Broad activities required to achieve an objective, control a critical success factor, or overcome a barrier.
Actions: Specific steps to be taken—by whom and when—to implement a strategy.

A vision statement of the role of genetics in health and society might include the following:

- An overview of the current status of genetic research and the scope of efforts to translate scientific progress into improved health for society;
- The desired future scientific, clinical, and societal goals for genetics;
- Information about existing and potential gaps, barriers, and areas for improvement that need to be addressed in order to meet these goals for genetics; and
- An exploration of the extent to which genetic technologies and genetic information may be different from other medical technologies and medical information and the extent to which special oversight and/or education may be needed if exceptionalism is determined to exist.

SACGT Efforts

SACGT did not develop a vision statement for genetics or genetic testing.

Policy Considerations

Vision statements are inherently broad and idealized. If SACGHS were to develop and recommend a vision statement that presented a detailed picture of the future of genetics in health and society, and if it were accepted by the Secretary, it could function to focus and guide current decision-making. It might also inform decision-making in the other departments and agencies represented on SACGHS. However, reaching consensus on a vision may not be a straightforward process. Making the vision sufficiently general enough for it to remain timely and relevant in the light of new scientific developments also might be challenging. In addition, once a vision statement is produced, public perception of the Committee's objectivity and impartiality in addressing other issues might be affected.

Is the determination of a vision of the future of genetics in health and society the role of SACGHS? Is SACGHS especially well suited and structured to articulate a broad vision, given the breadth of public perspectives and governmental agencies it includes?

Would a vision include recommendations to the Secretary about how HHS can contribute to its realization? For example, at the federal level, implementation of such recommendations would involve the efforts of many agencies and departments. Would it also necessitate the appointment of a high-level government official to coordinate and oversee these efforts?

Could a vision statement be a useful tool for the Committee itself, for example, to be used as part of the process of setting priorities or to help to focus Committee recommendations? Would a vision statement provide SACGHS a metric for defining the successful integration of genetics into health care and society?

Could the Committee consider recommending that HHS also develop a vision for genetics? Would this HHS vision be developed in addition to a SACGHS vision or perhaps instead of a SACGHS vision? If HHS developed a vision, it might necessarily relate only to the role of genetics and genetic technologies in health care and public health and be otherwise focused on and limited by the mission and role of HHS. On the other hand, could an HHS vision statement have some advantages, such as, for example, those of being implemented more quickly or having a more direct effect on policy development?

OUTCOME

The Committee decided that although the development of a vision statement is important, it is not the highest priority issue for SACGHS at this time. The Committee decided instead to prepare this report outlining its priority-setting process.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Coverage and Reimbursement of Genetic Technologies Issue Brief

Issue Statement

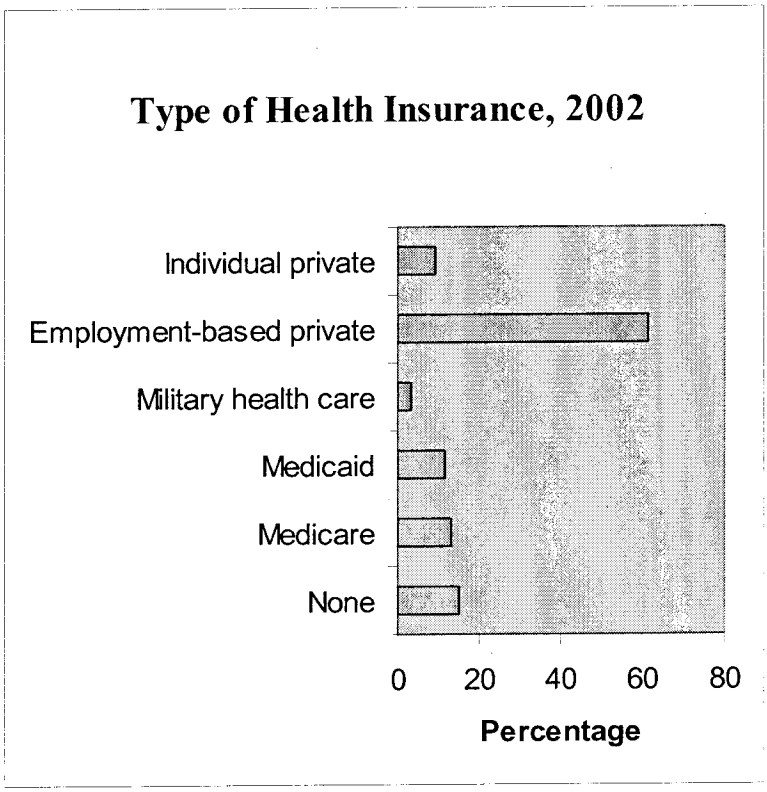
In the U.S. health care system, health insurance affects the cost of and access to health care at both the system and individual levels, and it affects the quality of the care delivered. Decisions made by public and private health plans about whether to provide coverage and about the level of reimbursement can influence the quality and cost of health care and can influence individuals' access to a particular provider, service, procedure, or test. Insufficient data for making coverage and reimbursement decisions, misunderstandings about the costs associated with genetic technologies, and new challenges that genetic technologies pose to the paradigm of health insurance (e.g., the potential need for testing non-plan family members to obtain meaningful test results for a plan member) all may add to the difficulty in making decisions about coverage and reimbursement for genetic services. Questions relevant to this issue include the following: Is coverage and reimbursement a significant barrier to consumer access to genetic technologies? What actions would facilitate coverage and reimbursement decisions about genetic technologies? Are there any key differences between genetic services generally and any other medical treatments, interventions, or technologies that would influence the formulation of reimbursement rates or coverage decisions?

Relevance to the SACGHS Charter

This issue relates to one of the seven functional categories identified in the SACGHS charter—assessing how genetic technologies are being integrated into health care and public health.

Background

In the United States, health insurance is a key factor in access to health care and health outcomes. Eighty-five percent of Americans have some health insurance coverage, either through a private health plan—purchased individually or obtained through an employer—or a public insurance program, such as Medicare or Medicaid (see figure).



Medicare provides health insurance to 39 million Americans who are 65 years old and over and who are less than 65 years old with a disability or end-stage renal disease. The Centers for Medicare & Medicaid Services (CMS) is the Federal agency responsible for administering the Medicare program. Coverage policy decisions are usually made locally by contractor advisory committees or, in some instances, nationally by the Medicare Coverage Advisory Committee. National Medicare policy

currently includes coverage for cytogenetic analyses for monitoring leukemia and myelodysplastic patients, for prenatal diagnosis of chromosomal abnormalities, and for failure of sexual development. A few local Medicare policies have been developed for HER-2/neu testing and BRCA testing. To be eligible for Medicare coverage, the use of a genetic technology must be deemed reasonable and necessary. By law, Medicare cannot cover screening tests conducted in the absence of signs, symptoms, and/or personal history of disease.

