Secretary's Advisory Committee on Genetics, Health, and Society
Summary of Thirteenth Meeting
July 10, 2007
Bethesda, Maryland

Committee Members Present

Reed Tuckson, M.D., Chair
Sylvia Mann Au, M.S., C.G.C.
Chira Chen
James P. Evans, M.D., Ph.D.
Kevin FitzGerald, S.J., Ph.D., Ph.D.
Julio Licinio, M.D.
Barbara Burns McGrath, R.N., Ph.D.
Steven Teutsch, M.D., M.P.H.
Marc S. Williams, M.D., FAAP, FACMG

***Ex Officios*/Alternates Present**

Gurvaneet Randhawa, M.D., M.P.H. (HHS/Agency for Healthcare Research and Quality)
Muin J. Khoury, M.D., Ph.D. (HHS/Centers for Disease Control and Prevention)
Madeline Ulrich, M.D. (HHS/Centers for Medicare & Medicaid Services)
Steven Gutman, M.D., M.B.A. (HHS/Food and Drug Administration)
Deborah Willis-Fillinger, M.D. (HHS/Health Resources and Services Administration)
Alan Guttmacher, M.D. (HHS/National Institutes of Health)
Robinsue Frohboese, J.D., Ph.D. (HHS/Office for Civil Rights)
Anand Parekh, M.D., M.P.H. (HHS/Office on Public Health and Science)
Martin Dannenfelser (Administration for Children and Families)
Michael Amos, Ph.D. (Department of Commerce)
Scott McLean, MC, USA (Department of Defense)
Daniel Drell, Ph.D. (Department of Energy)
Sherrie Hans, M.D., Ph.D. (Department of Veterans Affairs)

Executive Secretary

Sarah Carr, NIH Office of Biotechnology Activities

TUESDAY, JULY 10, 2007

Welcome and Opening Remarks

Reed V. Tuckson, M.D.
SACGHS Chair

Dr. Reed Tuckson, Chair of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS), welcomed those in attendance and stated that the public was made aware of the meeting through notices in the Federal Register, as well as announcements on the SACGHS website and listserv. He encouraged members of the public who wished to address the Committee to register for the public comment session. Dr. Tuckson explained that SACGHS quarterly meetings usually take place over a period of 2 days; however, because of the importance of the charge from the Secretary of Health and Human Services (HHS) on the oversight of genetic testing, one day had been devoted to a meeting of the Oversight Task Force. Dr. Tuckson noted that on April 27, 2007, the Committee sent a letter to Secretary Leavitt thanking him for his leadership in addressing oversight issues and for directing the SACGHS inquiry. The letter also expressed the Committee's interest in two Senate bills that would affect genetic testing: The Laboratory Test Improvement Act (Senate bill 736), and the Genomics and Personalized Medicine Act (Senate bill 976).

Dr. Tuckson stated that the Evaluation Task Force, which was created at the previous meeting, would delay its work until the oversight report was completed. Resources were being heavily invested in responding to the oversight charge, and the knowledge gained from the oversight effort would carry over to the goals of the new Task Force.

Dr. Tuckson stated that a vote on the Genetic Information Nondiscrimination Act (GINA), H.R. 493, was expected soon. GINA would prohibit genetic discrimination in health insurance and employment. Dr. Tuckson reported that the Centers for Medicare & Medicaid Services (CMS) provided comments on the 2006 SACGHS report on coverage and reimbursement of genetic tests and services. Dr. Marc Williams had volunteered to review the comments and help the Committee determine the type of follow-up needed. Dr. Tuckson welcomed Dr. Madeline Ulrich from CMS, who was attending on behalf of *ex officio* Dr. Barry Straube.

Dr. Tuckson introduced Dr. Cathy Fomous, who recently joined the Office of Biotechnology Activities (OBA) as a policy analyst, supporting SACGHS and an NIH program aimed at harmonizing clinical research policy. She previously worked at the National Library of Medicine, where she directed content development for the genetics home reference website. Dr. Fomous is a certified genetic counselor, and earned her doctoral degree in genetics from Georgetown University. Dr. Tuckson also introduced Ms. Natalie Vokes, who joined the OBA staff as a summer intern and was assisting with the study of gene patents and licensing. Ms. Vokes graduated with a degree in chemistry from Williams College and was the recipient of a 2-year fellowship to study the philosophy of science at Cambridge University.

Dr. Tuckson provided an overview of the agenda. Following an update on the status of the pharmacogenomics and oversight projects, the meeting would focus on gene patents and licensing, including an international roundtable. At the completion of the patent sessions, Dr. Katrina Goddard of the Centers for Disease Control and Prevention (CDC) would provide an update on public awareness of direct-to-consumer (DTC) tests. Executive Secretary Sarah Carr reviewed the rules of ethical conduct

governing Committee members as special government employees and Dr. Tuckson turned the floor over to Dr. Kevin FitzGerald, Chair of the Pharmacogenomics Task Force.

Update on the Development of the SACGHS Pharmacogenomics Report

Kevin T. FitzGerald, S.J., Ph.D., Ph.D.
SACGHS Pharmacogenomics Task Force Chair

Dr. FitzGerald stated that the draft pharmacogenomics report was released for public comment on March 23, 2007, which coincided with the release of Secretary Leavitt's personalized health care initiative. During the public comment period, the draft report was disseminated through the SACGHS website and listserv and to 283 other interested individuals and organizations. The public comment period ended June 1, 2007. The Pharmacogenomics Task Force received a total of 57 sets of public comments from Federal Government agencies; private companies, such as Abbott, Amgen, Eli Lily, and Genzyme; organizations such as the Blue Cross Blue Shield health plans, the American Medical Association, nursing associations, pharmaceutical organizations, and the Personalized Medicine Coalition; and individuals representing academia, health care providers, researchers, and others.

The Task Force was in the process of analyzing the responses received, after which they would be incorporated, as appropriate, into the draft report and recommendations. The revised draft would be sent to Committee members at the end of October for review in preparation for the November 2007 SACGHS meeting. The goal was to finalize the recommendations in November so that the final report could be transmitted to the Secretary in February 2008 and be released to the public in March 2008.