Medicaid provides coverage for about 29 million Americans with low income and limited resources, including children, the aged, the blind, and/or the disabled. The program is administered and funded by the states with matching funds from the Federal government. CMS has federal oversight authority over the Medicaid program. Although some minimum benefits are defined at the federal level, states have the latitude to add benefits, including genetic technologies, and to determine how they will deliver services according to the needs of their populations.

Private health insurance (usually provided through an employer) takes two main forms: managed care and indemnity insurance. These differ in how services are paid, who submits claims, and what benefits are covered. States can mandate minimal coverage standards for health plans operating in their jurisdiction (with the exception of health plans provided by self-insured employers, who are exempt from state insurance laws under the Employee Retirement Income Security Act).

For the most part, coverage decisions, including those for genetic technologies, are made by private insurers on a case-by-case basis or by the issuance of formal coverage policy decisions that apply to all plan holders. Several large private health insurers have formal policies for genetic technologies, including prenatal diagnostic testing, preimplantation genetic diagnostic testing, BRCA and colon cancer screening, and HER-2/neu testing. Most formal policies include criteria that must be met as a condition for coverage, such as the presence of evidence-based risk factors (e.g., symptoms, family history) or that the results will influence treatment decisions. The adjacent box lists some of the considerations that health insurers use in making coverage decisions.

Considerations in Making Coverage Decisions for New Technologies

- **Is it FDA approved?**
- **Do clinical trials demonstrate medical necessity?**
- **Are there practice guidelines that recommend its use?**
- **What do the experts and professional organizations say about it?**
- **Is it experimental?**
- **How much does it cost?**
- **How much money will this new technology save us?**
- **Are there any administrative, social, legal, or political factors that should be considered?**
- **Does the public approve of its use?**
- **Do other healthcare payers already cover it?**
- **Is a CPT code available?**

Services are billed to health insurers using Current Procedural Terminology (CPT) codes, which are established by the American Medical Association (AMA). If the service or technology is covered under the patient's health insurance plan and is medically appropriate for the patient's condition or diagnosis, the provider or laboratory will be reimbursed.

Health insurers typically reimburse a predetermined percent of the billed charges, or reimburse based on fee calculations that take into account the plan holder's scope of benefits, the type of provider (i.e., generalist versus specialist, contracted provider versus non-contracted), and the location of service (i.e., geographic adjustment). Medicare payment rates are extremely important, as they establish the upper

limit of what Medicaid can pay for the same service and may provide a basis upon which private health care payers, particularly smaller plans, determine payment amounts. The Clinical Laboratory Fee Schedule, established by CMS, determines Medicare's payment amount for laboratory tests, including genetic tests. The laboratory fee schedule sets payment at 60 percent of prevailing local rates.

SACGT Efforts

At its November 2000 meeting, SACGT held a roundtable to explore current practices and policies for reimbursement of genetic tests and testing services by the various types of public and private health insurance. The goal of the session was to enhance the Committee's knowledge of reimbursement issues and provide a foundation for its exploration of reimbursement issues and access to genetic tests and services. The Committee heard about the practices and policies of Medicare, Medicaid, managed care, and indemnity insurance regarding genetic testing services.

Two reports were in development related to coverage and reimbursement of genetic services. The purpose of the first report, *Coverage and Reimbursement for Genetic Education and Counseling Services*, was to examine the limitations of existing reimbursement and billing mechanisms and policies for genetic education and counseling and their potential impact on access to genetic services. The purpose of the second report, *Coverage and Reimbursement for Genetic Testing Services*, was to provide a broad study of coverage and reimbursement for genetic services, including the identification of challenges in obtaining and providing reimbursement for them. A draft of the first report and a proposed outline of the second report were presented to SACGT in May 2002. The Committee concluded that appropriate next steps would include 1) drafting a letter to the Secretary expressing an urgent need for data on the health and economic value of genetic services, including genetic testing and genetic education and counseling, and requesting that an assessment of existing data and the delineation of additional data needs and research strategies, methodologies, and priorities be conducted and 2) convening a roundtable of individuals who have a role in or who are affected by coverage and reimbursement decisions for genetic services. The second step was driven largely by agreement that research to support evidence-based coverage and reimbursement decisions is needed before recommendations in this area can be acted upon. No further action was taken on this issue because SACGT's charter was not renewed.

Policy Considerations

Genetic services can empower patients to make informed health care decisions for clinical management and intervention purposes. Furthermore, genetically tailored health care has the potential to improve the quality of care and reduce costs by helping to determine whether a particular treatment, drug, or test is a) necessary or unnecessary (e.g., earlier and more frequent mammography in women with a family history of breast cancer but who test negative for BRCA 1/2 may be unnecessary); b) effective or ineffective (e.g., pharmacogenetic testing may indicate that individuals with a particular genetic marker will be unresponsive to a drug); and c) beneficial or harmful (e.g., pharmacogenetic testing may indicate that individuals with a certain genetic marker are at increased risk of suffering the adverse side effects of a drug).

Although many genetic technologies can offer a means for preventing the onset of disease, the costs of such preventive services are incurred immediately, while the benefits, in terms of savings resulting from the avoidance of disease onset, may not be realized until much later, perhaps after the consumer changes health plans. For this reason, health plans may be hesitant to extend coverage to preventive services. However, many health plans, especially health maintenance organizations, are beginning to realize the benefits of offering such services and may be becoming more receptive to providing coverage.

Health plans also face several logistical challenges when considering the coverage, reimbursement, and delivery of genetic services. At this time, insufficient evidence of clinical and cost benefit exists to convince health insurers of the value of many genetic technologies. Furthermore, because many genetic technologies provide information about the risk of diseases that currently lack any proven strategies for prevention or delay of onset, justifying their medical necessity can be problematic. No national consensus has been reached about how to assess the value of genetic technologies that provide non-therapeutic information that consumers may desire for non-medical purposes (e.g., family or estate planning) and whether the informational value alone should warrant health insurance coverage. Also, some genetic technologies require testing of family members (who may not be health plan members) for correct interpretation of the plan holder's genetic risk. Health care payers are reluctant to pay for genetic testing on individuals who are not members of their health plan. In addition, some plans (e.g., Medicare) preclude coverage for the screening of healthy individuals entirely.

As with many health services, reimbursement amounts for genetic technologies and services may be insufficient to cover actual costs and may not adequately reflect the time and effort involved. Insufficient reimbursement could prevent consumers from being able to access appropriate genetic technologies and it also may discourage investment in genetics research and the development of genetic technologies. On the other hand, with finite dollars available to spend on health care, increasing coverage and reimbursement of genetic technologies may not be an optimal use of these limited funds, and current reimbursement rates for genetic technologies may serve as an incentive to manufacturers and laboratories to work toward reducing the marginal cost of genetic technologies. Data demonstrating the extent to which lack of coverage and insufficient reimbursement limits access and constrains research and development are scant, but they would be valuable for making evidence-based policy decisions. Also, any recommendations in this area should be measured against other health care concerns, including rising health care costs, the increasing number of uninsured, rising insurance premiums, and the need for coverage of other health services.

Because the U.S. health care financing system is complex and involves numerous stakeholders, recommendations on coverage and reimbursement would need to target all sectors—Federal agencies and programs (e.g., CMS/Medicare, Agency for Healthcare Research and Quality, Health Resources and Services Administration, Federal Employee Health Benefit Plan, military health plan), state agencies and programs (e.g., Medicaid, SCHIP), and the private/professional sector (e.g., AMA, employers, private health insurance companies) in order to have any significant impact. Creating change in coverage and reimbursement policies and practices in the private sector will be challenging and may be more feasible if recommendations are directed at federal and state governments. For example, because private health plans are highly influenced by Medicare policy, changes in the federal program may lead private plans to implement similar changes.

The national stature of SACGHS and its recommendations may stimulate change in the private sector if the recommendations gain the attention of health plans and their voluntary implementation is seen as feasible and "good practice." Recommendations aimed at federal programs may be potentially effective because of to SACGHS' placement within the Department of Health and Human Services (HHS) and its advisory role to the HHS Secretary. Recommendations aimed at Medicare, however, may require congressional approval if they call for changes beyond CMS' and HHS' legislatively mandated scope of authority.

OUTCOME

The Committee regarded coverage and reimbursement as a high-priority issue requiring further in-depth study. This issue was ranked #1 in this category.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Large Population Studies
Issue Brief

Issue Statement

Genetic variability within and across populations is becoming the focus of research into the cause, prevention, control, and cure of many chronic diseases. Currently, a number of countries around the world have begun to undertake national population studies that capitalize on genome-wide scanning for single nucleotide polymorphisms and haplotypes that can provide population-based information about associations between common polymorphisms and common diseases. U.S. investigators have carried out many smaller scale studies which, while important and informative on their own, do not have the statistical power needed to definitively detect some associations between environmental factors, genetic markers, and disease. Some policy questions relevant to large population studies in the United States include the following: How important is it to mount a large population cohort study in the United States? What role does the heterogeneity of the U.S. population play in assessing the value and importance of such a study? If a large population study is determined to be useful and warranted, how should the many complicated scientific, ethical, and practical challenges of conducting it be addressed? What should be the role of the Federal government in such a study? Are there obstacles that would make the conduct of such a study especially difficult in the United States (e.g., the lack of a universal health care system or the lack of a uniform electronic medical record system)?

Relevance to the SACGHS Charter

This issue is relevant to one of the seven functional categories identified in the SACGHS charter—identifying opportunities and gaps in research and data collection efforts.

Background

The completion of the sequencing of the human genome is facilitating research into the role of genetic variation in common, complex diseases, such as diabetes, which involve both genetic and environmental factors. This new knowledge has led to the establishment of population databanks in many countries, including Iceland, Estonia, the United Kingdom, Sweden, Japan, Canada, Latvia, Scotland, Iran, and Singapore. Research with data from the Icelandic Health Sector Database already has led to the discovery of several disease susceptibility genes for conditions such as obesity and osteoporosis. However, it is not clear what the applicability of these findings will be to populations outside of Iceland.

Several new smaller scale databases have been undertaken in the United States, including the Howard University GRAD Biobank, Northwestern University's NUgene initiative, and the Marshfield Clinic Personalized Medicine Research Project. These efforts have limited value, because they do not represent the heterogeneity of the U.S. population and therefore lack the statistical power of a large-scale study and may allow data access to only a small part of the research community.

There are many ongoing longitudinal large cohort studies in the United States that include a genetics component, but that were created for different purposes, including the National Health and Nutrition Examination Survey and the Framingham Heart Study. In addition, plans are under way to carry out a large longitudinal cohort study of children that will explore their health, environment, and genetics. The National Children's Study, authorized by the Children's Health Act of 2000, is a multi-agency effort led by the National Institute on Child Health and Human Development and involving the National Institute of Environmental Health Sciences, the Centers for Disease Control and Prevention, and the Environmental

Protection Agency. The study is still in the planning stages, but its long-range goal is to enroll, follow, and collect data from 100,000 children over 21 years. Current efforts are now under way to ensure the full representation of America's diverse population and to address the significant ethical, legal, and social issues inherent in this type of study.

Large population genetic-related databases generally have the following goals: mapping susceptibility genes for complex disease; determining the role of genetic variation in the variability of response to pharmaceuticals and treatments; and understanding gene-gene and gene-environment interactions in common disease. Some databases focus on homogeneous populations, which because of founder effects can facilitate the identification of susceptibility genes and relevant genetic variation. Both Iceland and Quebec have taken this approach, capitalizing on the unique makeup of their populations. Estonia and the United Kingdom, among others, are utilizing their databases to uncover genetic variation within more heterogeneous populations.

In April 2003, following the completion of the sequencing of the human genome, the National Human Genome Research Institute published an extensive framework outlining areas for future research in the area of genomics. This framework identified the need for a "large longitudinal population-based cohort study" to help elucidate the contribution of genetic variation to common disease.[19]

Current Status

The National Institutes of Health (NIH) currently is exploring whether a large national population study involving between 500,000 and 1,000,000 people could be undertaken to identify genetic and environmental risk factors in diseases that are of major public health concern and to advance the field of pharmacogenomics. Its potential benefits would include identifying the major susceptibility factors (genetic and environmental) for common diseases of public health consequence in the United States; determining the true population risk of genetic variants; elucidating the effect of environmental factors on disease; and identifying gene-gene, gene-environment interactions of major consequence. NIH will be assessing scientific, technical, and practical issues, as well as ethical, legal, and societal matters for such a study. The development and implementation of a large population study in the United States would entail a lengthy process, because of the numerous stakeholders involved, funding considerations, and the complexity of the undertaking.

Interest in establishing large population databases also is being explored at the state level. For example, the North Carolina House of Representatives recently passed a bill creating a DNA database for research purposes. The bill allows for the voluntary collection of DNA samples, which would be de-identified prior to entry into the database. Researchers, academic institutions, and biotechnology companies could access this databank for a set fee.