Dr. Tuckson thanked Dr. FitzGerald and turned the floor over to Dr. Marc Williams, who was speaking on behalf of Oversight Task Force Chair Andrea Ferreira-Gonzalez. Dr. Williams had chaired the full-day meeting of the Task Force that was held the previous day.

Report from the SACGHS Task Force on the Oversight of Genetic Testing

Marc S. Williams, M.D.
SACGHS Oversight Task Force Member

Dr. Williams reviewed the Secretary's charge to the Committee on oversight and placed it in historical perspective. He noted that in 1997, a National Institutes of Health/Department of Energy (NIH/DOE) Task Force recommended consideration of a genetics testing specialty under the Clinical Laboratory Improvement Amendments (CLIA) and mandatory proficiency testing for all laboratories conducting genetic testing. The NIH/DOE Task Force also recommended the establishment of a standing advisory committee to address genetic testing issues. This recommendation led to the formation of the Secretary's Advisory Committee on Genetic Testing (SACGT), SACGHS' predecessor.

In 2000, SACGT recommended that the Food and Drug Administration (FDA) be responsible for the review, approval, and labeling of all new genetic tests that moved beyond the basic research phase, using a novel, streamlined process. The Committee also recommended that CLIA be augmented with specific provisions to ensure the quality of laboratories conducting genetic tests, that data collection efforts continue after genetic tests reached the market, and that CDC coordinate public/private sector

collaboration. Dr. Williams pointed out the similarity of these issues with those represented in the Secretary's charge.

In January 2001, HHS responded to the SACGT report. They accepted the recommendations and indicated that the following actions would be implemented over time as resources allowed: FDA oversight of genetic tests to include laboratory developed tests (LDTs) and genetic test kits, postmarket data collection by CDC (possibly to be required of test developers and other payers), and CMS development of new CLIA regulations for expanded oversight of genetic testing laboratories. However, between 2001 and 2007, several factors affected that response. Questions were raised about FDA's authority to regulate LDTs. FDA issued a guidance stating that it had regulatory authority over the analyte specific reagents (ASRs) that are sometimes used in the development of LDTs. Another guidance stated that FDA had review requirements for laboratory developed *in vitro* diagnostic multivariate index assays (IVDMIAs).

In addition, the plans of CMS significantly changed in 2006. The agency halted a Notice of Proposed Rulemaking (NPRM) for CLIA, indicating that CLIA already certifies genetic testing laboratories and if new standards were developed, they would become outdated before publication because of the rapid changes within this specialty. CMS also stated that a genetic testing specialty would not solve the gap in clinical validation of LDTs and would not address concerns about the lack of proficiency testing and the lack of data on unique problems with genetic testing laboratories. In lieu of developing a genetic testing specialty, CMS planned to provide CMS surveyors with expert guidance to assess genetic testing laboratories; develop alternative proficiency testing mechanisms, for example, interlaboratory comparisons; develop educational materials; maximize the expertise of accreditation organizations; seek guidance from FDA and CDC on review of complex and analytical test validations; and collect data on genetic testing laboratory performance.

In March 2007, SACGHS received the Secretary's charge and created the Oversight Task Force. During six meetings of the full Task Force via teleconference, the report outline and scope were developed. The Steering Group (i.e., the five SACGHS members on the Task Force) met periodically by phone to address broad issues. Teams were assigned to develop each chapter, meeting as needed to refine their drafts. The focus of the work was to identify gaps in knowledge and discuss actual and potential harms, so that recommendations to address problems in oversight could be developed.

Dr. Williams described the content of each chapter of the report. Chapter 1 provided the background and scope of the report, the balance of harms and benefits of genetic testing, and an overview of the report. It acknowledged genetic exceptionalism as a social and policy reality. Chapter 2 described current and future trends in laboratory technology. Chapter 3 focused on analytic validity, proficiency testing, and clinical validity. Chapter 4 addressed the challenges inherent in clinical utility, which is not subject to regulation, and the importance of evidence development. Chapter 5 focused on effective communication in the pre- and post-analytic phases of testing and clinical decision support for patients and providers, which must incorporate evidence-based clinical guidelines. Chapter 6, which was not yet developed, was to provide a summary of recommendations.

The Task Force planned to develop recommendations based on the meeting held the previous day. The recommendations would initially be developed by the chapter teams and would be sent to the Steering Group for review. The Task Force planned to develop the second draft of the report between July and September of 2007, and to hold a second face-to-face meeting on September 5. Input from key stakeholders would be sought and incorporated, after which a draft report would be sent to SACGHS

members prior to the November 19-20 SACGHS meeting. From November 21-30, SACGHS comments would be incorporated and the draft would be prepared for public comment. The public comment period was scheduled for December 3, 2007, through January 7, 2008. Public comments would be analyzed in January. At the February 2008 SACGHS meeting, the Committee would have the opportunity to discuss the comments received, propose revisions to the report, and approve a draft for submission to the Office of the Secretary (OS). Edits resulting from the meeting would be incorporated and the penultimate draft would be submitted to OS. In March, the final report would be edited and published, with a final review by SACGHS taking place via email on April 16. Formal submission to the Secretary is planned for April 30, 2008. Dr. Williams asked the Committee if the Task Force's approach to the organization and scope of the report appropriately reflected the Secretary's charge.

Dr. Tuckson, Dr. Julio Licinio, and Dr. Barbara Burns McGrath stated that the report was well done, comprehensive, and had an appropriate scope. The full Committee agreed. Dr. Tuckson commented on the importance of ongoing communication with the Certification Commission for Health Information Technology (CCHIT), which is part of the America's Health Information Community (AHIC). The goal of CCHIT is the certification of electronic medical records, which overlaps with the oversight report in the area of evidence-based decision support. Dr. Michael Amos commented that the National Institute for Standards and Technology (NIST) and AHIC were working together closely to develop standards for interoperability and intercommunication among all electronic health record systems.

Dr. Tuckson commended the Task Force on their work and asked that SACGHS receive intermittent updates on the status of the report prior to the November 2007 meeting. He turned the floor over to Dr. Jim Evans, who led the session on gene patents and licensing practices, which included a roundtable on international patenting and licensing practices and a presentation on pending legislation in the United States.

Session on Gene Patents and Licensing Practices

Overview of Session
Jim Evans, M.D., Ph.D.
SACGHS Gene Patents and Licensing Task Force Chair

Dr. Evans provided an overview of the session's goals. He commented on recent public attention to the issue of gene patenting and noted that both chambers of Congress were working on patent reform legislation. He said SACGHS prioritized the issue of gene patents and licensing practices as a priority issue in 2004, but since the National Academy of Sciences (NAS) was in the process of formulating a report on the subject, the Committee deferred its efforts until the report was published. In the fall of 2005, a group of SACGHS members reviewed the NAS report and found that the report was heavily focused on issues of research, but did not fully address the issue of patient access to patented genetic tests.

In June 2006, the Committee held an informational session and decided to move forward with an in-depth study that would focus on the effects of gene patenting and licensing practices on patient access to genetic tests. The Task Force on Gene Patents and Licensing Practices and Patient Access to Genetic Tests was established, which refined the proposed scope for the study and outlined a work plan. In the spring of 2007, the Duke University Center for Genome Ethics, Law, and Policy (GELP) agreed to assist the Task Force. At the March 2007 SACGHS meeting, the Committee received a primer on gene patents and licensing that provided the background necessary to understand key issues. In May 2007, the Task Force discussed next steps and planned the international roundtable so that the Committee could learn about the

impact of gene patents and licensing practices in other countries, and strategies employed to minimize adverse effects to patient access.

Dr. Evans presented the study's scope, which included an evaluation of the positive and the negative effects of current gene patenting and licensing practices on patient access to genetic technologies in the United States. The focus would be on gene patents for health-related tests (e.g., diagnostic tests, predictive tests, other clinical purposes). Dr. Evans explained the Task Force's use of the terms "clinical access" and "patient access." He said that clinical access referred specifically to the ability of physicians to order genetic tests. Dr. Evans noted that the scope would also consider the effects of gene patenting and licensing practices on translational research, i.e., moving technologies into the clinical arena.

Dr. Evans described the three components of the study plan, which would take place in parallel. Part 1 consisted of data gathering and analysis through a literature review, expert consultations, case studies, and possibly, additional research. This effort was spearheaded by the Duke team. Part 2 would involve gathering public perspectives. Part 3 focused on obtaining international perspectives, which would be accomplished through the day's roundtable. The information gathered from these three study components would be analyzed and synthesized to create a draft report that would be released for public comment and lead to a final report to the Secretary. Dr. Evans introduced the members of the Duke team that were present: Dr. Bob Cook-Deegan, Mr. Ashton Powell, Dr. Subhashini Chandrasekharan, Ms. Deidre Parsons, Ms. Lee Hong, Ms. Catherine Colaianni, Dr.Carla Rydholm, Ms. Swathi Padmanabhan, Ms. Shreya Prasad, and Ms. Elana Berger.

Dr. Evans introduced the presenters and moderated the roundtable discussions.

Update on U.S. Patent Reform Initiatives
Judge Pauline Newman
Circuit Judge, U.S. Court of Appeals for the Federal Circuit

Judge Newman presented arguments in favor of and arguments against pending legislative proposals that related to the health of the patent system: H.R.1908 and S.1145 (based on Senator Leahy's "Manager's Amendment" of June 2007). She stated that the purpose of patent law is to bring technology to the public, not to withhold it or create artificial barriers to its utilization. Judge Newman noted the strong lobbying efforts by numerous parties with interests in the patent system. She said the software industry was trying to weaken the patent system, and their efforts were being opposed by the university community and pharmaceutical, biotechnology, and other industry groups.

Judge Newman described two significant changes proposed in the Leahy amendment that would affect technical aspects of patent law. The first was a move from the "first-to-invent" system to the "first inventor-to-file" system. Currently, if there are competing patent applications for authentic, concurrent inventions by different people, the Patent Office runs an interference proceeding to determine who the first inventor is, and that person receives the patent. The legislation would change this system so that the first person to file with the Patent Office would receive the patent. A safeguard would remain in place so that the person who lost the race to the Patent Office could claim that the other party stole the invention, i.e., "derived" it. Arguments in favor of this change are that 1) the rest of the world has a first-to-file system, so the change would move in the direction of a unified, multinational approach; 2) most entities already operate according to a first-to-file system to protect their patents internationally; 3) less than 1 percent of patents have the kind of conflicts that warrant expensive interference proceedings, and in most

cases, the first party to file usually prevails; and 4) the first party to file approach provides certainty to applicants that a later filer will not establish an earlier invention date.

Arguments against the first-to-file system include concerns about creating a premature race to patent before inventions were adequately proven. Such races would divert financial resources away from research and development and into legal services for filing before the value of the invention was fully known, which smaller entities would not be able to afford. Although a 1-year grace period is currently included in the legislation, many universities also want a grace period that allows university researchers to publish their findings prior to patent filing. Judge Newman stated that, at one time, small business groups opposed changing to the first-to-file system, but dropped their opposition because of their interest in international activities.

Judge Newman described a second issue related to post-grant cancellation proceedings, which she called the "second window." The "first window" after a patent is granted is a 1-year period of time during which a post-grant cancellation proceeding can be conducted for any reason. In other countries, this is called an opposition proceeding. A second window would be an administrative proceeding that could declare a patent invalid without litigation. An infringement claim could be submitted to the Patent Office at any time and the public would be able to submit information to the patent examination process that examiners had not previously or adequately considered. Judge Newman noted PTO's challenge in recruiting sufficiently qualified patent examiners to handle the many emerging changes in technology. She said there are too few experienced examiners in the Patent Office, which could lead to mistakes in the granting of patents.

Arguments in favor of a second window include the fact that litigation is expensive and burdensome for both sides, the idea that the year-long first window is too short, and that second-window proceedings would usually be conducted in the context of a charge of infringement, which would likely achieve the correct result as to validity. If the patent claim were sustained in such a proceeding, it could not be challenged again in court.

There are several arguments against a second window, including claims that patents that are successfully challenged are usually those for which the invention has been developed, commercialized, and proven profitable. A second window could tempt opportunistic attacks to gain a share of the profits. The process could also change the landscape of licensing negotiations, because the patentee would, by definition, be in a weaker position as a matter of law, even though the specifics of an invention had not been investigated. Critics say the potential abuses in this situation could outweigh the advantages. They state that, to acquire risk capital, as well as other capital investment, there must be a reliable patent. A second window would allow for judicial review of patent validity. The "Big 10" universities took a strong position on this issue, stating that if patents are to have value to investors, there must be some finality to the administrative process. The absence of a second window does not prevent the challenge of a patent in court. Judge Newman noted that a 1-year opposition period (first window) has usually proven sufficient in other countries.