SACGT Efforts

SACGT did not explore policy questions relevant to large population cohort studies aimed at advancing knowledge of the role of genetic variation in common, complex diseases.

Policy Considerations

Advocates of establishing a large population study believe that such a study is a necessary step in the translation of knowledge gained from the sequencing of the human genome. A large population database

[19] Collins, FS; et al. A vision for the future of genomics research: a blueprint for the genomic era. *Nature* 2003;422(6934):835-847.

may go a long way toward permitting the full benefit of genomic research to accrue to the American public. Realizing the full promise of genetic medicine may depend on establishing a large population database. Without such a resource, the public may begin to question whether we are fully capitalizing on the value of the Human Genome Project.

Notwithstanding the benefits of the knowledge that could be gained from a U.S. population database, there is some debate about whether it is necessary to create an entirely new database or if instead existing studies could be expanded or consolidated. In addition, some suggest that efforts should be made to collaborate with investigators in countries that already have established large population databases. However, the associations uncovered through those databases may not be applicable to the U.S. population. The unusual heterogeneity of our population and its unique genetic variability (as well as potential differences in environmental factors between some other nations and the United States) may suggest that a database is needed here in order to uncover the most relevant gene-environment-disease associations. Furthermore, it is not clear that either larger non-U.S.-based or smaller U.S.-based cohort studies will afford sufficient data access to meet the needs of the research community in increasing the knowledge base.

The implementation of a large population cohort study raises a number of scientific, technical, and policy considerations:

- Scientific issues include obtaining adequate sample size to identify gene-environment and gene-gene associations with common diseases; following the dispersed and mobile participants over a decade or longer; maintaining the cohort (not having a fixed sample size); and incorporating rapid changes in information regarding environmental exposures and advances in measurement techniques/standards.

- Information technology infrastructure and informatics capacity are critical to managing and standardizing large amounts of data. The lack of a standardized electronic medical record system in the United States and a centralized repository for medical records may be problematic, because information about patients is not collected in a standardized format, limiting its comparability for research purposes.

- Measures protecting the confidentiality and privacy of the collected information and preventing potential misuses, such as discrimination or stigmatization, will be critical. They also will need to be balanced with the value of broad access to primary (de-identified) data in order to help speed the realization of benefits.

- The lack of a universal health care system in the United States may make data collection difficult and may affect the study's diversity and therefore the extent to which disease associations that vary between populations will be detected. From an ethical perspective, given the magnitude of the human and financial investment and the reality that millions of uninsured Americans will not have access to the resulting benefits, distributive justice and equity issues may be particularly salient.

- Other ethical issues include ensuring valid informed consent, including consent for unanticipated future uses, and the concurrence of identifiable communities and populations; equitable distribution of the benefits and risks of the research; the potential for stigmatization based on disease associations with socially defined groups; and difficulty in categorizing populations in a scientifically meaningful and valid way.

Carrying out a project of this magnitude and scope would undoubtedly require the involvement of multiple agencies and the support of the Administration and Congress, scientific and medical communities, and the public. Given that NIH and others in the Department of Health and Human Services (HHS) currently are assessing whether such a project could and should be mounted, a SACGHS recommendation about the value of a large population study may be especially useful at this juncture. Because the issue is still in the formative stages, with fuller NIH and HHS exploration ongoing, an appropriate role for SACGHS beyond such a recommendation may be to keep abreast of agency developments.

OUTCOME

The Committee regarded large population studies as a high-priority issue requiring further in-depth study. This issue was ranked #2 in this category.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Pharmacogenomics
Issue Brief

Issue Statement

Individuals may respond differently to drugs because of differences in their genetic makeup or the heterogeneity of the disease being treated. Genes play a role in how individuals react to drugs—how effective they are and whether they cause adverse reactions. Pharmacogenomic (PG) testing may offer a more individualized approach to medicine through the identification of genetic determinants that help to target the appropriate pharmaceutical interventions to individuals based on the molecular nature of their disease and their individual genetic variation in drug targets, drug transporters, and drug-metabolizing enzymes. For the purpose of this brief, the term *pharmacogenomics* is defined broadly to encompass interindividual differences in whole-genome or candidate genes and alterations in gene expression or inactivation that may be correlated with pharmacological function or response to drugs and will encompass all of the technologies described by terms such as *pharmacogenetics*, *toxicogenomics*, and *toxicogenetics*. Pharmacogenomics also is being applied in the identification of new targets for drug development and in the evaluation of candidate drugs in the laboratory and in clinical drug trials. Notwithstanding the promise of this field, there are many scientific, clinical, and policy issues surrounding pharmacogenomics. These issues include questions about how the clinical validity and utility of pharmacogenetic tests will be established; whether and how pharmaceuticals already on the market will be reassessed; and how access to clinical trials and marketed technologies can be enhanced. Other relevant questions include the following: Does current evidence indicate that these technologies can improve health care outcomes, costs, and quality? Are there measures that the Federal government can take to improve the chance of success? Is current research sufficient for the full potential of pharmacogenomics to be realized? Could these technologies have unintended adverse consequences, such as creating more orphan diseases or increasing health care costs and health disparities? How will this technology best be integrated into the health care system?

Relevance to the SACGHS Charter

This issue relates to a number of the functional areas identified in the SACGHS charter, including assessing the integration of genetic technologies into health care and public health; studying the clinical, ethical, legal, and societal implications of new medical applications; and identifying opportunities and gaps in researching data collection efforts.

Background

PG tests are likely to be used initially to assure safety or predict adverse events. For example, a test to identify variation in the thiopurine s-methyltransferase (TPMT) gene in patients with acute lymphoblastic leukemia already is in use, although not required, for patients receiving the chemotherapeutic agent 6-mercaptopurine. This chemotherapeutic agent is toxic in children with a known TPMT variant with a frequency of approximately 1/300. Pharmacogenomics can be used to predict the safety and efficacy of drugs based either on the genetic profile of the disease or on individual genomic variation, such as with TPMT, or polymorphisms in CYP2D6 or 2C9.

Clinical trials to demonstrate the safety and efficacy of drugs usually cannot capture and describe all of the therapeutic variation that will be seen when a drug is introduced into larger, more diverse populations or the general population. After drugs are brought to market, they may be found to cause adverse effects or to be ineffective in subsets of individuals. A combination of genetic and environmental factors may

explain these differential effects. Pharmacogenomics promises a more individualized approach to medicine, which may reduce the human and economic costs of adverse drug effects. Understanding the wide variation in metabolic rates for common drugs among individuals could lead to more precise drug selection and dosing, reducing the often months-long process of finding the correct drug at the right dose. In the future, when genetic information may tell us the common diseases to which we are more susceptible, pharmacogenetics may help pinpoint which drugs or therapies will have maximal health benefits and minimal risks.