Dr. Evans asked Judge Newman if there are remedies that could be brought to bear on different aspects of patent practice that would mitigate some of the bluntness of patent law. She replied that, based on arguments made by the software industry, it would be appropriate to think about whether the rules should be modified in cases where the patentee has not made a commercial investment. This principle could apply to scientists in universities seeking to license their inventions with no intention of developing and exploiting them. Judge Newman said that a strengthened role for licensing entities was under

consideration because of a recent Supreme Court decision stating that a licensee can challenge a patent at any time. The balance of the negotiations shifts for scientists and their supporters in universities when their interest is in licensing for the purpose of moving a scientific development into public use, not just to provide a financial return to the university. She was not sure whether such a shift creates a disadvantage. If incremental steps are no longer viewed favorably by decisionmakers in patenting, Judge Newman questioned the effect on the development of the science, its movement to the laboratory bench, and into public use. She was concerned that new discoveries might never reach the clinic. Dr. Evans noted that the imperative to the Committee with regard to diagnostic and predictive tests was to develop recommendations concerning patient access and public health, not just commerce.

International Roundtable on Gene Patents and Licensing Practices

Dr. Evans introduced the international roundtable by stating that the purpose of the session was to gather background information on the gene patenting and licensing practices of other countries. Information would be presented to the Committee that would compare and contrast the enforcement of intellectual property rights for patented genes in the U.S. and in countries with government-sponsored healthcare systems. The processes used by international groups to develop reports and recommendations on gene patents and licensing strategies would also be explored.

Overview of the International Gene Patents and Licensing Practices Landscape

Richard Gold, S.J.D., LL.M., LL.B.
Director, Centre for Intellectual Property Policy
McGill University, Montreal

Dr. Gold is an expert in law, technology, commerce, and ethics and principal investigator of the Intellectual Property Modeling Group, a transdisciplinary research team investigating intellectual property regimes. He joined the meeting via telephone from Geneva.

Dr. Gold stated that the international patent debate began in the U.S. with the patenting of biotechnological inventions in 1980. Other patent offices in developed nations followed suit. In 1982 and 1985, the Organisation for Economic Cooperation and Development (OECD) published studies concluding that only the U.S. and Japan had laws that sufficiently addressed biotechnological inventions. In 1983, the World International Property Organization (WIPO) Group of Experts called for international harmonization of laws concerning biotechnology.

The European Commission issued a white paper in 1985 stating its intention to act in the area of biotechnology, and in 1988, introduced a draft directive that dealt with the legal protection of biotechnological inventions. The Commission's view was that the directive merely clarified existing patent law in Europe, stating that biotechnology (including genes) was patentable. They were surprised by the negative reactions received from religious and ethics communities, which actively joined in the debate. The European Parliament defeated the Commission’s draft directive in 1995. The Commission introduced a new version of the directive in late 1995 that recognized the ethical issues inherent in human gene patents, including the concept of owning life.

In July 1998, both the European Parliament and the Council passed the directive, with several amendments targeted at ethics, including a clause dealing with exceptions for patentability when moral problems arise. The final version of the directive has some ambiguous language. Although Article 3.2 calls for the patentability of all artificial or isolated biotechnological material, Article 5, which relates to

gene patents, introduced some contradictions. The first section of Article 5 states that the human body, at various stages of formation, is not patentable, including the simple discovery of one of its elements. This seems to imply that genes cannot be patented. However, the second article says that an element taken out of the human body and isolated, or created artificially through a technical process, can be patentable, even if the structure is identical to that found in nature. Dr. Gold said there seemed to be a contradiction between these two articles. He noted that the third section of Article 5 states that the industrial application of a sequence or a partial sequence of a gene (which is roughly equivalent to the utility standard in the U.S.) must be disclosed in the patent application.

Dr. Gold explained that there is a dual system for patents in Europe. Most countries issue their own patents if they are filed locally. However, the European Patent Convention is used more often. Although the European Patent Convention and the European Patent Office include most of the same states, they are not part of the European Union (EU). To achieve an alignment between the directive's statements about patentability of biotechnology and knowledge that includes patents, a corresponding change was needed to the European Patent Convention. Some countries opposed this change. It was brought in through a regulation stating that it only clarified existing law, because a regulation requires a lesser majority to approve. The directive also called for the creation of an ethics committee to report back on programs every 5 years.

At about the same time, a patent for a specific gene was rejected in the Opposition Division based on a lack of industrial application. During this procedure it was stated that, for a gene to be patentable, the application cannot be purely speculative or hypothetical concerning the function of the gene. They developed the criteria that the application must be specific, concrete, and credible, which corresponds to the utility standard in the U.S. Therefore, formal patent law in Europe and the United States were beginning to align. Both were advancing at about the same pace and coming to similar conclusions. One exception between the two systems is Europe's fairly restrictive approach to the patenting of stem cells.

Dr. Gold discussed patent law in Canada, where there is no specific legislation on gene patents. However, in 2004, the Supreme Court of Canada made a definitive statement in a decision between Monsanto and a farmer, which had to do with genetically modified canola. The canola seeds spread onto the farmer's land and he was sued for patent infringement. The patents in that case were on the genes and the cells containing the genes. There was no patent issued on the plant, because Canada does not issue patents on whole plants or whole animals. The Supreme Court ruled that gene patents are valid and a patented gene gives rights over an entire organism.

The law in Brazil is ambiguous about whether patents can be granted for genes, because the Patent Office has never been challenged on its position. China permits gene patents, and some Chinese government-owned companies have large financial stakes in them. In 2005, India reformed its Patent Act to be in compliance with the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement, and India now permits gene patents. Gene patenting in developing countries is fairly low. Broad gene patenting generally does not occur in countries lacking a fairly significant scientific infrastructure.

Dr. Gold stated that although there has been some international alignment of rules about gene patenting, conflicting policy responses have been issued. A 2002 statement by the Canadian House of Commons Standing Committee on Health said that patents issued on DNA sequences were repugnant, and the legislators did not seem to realize these patents existed. In 2004, the National Research Council, which has a mandate to conduct research in the interest of Canadians, publicly recognized that patents are important to innovation. While the European Parliament passed a directive that seemed to support the

patenting of human genes, in 2001, the European Parliament indicated that gene patents should not be issued. These contradictions suggest an unsettled public policy situation with concerns similar to those in the U.S., including ethical questions about owning life, how gene patents affect research, and patent criteria.

Dr. Gold said the biggest differences lie in the area of public health care. Since most OECD countries have a public health care system, the strongest voices trying to effect change are the health departments responsible for service delivery. They are concerned about the effects of gene patents on research and on the delivery of health care. Representatives of these departments raised the issue as a general matter, and governments or institutions within various countries conducted analyses. The Australian Law Reform Commission was mandated by the government to look at the issue of gene patents. The Canadian Biotechnology Advisory Committee, on a joint mandate from Health Canada and Industry Canada, was asked to examine the implications of gene patents on research and health care delivery. The World Health Organization (WHO) looked at questions of access related to the effect of gene patents. The 2002 Nuffield Council also studied the policy issues associated with the patenting of genes.

The general conclusion of these studies was that gene patents should be allowed, but should be well managed. Many discussions took place about levers that could be provided to health administrators that would give them the power to control the introduction of new medicines. There was little appetite for patent reform, either in the reports or by the governments. The differences focused on specific issues. In Europe, there was an effort to fight Myriad's patents for the familial breast cancer genes, BRCA1 and BRCA2, through the opposition process and most of the Myriad patents were invalidated at the initial opposition stage. In Canada, the response was to ignore the Myriad patents on the basis that they might not be valid or might not apply. Generally, no payments are made to Myriad and no licenses exist in Canada, with the exception of Quebec.

Other responses at the international level shifted the focus from changes in patent law to changes in practice. They aimed at moving beyond the Myriad debate to consider the ways in which gene patents differ from other patents. There was a general view that, even though the law does not require it, it is preferable for gene patents to be nonexclusively licensed, although exclusive licenses might be justified in certain circumstances. For example, the feeling was that there should be accommodations for health care providers so they can control the availability of treatment, which would mean having local licensees. Many of the concerns at the international level were similar to those in the United States, e.g., researcher access, follow-on research, and the development of alternative clinical therapies or diagnostic kits. The primary difference was found in the public health care setting, where authorities were concerned about the roll-out of genetic testing for several reasons. Public authorities wanted the ability to conduct technology assessments and control which technologies were introduced, how and to whom they were introduced, and the services offered in relation to new technologies. During actual health care delivery, there were several points at which a patent owner could intervene in these types of decisions, which was a major concern in most countries.

The most significant concern was related to the business models used to provide genetic services. Health care administrators felt that the business model used for genetics did not provide enough flexibility to the public health care system and that traditional models of technology dissemination do not work in these settings. Patent law was viewed as not having sufficient levers to discipline the market to provide better models. Since the governments have very little bargaining power in these situations, their only recourse is to ignore the patents.

Dr. Gold discussed the lessons learned from the international analyses. He stated that the polarization of views internationally is similar to that in the United States. On one hand, there are those who believe that gene patents create a technical issue having to do solely with private sector incentives to innovation. On the other hand, there are those who believe gene patents raise fundamental ethical and religious questions. Both internationally and in the U.S., there are concerns about the effects of gene patents on research and relatively little concern about developing countries, as there is no evidence of significant gene patents in developing countries.

Internationally, the primary concern is the effect on public health care administration. The belief is that licensing practices are part of the solution, but not the entire solution. Europe and Canada have made advances chiefly by refusing to respect patents that are exercised in a manner they find unsuitable. Dr. Gold concluded by stating that the U.S. debate is more limited because the issue of public health care systems does not come into play. However, no country has found a stable solution. There is a standoff internationally and a lack of willingness to undertake even modest patent reforms that would provide policy levers for health care administrators.

BRCA Testing in the United Kingdom
Shobita Parthasarathy, Ph.D.
Assistant Professor, Public Policy
Gerald R. Ford School of Public Policy
University of Michigan

Dr. Parthasarathy conducts research on the politics of science and technology in the U.S. and abroad. She authored the book, "Building Genetic Medicine: Breast Cancer, Technology, and the Comparative Politics of Health Care."

Dr. Parthasarathy said she would address the Myriad Genetics case, as well as the comparative politics of biotechnology patenting in the U.S. and Europe. She reviewed the history of the discovery and patenting of the BRCA genes. BRCA1, a breast cancer gene, was discovered by Myriad Genetics in Utah in September 1994. In December 1995, a United Kingdom Cancer Research Campaign-funded group in London announced the discovery of BRCA2. Myriad disputed this, and both Myriad Genetics and the U.K. group applied for multiple patents at the U.S. Patent and Trademark Office (USPTO) and at the European Patent Office (EPO). The U.K. group filed for a defensive patent and stated that they wanted to ensure that Myriad would not have a monopoly on the fate of the breast cancer gene patent and the related genetic test. The British group licensed the patent to the American company Oncormed, which had applied for patents on a different consensus sequence of the BRCA1 gene. Several conditions were part of this licensing agreement: the British National Health Service (NHS) received free access so that the license would not impinge on the development of NHS testing systems, the NHS required that the patent be sublicensed to avoid a monopoly, and guidelines for genetic counseling were established.

From 1996 to 1998 in the U.S., a competitive environment emerged among four major providers (the Genetics and IVF Institute, the University of Pennsylvania, Oncormed, and Myriad Genetics) that offered testing for the full gene sequences of the BRCA1 and BRCA2 genes. Some offered mutation testing through the Ashkenazi Jewish panel. Myriad Genetics used its legal position and strong economic resources to shut down the other three testing services.

In the U.S., Myriad Genetics' testing system uses a straightforward commercialization of their patented technologies, offering a state-of-the-art laboratory service. Their focus is on DNA analysis. Genetic

counseling is not required. The test can be offered through any physician and is marketed widely to primary care physicians. Risk and disease management options for those testing positive are often defined by the mutation status. The drug tamoxifen was accepted by Myriad as a treatment option. Dr. Parthasarathy noted that full sequence analysis of both breast cancer genes costs approximately $3,000. Although it is reimbursable through insurance, many women choose to pay for the test out of pocket to avoid possible employment discrimination.