Pharmacogenomics also has the potential to assist in drug development. PG research can be used in the early phases of drug development to identify potential drug targets or biological pathways that may be most effective in treating disease. Pharmacogenomics also can be used to eliminate drugs with serious side effects from the pipeline before a significant investment has been made in them. For example, it has been estimated that 30 percent of drugs currently on the market are metabolized by two P450 enzymes shown to have significant allelic variation in the population.[20] Drugs metabolized by these P450 enzymes may be expected to have adverse effects on a subset of people. This is an important public health consideration, because adverse drug reactions may cause as many as 100,000 deaths per year in the United States at an estimated cost of $76 billion.[21]

PG studies might lead to the development of tests that would identify individuals likely to have adverse events, permitting appropriate selection of study populations in clinical trials. This can result in bringing to market an important drug that has been shown to be effective in a subset of the population, but that may have failed in clinical trials in an unselected population. It also could allow potentially useful drugs that have caused adverse effects in some individuals to be used safely in the remainder of the population. However, concern has been raised that research on potentially important drugs may be stopped if genetic data suggest that the population in which the drug will be useful is too small or is otherwise not expected to constitute a profitable market. In addition, the pharmaceutical industry has very little incentive to conduct PG studies on already-marketed drugs or generic drugs. Such studies are expensive, appear to offer no market advantage for their sponsor, and may result in the identification of persons for whom the drugs would be ineffective, thereby creating a stratified market for the products.

Most PG data produced by pharmaceutical companies are not publicly available, making it difficult to know the extent of industry use of this technology in the drug development process. The expanding role of pharmacogenomics in medicine is apparent, however, in the growing scientific literature that includes PG data, the number of new journals devoted entirely to the subject, recent draft Food and Drug Administration (FDA) guidelines for pharmacogenomics data submission, and the increasing amount of money being spent on PG research and development. Despite the promise of and obvious interest in pharmacogenomics, there are skeptics, and several articles recently have been published suggesting that the enthusiasm may be premature. For example, Haga et al. [22] have suggested that gene disease links may be weaker than originally predicted and that there may be difficulty in establishing the scientific validity of PG. Lindpainter[23] concludes that pharmacogenomics will provide new ways to diagnose and treat disease in the near future, but that the advances will be incremental and unlikely to dramatically change medical practice.

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[20] Abbott, A. With your genes? Take one of these, three times a day. *Nature* 2003;425:760-762.
[21] Brazell, C; Freeman, A; Mosteller, M. Maximizing the value of medicines by including pharmacogenetic research in drug development and surveillance. *J Clin Pharmacol* 2002;53:224-231.
[22] Haga, S; Koury, MJ; Burke, W. Genomic profiling to promote a healthy lifestyle: not ready for primetime. *Nat Genet* 2003;43:347-350.
[23] Lindpainter, K. Pharmacogenetics and pharmacogenomics in drug discovery and development: an overview. *Clin Chem Lab Med* 2003;41(4):398-410.

Current Status

Regulatory Initiatives. In November 2003, FDA published a draft *Guidance for Industry Pharmacogenomic Data Submissions* for public comment. FDA points out in the guidance that like any other data used for decision-making during drug development, such as to select study populations or to inform final drug labeling, genetic information is subject to existing FDA requirements for disclosure to the agency. However, the guidance also states that FDA currently considers most PG data to be exploratory and, as such, inappropriate for use in the regulatory process. The guidance reflects FDA's recognition of the potential public health benefits of PG data and aims to encourage its application in drug development. In order to prepare for the future incorporation of pharmacogenomics into drug development and health care, the guidance proposes the implementation of a Voluntary Genomic Data Submission process. The agency also is drafting new guidance that will outline the review process for jointly marketed diagnostic-therapeutic products.

Private sector interest also has been evident in developing regulatory guidelines. The Consortium on Pharmacogenetics was founded with financial support from GlaxoSmithKline, IBM, and the First Genetic Trust to address regulatory and ethical public policy issues surrounding pharmacogenetics. The consortium members included bioethicists with public policy expertise and policy experts from the pharmaceutical and biotechnology industries. Through a series of meetings between November 2000 and October 2001, the consortium developed recommendations that are published in the document *Pharmacogenetic Consortium Report: Ethical and Regulatory Issues in Research and Clinical Practice.*

Research Initiatives. Federal research efforts in pharmacogenomics are under way. The National Institutes of Health (NIH) supports extensive research in this area. A salient example is the National Institute of General Medical Sciences' Pharmacogenetics Research Network, which supports multidisciplinary research groups addressing research problems in pharmacogenetics. Its main goal is to advance understanding of how drug response phenotypes correlate with genetic variation. The participating centers in the network also are developing a public database, PharmaGKB, to provide reference data, population frequencies, mechanistic understanding, and information about the possible clinical impact of PG research. Other institutes within NIH are funding research that will underpin and advance the field. The National Human Genome Research Institute supports projects and public-private partnerships aimed at developing tools that will advance the field of pharmacogenomics, including the HapMap project and the SNP Consortium.

Many other public and private organizations are contributing to the production of databases and database standards, including the European BioInformatics Institute, the MicroArray Gene Expression Data Society, and Japan's Center for Information Biology Gene Expression. Foundations also are supporting research in this area. The Health and Environmental Science Institute of the non-profit International Life Sciences Institute is studying micro-array methodologies for measuring alterations in gene expression, working toward developing publicly available data and contributing to the development of public international databases of gene expression data and key biological parameters.

SACGT Efforts

SACGT did not specifically look at pharmacogenomics; however, its recommendations on the oversight of genetic testing apply to the development and use of PG tests (see the *Oversight Issue Brief*).

Policy Considerations

Many believe that pharmacogenomics has the potential to bring about fundamental changes in the way medicine is practiced. However, there are still many questions about how the integration of

pharmacogenomics into clinical medicine will be achieved and its effect on the health care system. Is there a need to assess the potential of pharmacogenomics and the barriers to the realization of the full potential of pharmacogenomics? What regulatory mechanisms will be in place for the evaluation of PG data and tests? FDA currently is working on several guidance documents that are intended to assist industry in the use of PG data in drug discovery and development and to aid in bringing PG tests to market. However, many PG tests are likely to be homebrews and therefore subject to the same oversight gaps that currently exist in the genetic testing arena.