In the British system, all genetic testing is offered through the NHS because, to date, there are no private genetics clinics. Laboratory and clinical services are combined, often in hospitals, and NHS controls all genetics activities because they fund the services. Each local NHS region has a genetics clinic and most provide BRCA testing services. The extent to which the national NHS administration and the regional administrations control health policy and access often differs according to the service.

Dr. Parthasarathy stated that there are many similarities in patent policies among the U.K., European, and U.S. systems. One exception is the response to Myriad Genetics' BRCA1 and BRCA2 patents. The EU Biotech Patent Directive was introduced in 1988, but the public controversy became more widespread in the mid- to late 1990s, at the same time that Myriad Genetics' patents became an issue. General controversies also arose concerning other aspects of biotechnology patents.

In the early days of the NHS BRCA testing system, patent holders were not involved and Myriad Genetics was not in Britain. However, before too long, a group of health care professionals, patient advocates, scientists, and government officials attempted to create a national risk assessment and triage system dictating how genetic testing for breast cancer would be offered throughout the country. There was a strong focus on "getting it right," because BRCA testing was the first major genetic test for a common disease and it had the potential to become a model for other genetic tests that would follow. They created a risk stratification system based on family history information. Individuals have their family histories taken by primary or secondary care physicians and, based on that information, are classified into three categories: low, moderate, or high risk. Low-risk individuals are deemed not likely to have a gene mutation and receive no further attention. Individuals at moderate and high risk are offered access to a tertiary care center, i.e., the regional genetics clinic. Only individuals deemed high risk are offered access to testing and genetic counseling; moderate-risk individuals receive increased surveillance through annual mammograms and genetic counseling. Dr. Parthasarathy said the focus of the system is a broad public health approach: standardizing clinical care by identifying and managing individuals at risk according to family history. DNA analysis is an additional tool, rather than the focus of the system. She noted that tamoxifen is not approved in the U.K. or in the rest of Europe for women with BRCA mutations. It is considered unproven and has long-term adverse effects. In Britain's system, the client has a limited ability to demand access to services because the doctors and the NHS make decisions about access. However, the patient could pay for their own testing in the U.S. or in another European country.

In the late 1990s and early 2000s, Myriad Genetics, anticipating that their EPO patents would be issued, tried to shut down British services or force the NHS to pay royalties to the company. A vigorous opposition erupted among patient advocates, scientists, and health care professionals. They questioned the legitimacy of Myriad Genetics' patent rights, as well as the accuracy of the test and their focus on clinical care. Some of this opposition had already been mobilized in response to the EU directive and these groups worked together to take on Myriad Genetics. A temporary resolution was reached when Myriad opened a U.K. satellite laboratory, Rosgen, which offered free access to Myriad's services. NHS services were not affected; Rosgen provided an additional resource. Rosgen allowed access to their test only if people

received specialized genetic counseling first. Rosgen eventually liquidated for reasons unrelated to Myriad Genetics.

At this time, a number of scientists, health care professionals, governments, and patients in Europe formed a pan-European coalition to oppose Myriad's patent at the EPO. The Institute Curie, a scientific organization in Paris, took the lead in organizing 28 groups. Participants included 11 human genetics societies, 4 clinical genetics centers, 3 government health ministries, the European Parliament, 3 patient groups, a Swiss political party, and Greenpeace. Dr. Parthasarathy noted that the opposition mechanism provides an opportunity, within 9 months of a patent's issue, for any third party to challenge a patent. It is an important part of the patent process in Europe because it often narrows overly broad patents. The Myriad opponents were successful in having two of the patents revoked entirely and one narrowed significantly. Myriad Genetics now holds a patent on two BRCA gene mutations, but the decision is under appeal. Dr. Parthasarathy concluded by stating that health departments in Europe have played an important role in shaping the way gene patents are addressed.

BRCA Testing in Canada
Richard Gold, S.J.D., LL.M., LL.B.
Director, Centre for Intellectual Property Policy
McGill University, Montreal

Dr. Gold stated that he was an advisor to the Ontario government on the BRCA issue. He said the literature is missing the perspectives of some actors, including policymakers and Myriad Genetics. Therefore, a group discussion was held with some of those involved in or affected by the Myriad Genetics situation. Participants included Canadian government officials, a researcher in France who was advising the Institute Curie, and Dr. Robert Cook-Deegan's group from Duke University. He reported on the results of this investigation, listing three major problems: a lack of communication by Myriad Genetics and by the governments, a lack of trust on both sides, and institutional failure, primarily on the governmental side.

Dr. Gold focused on events in Canada. In 2000, Myriad Genetics and MDS Laboratories entered into a distribution agreement. MDS provided diagnostic laboratory services to various Canadian governments in the provinces and their largest client was the Ontario government. Dr. Gold noted that at the time, budget cutbacks were taking place in the provincial governments' health care systems and they were not adding new services to the list of those covered by public health care insurance, but they did allow private sector providers to offer some of the services that fell outside of their coverage. MDS saw their niche as finding and offering new, high-quality technologies that were not broadly available through the public system.

After MDS and Myriad Genetics signed the agreement, the policy unit in the Ontario health ministry was asked by the government procurement department to consider the right way to handle genetic technology services. The policy unit did not have a framework to address these questions and communication with Myriad Genetics halted. In May and June 2001, Myriad issued cease and desist letters to four provinces, including Ontario, stating that the government was funding laboratory services that violated their patent. In August 2001, the government of Ontario stated that there was no infringement of a valid patent. The presidents of Myriad Genetics and MDS Laboratories asked for a meeting with the Minister of Health, which took place in November 2001. Myriad Genetics and MDS Laboratories presented the Minister with 100 letters from scientists, one from U.S. Senator Orrin Hatch, and one from the American ambassador, stating that Canada was in violation of its trade agreements and the matter might be referred to the U.S. trade representative. This was seen by the Canadian government as exceedingly hostile. Dr. Gold

surmised that because the principle of a public health care system was considered paramount by the ministry, the Canadian government did not want to yield to a private U.S. company. Myriad Genetics made some strategic mistakes by raising the stakes and threatening trade sanctions.
In 2001, the Minister held a policy forum involving members of the public, academia, government, and industry. This meeting led to a seven-chapter report on genetic tests in January 2002, which was developed by the Ontario government. It described the challenges of coordinating technology assessments across Canada and coordinating the provision of services. One chapter dealt with intellectual property and stated that Canada needed policy levers to resist what was viewed as hostile maneuvering by Myriad Genetics. The Ontario government saw Myriad Genetics as having a one-size-fits-all approach to licensing that was not well integrated into the provincial health care systems and did not take into account the need for genetic counseling. All the provincial governments supported the Ontario report, including Quebec.

In response, the Biotechnology Industry Organization (BIO) intervened on behalf of Myriad Genetics and threatened to boycott the BIO 2002 General Meeting in Toronto. Myriad Genetics, with strong American political connections, also expected Ontario to bend. Ontario started a policy process in the provinces. Health Canada, which is responsible for the federal part of the health care system, participated. They also engaged in direct conversation with the unit in Industry Canada that was responsible for the Patent Act because they needed a policy lever to use as a threat. However, in the spring of 2003, the emphasis of the policy unit on gene patents waned because of the SARS crisis in Toronto. In October 2003, the government of Ontario changed and the new government did not see the Myriad Genetics controversy as a priority. In the fall of 2004, the matter was referred to the Canadian Biotech Advisory Committee (CBAC), which issues reports on biotechnology. In 2006, CBAC issued a report saying that gene patents were acceptable, but there must be policy levers within the Patent Act.

Dr. Gold explained how this series of events was seen by various actors. It was his opinion that Myriad Genetics entered the Canadian and European markets with the mistaken belief that these environments would be similar to the U.S. and without a full understanding of the public health care systems. Dr. Gold said Myriad Genetics was still operating under a deficit in the U.S. and was very short-staffed. Myriad Genetics maintained the exclusive license for the expensive proband testing (costing approximately $3000) and out-licensed the less expensive follow-on mutation testing (costing approximately $300). Because fewer family members than expected wanted follow-on testing, Myriad made much less money than anticipated.

Myriad Genetics claims they had a very broad view of research, i.e., scientists did not need to go to the company for a license to conduct research. They say that research includes the provision of genetic tests if conducted by the researchers, however, they did not want to outsource the proband or other testing for non-research purposes. Therefore, the University of Pennsylvania was accused by Myriad Genetics of infringement because of its outsourcing to academics in other departments and to others involved in commercial activity. The university viewed the outsourcing as legitimate under the research exemption, but Myriad Genetics disagreed.

Dr. Gold noted that Myriad Genetics contributed all of its mutation data to the Breast Cancer Information Core Database. The company said it was in their interest for other people to contribute as well, because more information would improve the test. Their only concern was whether large operations were outsourcing this information.

Dr. Gold said Myriad Genetics' international business model attempted to replicate the U.S. model, i.e., find local licensees who would provide mutation testing and send the proband testing back to the U.S. However, this model did not work in other countries. Public health authorities did not like the model because there was no ability to manage the health care system. In France, it is illegal to export blood samples. Also, Myriad Genetics never made a public proclamation that they would not prosecute the research community. There was also a great deal of ill will and a lack of trust because of previous patent battles.

Dr. Gold summarized the failures in the Myriad situation. There were several communication problems. Myriad Genetics interpreted the government's slow reaction as a refusal to accept their patents. The government viewed Myriad Genetics' quick escalation as an unwillingness to negotiate. Myriad Genetics missed the signal sent in Europe by the launch of the opposition. The opposition procedure in France was intended as a starting point for negotiations, with the goal of finding a solution for both sides. However, Myriad Genetics was not well advised and missed the opportunity France offered them. As a result, Myriad Genetics developed a poor reputation in the scientific community.

In terms of institutional difficulties, there was a lack of understanding by Myriad Genetics that the public and private sectors in other countries work in different time frames. Industry groups shunned Myriad Genetics instead of trying to mediate a solution. There was no governmental department that had the jurisdiction or the willingness to mediate the situation. Each side stood their ground and no one was willing to compromise.

Dr. Gold concluded that better communication would have solved many of these problems. An honest broker might have been able to instill trust between negotiating parties. He said the industry needs new business models for genetic testing services or they will not work, especially in a public health care system. In addition, new tools are needed for technology assessment and better integration into the health care system.

Q&A

Dr. Gurvaneet Randhawa asked how a public sector system can have leverage concerning the licensing or patenting of a gene that is linked to a disease or leads to an intervention that can improve public health. Dr. Parthasarathy stated that under the Bayh-Dole Act, if the government funds university research and a patentable invention results, the government does not get involved. She said that in the case of Myriad Genetics, researchers from the National Institute for Environmental Health Sciences (NIEHS) were involved in the initial BRCA1 research and NIH insisted that their inventors be put on the patent. Myriad Genetics put two individuals from NIEHS on the patent, but they had not received much compensation in the form of royalties. The extent to which NIEHS would have standing to influence how the patent was being used and licensed was not clear. Dr. Gold said there is no equivalent to Bayh-Dole in Canada. Each university develops its own set of rules in negotiation with its researchers. Ownership can be by the university, the researcher, or some combination. The federal government has no say and there are no march-in rights.

Dr. Debra Leonard asked Dr. Gold to expand on his point that licensing practices are not sufficient to protect gene patents for health care use. He replied that licensing guidelines are beneficial if people follow them, act reasonably, and communicate well. However, that is not always the case. Therefore, the policy units in Canada want targeted changes to patent law that would give them leverage in negotiations. Researchers wanted broad research exemptions that would allow them to proceed without fear of being

sued. Dr. Gold said the most effective policy levers should pose a real threat, but should never have to be invoked. Licensing guidelines are more likely to have an effect if the government knows it has leverage if things go wrong.

Dr. Tuckson asked how the rules apply to companies that operate internationally. Does trade rely on international politics between countries and pressure by the country of origin? Dr. Gold said that in some cases, ambassadors are brought into the process if there is a lack of compliance. He noted that U.S. companies do not seem to understand the public health care systems in other countries, e.g., Europe, Canada, and Australia.

Dr. Tuckson thanked the speakers and introduced the public comment session.