A significant portion of the population does not receive adequate health care now, and it is not clear how this potentially expensive technology will affect already-escalating health care costs. PG tests may be expensive and may increase the cost of drug development and drugs. On the other hand, the technology also has the potential to decrease costs and improve the quality of health care by optimizing pharmaceutical use, the fastest growing portion of health care costs. Because many drugs on the market today are metabolized by an extremely limited number of pathways, pharmacogenetic screening might not be prohibitively expensive. Although costs associated with testing could be initially high, they are non-recurring and, as such, may lead to savings in the short and long run (e.g., fewer office visits to optimize treatment, prevention of adverse effects, and better outcomes). The potential increased cost of drug development and diagnostic testing also would need to be balanced against this potential gain in health quality and decrease in both short-term and long-term health care costs.

Elucidating the role of genetic variation in common disease will require the statistical power of large cohorts. Will the current health care system infrastructure and research enterprise be able to support the clinical validity and utility determination of pharmacogenomics? How will study populations be chosen? Is this technology likely to create new disparities? Researchers in the HapMap project have used extensive community engagement that could serve as a model for community participation in large PG population studies. The Committee's actions could result in greater public acceptance and participation in the studies needed to validate PG tests.

There is the additional risk of stigmatization of communities that have higher frequencies of particular gene variants. Pharmacogenetic variation identified today may later be found to be associated with disease in the future. For example, a correlation between genetic variants at the HLA locus and increased susceptibility or resistance to SARS recently has been described in the literature. Pharmacogenomics may have unforeseen social impacts; for example, current notions of race and ethnicity may be challenged by the emerging PG data.

Will health professionals be adequately educated to facilitate the integration of pharmacogenetics into clinical practice? Will fears about the possible misuse of genetic information frustrate the use of this technology? How will coverage and reimbursement decisions be made with respect to this technology? Will patents on PG methodologies hinder research or increase industry participation? What should be the role of the Federal government in the complex issue of ensuring access to data used in or resulting from drug development?

Recommendations on ways to maximize the benefits and minimize the risks of pharmacogenomics could help ensure that this new technology is safely and appropriately integrated into research and health care, increase public awareness of the benefits and limits of this technology, and result in greater public acceptance of and participation in studies needed to validate PG research.

OUTCOME

The Committee regarded pharmacogenomics as a high-priority issue requiring further in-depth study. This issue was ranked #3 in this category.

This issue brief was prepared to facilitate the identification of SACGHS' study priorities; it does not represent the official views of SACGHS or of the United States Government.

Direct-To-Consumer Marketing of Genetic Technologies Issue Brief

Issue Statement

Concerns have been raised about direct-to-consumer (DTC) advertising of genetic tests and products, both in the arena of health care and in non-health-related areas. In addition, even greater concern has been raised about direct access to genetic tests and products. The marketing—that is, both the advertising and sale of medical services and products directly to consumers, has become a common and generally accepted practice. Many consumers view DTC advertisements as a source of information that can enable them to be better informed with respect to health and non-health-related genetic issues. In particular, with respect to health, DTC advertising may enable consumers to participate more fully in health care decisions and exercise more control over their health and well-being. On the other hand, like many other products and technologies, ranging from nutritional supplements to total body scans, many genetic technologies are being marketed with exaggerated claims or in some cases without independent confirmation of their clinical validity and utility. Yet the average consumer typically lacks the background to critically evaluate marketers' claims. Direct access to genetic technologies raises other concerns because their complex nature often necessitates careful interpretation by well-trained health professionals. The Food and Drug Administration (FDA) and the Federal Trade Commission (FTC) both have roles in protecting consumers from false and misleading advertisements in the health care arena, and FTC has a general responsibility for truth-in-advertising in all areas. Currently, however, neither agency is actively involved in monitoring advertisements for most genetic tests. Relevant policy questions might include the following: Do the risks of DTC advertising of genetic technologies outweigh its benefits? Does DTC advertising of genetic technologies raise greater concern and warrant more attention than DTC advertising of other medical products? Is direct access to genetic technologies a concern? Do current uncertainties, questions, and policy considerations require the attention of SACGHS?

Relevance to the SACGHS Charter

These issues are relevant to integration of genetic technologies into health care and public health, one of the seven functional categories identified in the SACGHS charter.

Background

DTC Advertising of Genetic Technologies. Pharmaceutical manufacturers formerly directed their advertising of prescription drugs to medical professionals. However, in the 1980s prescription drug makers expanded the marketing audience from health professionals to include the general public. In 1999, FDA issued a guidance document to assist sponsors in meeting requirements for DTC broadcast advertising of prescription drugs. That same year, FDA surveyed consumers and found DTC advertisements made them more aware of medical options, encouraged them to seek out medical care and advice, and prepared them more fully for discussions with providers about their options. This was the first in a series of FDA surveys aimed at understanding the impact of DTC advertising on doctor-patient relationships and prescribing decisions. Two follow-up surveys, one of consumers and one of physicians, were completed in 2002. The physician survey found that most agreed that the effect of DTC advertising was generally positive, but that it led to unnecessary anxiety on the part of patients and to pressure to prescribe name-brand medications. The American Medical Association supports consumer access to drug information, but is concerned that consumers may receive inaccurate or misleading information and may incorrectly believe that the advertisements have FDA approval. The National Health Council, a coalition of voluntary health organizations, issued a report in 2002 that recognized the value of DTC advertising in

providing important and often beneficial information to consumers, but also called for research to understand more fully the potential and impact of DTC advertising. In order to assist industry in providing consumers with useful and understandable risk and benefit information based on approved labeling, FDA issued three additional draft guidances in February 2004, one targeted specifically at device manufacturers.

FDA and FTC both have jurisdiction regarding labeling and advertising of drugs and devices. The Federal Trade Commission Act grants FTC broad jurisdiction over unfair or deceptive acts or practices and false advertisements for drugs, devices, and services. This jurisdiction includes advertising claims by marketers of genetic technologies. FDA, in its role in implementing and enforcing the Federal Food, Drug, and Cosmetic Act (FDCA) of 1938, regulates any statements that a manufacturer may make concerning a medical device, including advertisements and promotional labeling. The FDCA requires that manufacturers, packers, and distributors include certain information about the advertised product's uses and risks and that advertisements and labeling refer only to the use for which the drug or device was approved (i.e., its intended use). A product is considered misbranded under the act (and therefore, subject to enforcement action) if its labeling or advertising is false or misleading in any particular way or if it fails to reveal material facts. Off-label use cannot be promoted in advertisements and labels. Genetic tests sold as kits are considered to be devices and as such are subject to FDA regulation. Certain homebrew tests (those that do not use analyte-specific reagents, which are subject to FDA oversight) generally marketed as services fall into a regulatory gap, because FDA does not monitor their labeling and promotion. Therefore, FDA cannot require that warnings, contraindications, precautions, and side effects be included in promotional communications issued by or on behalf of laboratories for these services. See the *Oversight of Genetic Technologies Issue Brief* for additional background on the roles and responsibilities of the agencies involved in the oversight of these technologies.

A 1954 liaison agreement between the two agencies gives FTC primary jurisdiction for the advertising of foods (including supplements) and over-the-counter drugs and devices. However, FDA maintains jurisdiction over the intended use of over-the-counter drugs and devices. Thus, if a manufacturer or distributor misrepresents the intended use of a particular medical device, FDA has jurisdiction over whether the misrepresentation is in an advertisement or in the labeling. Responsibility for both the labeling and advertising of prescription drugs rests with FDA.

Laboratories providing non-health-related testing for paternity, familial relationships, or ancestry are easily accessed through the Internet. As with some health-related testing, the validity of some of these non-health-related tests may not be established, yet the extent to which FTC or FDA will regulate advertisements for non-health-related genetic tests is not clear. Although FTC's statutory authority would seem to encompass such tests, as with health-related genetic tests, the agency is not actively monitoring the field. FDA may not have the authority to monitor advertisements for test kits for non-health-related genetic tests.

Direct Access to Genetic Technologies. Direct access to clinical genetic tests as well as non-health-related genetic testing (e.g., paternity, familial relationships, or ancestry) is growing, particularly through the Internet. A 2003 study by Gollust et al.[24] identified 105 unique Internet sites that offered genetic services directly to consumers. Ninety-one of these sites (87 percent) offered only non-health-related testing such as parentage testing, identity testing, and DNA banking. Fourteen sites offered direct access to health-related genetic tests. Half of these sites did not require physician involvement. In addition, several sites offered neutraceutical remedies or therapies based on test results. The FDCA limits the ability of FDA to regulate nutritional supplements.

[24] Gollust, S; Wilfond, B; Hull, S. Direct-to-consumer sales of genetic services on the Internet. *Genet Med* 2003;5:332-337.

The United Kingdom's Human Genetics Commission produced the report *Genes Direct:Ensuring the Effective Oversight of Genetic Tests Supplied Directly to the Public* in March 2003. In the report, the commission acknowledges the right of persons to obtain information about themselves, free from state intervention unless there is risk of harm. Potential harms include overstating the role of genetics in common diseases; erroneous predictive health information that may cause individuals to delay seeking health care or adopt possibly harmful or expensive lifestyle changes; and inappropriate testing of non-consenting adults and children. The commission recommended that a statutory prohibition of DTC marketing of genetic testing was not necessary; genetics services and new predictive genetic tests should be accessible through the national health service; and health-related tests should not be offered directly to the consumer.

In the United States, state governments are responsible for regulating who may order laboratory tests and receive test results. As of last year, 21 states had no limits on access, 12 allowed limited access, and 17 prohibited direct consumer access to laboratory testing.[25]

In 2003, the American College of Medical Genetics (ACMG) developed a policy statement discouraging direct access to genetic testing without the involvement of an appropriately qualified health care professional to ensure appropriate use, interpretation, counseling, and follow-up.[26] ACMG cautions against self-ordering of genetic tests and use of genetic "home testing" kits, because of the complexities of genetic testing and the potential for harm.

Current Status

Although FTC has the authority to regulate false and deceptive marketing of genetic tests, to date it has not actively conducted enforcement in this area. In order to maximize its impact and limited resources, FTC focuses its attention on products or services that present significant safety concerns, make claims about serious diseases, and are being marketed on a nationwide basis. In addition, lack of consensus among practitioners about the validity of tests can make it difficult to distinguish false and deceptive promotion of genetic technologies from innovative new uses. In general, FTC does not get involved in medical practice.

In addition to issuing guidance aimed at helping manufacturers provide consumers with better risk and benefit information, FDA also is strengthening enforcement efforts by issuing warning letters for violations of the promotion rules. These efforts may improve the quality of information used in DTC marketing and deter advertising for unapproved uses. However, because homebrew genetic tests are not subject to FDA premarket review regulations, the agency also does not monitor their marketing and use, which may leave the consumer particularly vulnerable to false claims about this type of service.

The Clinical Laboratories Improvement Advisory Committee (CLIAC) is considering the issue of direct access to laboratory tests and deliberated on the issue at its September 2003 meeting. CLIAC concluded that direct access to genetic technologies requires monitoring and surveillance and indicated that it plans to monitor the issue.

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[25] From data presented by Dr. Toby Merlin, Associate Director for Laboratory Medicine in the Centers for Disease Control and Prevention's Division of Laboratory Systems, to the Clinical Laboratory Improvement Advisory Committee, September 2003.

[26] American College of Medicine Genetics Board of Directors. ACMG *Statement on Direct-to-Consumer Genetic Testing. Genet Med* 2004;6(1):60.

The National Human Genome Research Institute convened consumer and industry representatives and federal officials in a small roundtable meeting focused on current practices and trends in DTC advertising of genetic tests. One anticipated outcome from the discussions is the articulation of potential policy options for consideration, and possibly further development, by federal regulators and policymakers.

Some private sector efforts may be relevant. The National Coalition for Health Professional Education in Genetics (NCHPEG) is developing a web portal, Genetic Resources on the Web (GROW). This website will feature information on genetic education programs for non-genetic health professionals. The information has been reviewed by NCHPEG to evaluate the extent to which it addresses core competencies for health professionals in genetics and to consider its general accuracy about genetics and disease. However, GROW will not provide assurance that specific genetic tests are clinically valid, and it probably will not be useful for the general public. In addition, NCHPEG plans to develop standards for membership in GROW and to link to members' websites, with the expectation that users likely will find accurate and useful information though GROW members. GeneTests, a publicly funded medical genetics information resource (www.genetests.org), provides up-to-date information on genetic tests that is free to all interested parties.

SACGT Efforts

In its July 2000 report, *Enhancing the Oversight of Genetic Tests*, SACGT recommended that current FDA and FTC regulations be enforced in the area of genetic test promotion and marketing. The Committee also held a session at its November 2000 meeting on FDA and FTC regulations governing the labeling, promotion, and advertising of medical devices.

Policy Considerations

Consumers today expect to take a more active role in their health care decisions. DTC marketing of validated genetic technologies can help consumers make more educated choices regarding their health care when the information provided is complete and accurate. DTC advertising can affect physician-patient relationships by encouraging patients to see their physician and engage in a dialogue regarding their health care. DTC advertising also may cause patients to request tests or medications that are inappropriate for their condition from their health care provider or other professional, and direct access will permit individuals to be tested or to buy treatments without consultation with an expert to assure appropriate interpretation of test results or safety of treatment. In some cases, unvalidated genetic testing services, some of which may have potentially significant consequences, are being advertised and accessed over the Internet and elsewhere. In addition to the possible direct harm caused by inaccurate or misleading test results, these advertisements and services may have a negative effect on the public's overall trust in genetic technologies.

Given the perceived usefulness by both industry and consumers, DTC marketing is likely to continue. Is the current situation acceptable? Does DTC marketing of genetic technologies provide value to consumers? Does it really increase consumer control over their health care or provide consumers with services of social value, and is this an important consideration? Is the current regulatory framework sufficient to protect the public from the potential harms of DTC advertising and direct access? Because homebrew genetic tests are not subject to FDA premarket review regulations, and the agency also does not monitor their marketing and use, are consumers particularly vulnerable to false claims about this type of service? How can the public be assured that they are receiving complete and accurate information about genetic technologies that are advertised? At the October 2003 meeting, SACGHS discussed the need for an accreditation system to assist consumers in judging the validity or accuracy of websites providing genetic information. Would the establishment and operation of such a system be an appropriate

governmental role, or would it be a more appropriate function for the private sector? Is further consideration of this idea warranted?

Additional economic and market considerations not addressed in this brief also may need to be considered. For example, DTC marketing costs are included in the cost of drug development. These costs constitute less than 20 percent of pharmaceutical marketing expenses, but they may have an effect on health care costs. Is the value derived from DTC advertising enough to compensate for the increase in health care costs? Do the economic considerations warrant further study?

DTC advertising of genetic technologies and services has the potential to facilitate integration of these technologies into health care by educating the public and health providers about them, increasing awareness of their availability, and enhancing their appropriate use. Consumers also may derive value from free access to personal non-health-related genetic information. However, direct access to genetic testing and technology is more controversial than DTC advertising and may warrant increased scrutiny. Genetic testing results can be complex and may require a trained professional for interpretation and application to an individual's unique health concerns. Is it possible to distinguish tests appropriate for DTC from tests that should be accessed only through a heath care provider? Should access to any non-health-related tests be restricted? Who should/could produce such guidance? What effect does direct access have on access to health care overall? Although SACGHS may be able to bring attention to the direct access issue, any recommendations may have limited impact because states regulate who may order tests and receive the results.

OUTCOME

The Committee regarded DTC marketing of genetic technologies as a high-priority issue requiring further in-depth study. This issue was ranked #4 in this category.

GLOSSARY

Analytical validity – describes how well a test performs in the laboratory—that is, how well a test measures the property or characteristic it is intended to measure.

BRCA 1 and BRCA 2 – genes associated with hereditary breast and ovarian cancer.

Clinical utility – the usefulness of the test and the value of the information it provides from a medical standpoint. If a test has clinical utility, it means that the results, positive or negative, provide information that is useful for the clinical management of a patient's care, because the information can be used to predict an effective treatment or preventive strategy.

Clinical validity – the accuracy with which a test predicts the presence or absence of a clinical condition or predisposition.

Cohort study – a study that observes a designated group(s) over a period of time to determine whether and under what circumstances (e.g., environmental exposures) the outcome of interest (e.g., disease) develops.

Coverage – as defined by the health plan or insurance contract, the scope of services, technologies, and procedures provided by an insurer and the extent to which and circumstances under which they are reimbursed.

Diagnostic – aiding in the identification of a specific disease in a symptomatic individual.

Direct-to-consumer marketing – the advertisement and sale of a product directly to the general public through various means, such as television and the Internet.

Genetic determinism – the idea that genes are solely responsible for an individual's physical characteristics and/or behaviors.

Genetic discrimination – differential treatment of similarly situated people on the basis of their genetic information or their family members' genetic information.

Genetic enhancement – the act of manipulating an individual's genes with the goal of providing improved traits.

Genetic exceptionalism – the idea that genetics information is inherently unique from other types of medical information and should receive special consideration.

Genetic predisposition – increased susceptibility to conditions, behaviors, or diseases because of one's genetic composition.

Homebrew – laboratory tests that are developed and performed in-house and that are provided as clinical laboratory services (as opposed to test kits).

Indemnity – type of health insurance in which providers or plan members are reimbursed on a fee-for-service basis regardless of who provides the service.

Orphan disease – a rare disease or condition that affects fewer than 200,000 individuals in the United States.

Pharmacogenetics – the study of interindividual variations in DNA sequence related to drug absorption and disposition (pharmacokinetics) or drug action (pharmacodynamics), including polymorphic variation in the genes that encode the functions of transporters, metabolizing enzymes, receptors, and other proteins.

Pharmacogenomics – the study of interindividual differences in whole genomes or candidate genes and alterations in gene expression or inactivation that may be correlated with pharmacological function or response to drugs, and will encompass all of the technologies described by such terms as *pharmacogenetics*, *toxicogenomics*, and *toxicogenetics.*

Public health – the science and practice of protecting and improving the health of a community by preventive medicine, health education, control of communicable diseases, application of sanitary measures, and monitoring of environmental hazards.

Reimbursement – payment given for products or services rendered.

Screening – testing or examining a population for the presence of a disease or disease risk factors.

ACRONYMS

ADA – Americans with Disabilities Act
AMA – American Medical Association
ASRs – Analyte Specific Reagents
BRCA 1 and BRCA 2 – Breast Cancer Gene 1 and Breast Cancer Gene 2
CAP – College of American Pathologists
CDC – Centers for Disease Control and Prevention
CLIA – Clinical Laboratory Improvement Amendments
CLIAC – Clinical Laboratory Improvement Advisory Committee
CME – continuing medical education
CMS – Centers for Medicare & Medicaid Services
DOE – Department of Energy
DTC – direct-to-consumer
EEOC – Equal Employment Opportunity Commission
ELSI – ethical, legal, and social issues
ERISA – Employee Retirement Income Security Act
FDA – Food and Drug Administration
FDCA – Food, Drug, and Cosmetic Act
FTC – Federal Trade Commission
HHS (also DHHS) – Department of Health and Human Services
HIPAA – Health Insurance Portability and Accountability Act of 1996
HRSA – Health Resources and Services Administration
IVD – in vitro diagnostic device
JCAHO – Joint Commission on Accreditation of Healthcare Organizations
NAS – National Academy of Sciences
NCHPEG – National Coalition for Health Professional Education in Genetics
NHGRI – National Human Genome Research Institute
NIH – National Institutes of Health
OHRP – Office for Human Research Protections
PG – pharmacogenomic
SACGHS – Secretary's Advisory Committee on Genetics, Health, and Society
SACGT – Secretary's Advisory Committee on Genetic Testing
USPTO – United States Patent and Trademark Office