Public Comment

Amy Miller
Public Policy Director
Personalized Medicine Coalition

Dr. Miller said the Personalized Medicine Coalition (PMC) represents academic, industrial, patient, provider, and payer groups that seek to advance the understanding and adoption of personalized medicine for the benefit of patients. Her comments focused on issues addressed in the SACGHS draft report on pharmacogenomics (PGx). The PMC believes that business incentives for pharmacogenomic products are needed and they are creating a list of incentives to advance PGx. The PMC is also developing a privately funded medical education program on PGx to address gaps in genetics education and lists of payer principles for reimbursement of PGx products. Ms. Miller noted that the SACGHS report suggested reimbursement of prevention services as a Medicare benefit, and the PMC was in support of this idea. Dr. Kevin FitzGerald asked Ms. Miller to provide the PGx Task Force with the list of incentives for pharmacogenomic products when it was completed.

Chris Colwell
BIO
Biotechnology Industry Organization

Ms. Colwell stated that BIO represents more than 1,100 biotechnology companies, academic institutions, and State biotechnology centers. They deal with health care, environmental, agricultural, and industrial companies, including a large number of companies that are heavily invested in research and commercialization activities and pharmacogenomics research tools and molecular diagnostics. Ms. Colwell stated that intellectual property protection is essential to the success of biotechnology companies, as patents provide the necessary insurance for investors so that new processes can be developed. She commented on the SACGHS PGx report, recommending a more comprehensive discussion of the economic factors surrounding pharmacogenomics, particularly reimbursement policies. BIO believes the report should indicate where enhanced congressional appropriations would be required to implement the recommended initiatives, since funding for NIH has failed to keep pace with biomedical research inflation. BIO and a number of other stakeholders were supporting an increase in NIH funding of up to $30.8 billion for FY 2008. Dr. FitzGerald asked Ms. Colwell to provide more information on BIO's views on reimbursement policies.

Catherine Wicklund
President, National Society of Genetic Counselors (NSGC)

Ms. Wicklund stated that NSGC represents over 2,000 genetic counselors that practice in a variety of medical specialties, academia, research, public policy, and biotechnology, and they advocate for the profession. She stated that access to quality genetic tests and services is extremely important. As genetic counselors often explain the benefits and limitations of genetic testing to patients, they must discuss test inaccuracy or misinterpretation. NSGC therefore applauded the Committee's efforts to improve regulation that ensures the analytic and clinical validity of genetic tests. NSGC believes that it is important that there is pre- and post-test consumer education and counseling provided by properly qualified individuals who can conduct proper evaluation of family history, order appropriate tests, and accurately interpret results. For this reason, it is imperative that non-genetic health care professionals have at least a minimum level of genetics competence and collaborate with genetic specialists when appropriate. NSGC also thinks it is critical to assess and satisfy consumers' needs for information that will empower them in making decisions about testing. The organization offered to collaborate with SACGHS to develop guidelines in this area for the Secretary.

Concerning coverage of and access to genetic services, NSGC is pursuing the recommendations outlined in the February 2006 SACGHS report. They prioritized efforts to improve consumer access to genetic counselors. NSGC has been successful in enacting licensure bills in several States and is working with policymakers in Congress to recognize genetic counselors as CMS providers under Medicare.

Dr. Tuckson thanked Ms. Wicklund for her comments, and urged genetic counselor organizations to come together to resolve differences of opinion. The Committee had heard varying viewpoints from several organizations.

Sharon Terry
Coalition for 21st Century Medicine

Ms. Terry said the Coalition for 21st Century Medicine represents innovative diagnostic companies, clinical laboratories, policymakers, researchers, physicians, venture capitalists, and more than 30 patient advocacy groups, including the Genetic Alliance. It believes that access to advanced diagnostic products and services is vital to the future quality and affordability of personalized health care. The Coalition shares HHS's focus on personalized medicine and the Congress and FDA's goals of assuring that treating physicians and their patients have access to safe, accurate, and reliable information. Ms. Terry said the Coalition was looking forward to FDA reissuing draft guidances for IVDMIAs and ASRs to allow all interested stakeholders an opportunity to review and comment on the documents. She said they met privately with FDA leadership in December 2006 and May 2007 to provide comments. The Coalition expressed concern that, if implemented in their current form, the draft guidances for IVDMIAs and ASRs could result in adverse, unintended consequences. Ms. Terry said Congressional action and the resulting novel or substantially modified statutory authority could ultimately supersede the draft guidances in important ways. She urged the Department to be clear in its intentions, so that all entities were working toward the same end. Ms. Terry said the Coalition would continue to educate key stakeholders about the importance of innovative diagnostics and their role in health care.

With regard to CMS, she said the Coalition would continue to emphasize the importance of CLIA in assuring that patients and physicians have timely access to accurate, reliable, and safe advanced diagnostic medicine. The Coalition believes that enhancing and strengthening existing requirements under

CLIA by issuing a genetic testing specialty would address some of these concerns. CMS indicated in letters and in the HHS regulatory agenda that it was going to proceed with an NPRM for a genetic testing specialty, but this effort was subsequently halted. The Coalition believes that any regulation of laboratory developed tests, including genetic tests, should be risk-based, rather than technology-based. Ms. Terry stated that GINA is a critical component of personalized medicine and asked that SACGHS recommend to the Secretary that he express his strong support for the Act.

Session on Gene Patents and Licensing Practices (continued)

Comparison of the Patent System of the U.S. and Select Countries
Joseph Straus, Ph.D.
Professor of Law, University of Munich
Director, Max-Planck Institute for Intellectual Property, Competition, and Tax Law
Chairman, Managing Board of the Munich Intellectual Property Law Center

Dr. Straus focused on differences between the U.S. and Europe with regard to gene patenting. He stated that the primary difference is that Europe takes a statutory approach, rather than a case law approach, which began with the European Directive adopted in 1989 and renewed in 1998. He said that a number of patent issues in Europe had not yet been decided because the courts had not had the opportunity to apply the rules in practice.

The European Directive has specific provisions that address the eligibility of genes for patent protection. Dr. Straus said that under these provisions, genomic sequences can be patented if they are not just discoveries of simple genomic sequences. Europe also ensures that gene sequences as biochemical substances can be patented. The Directive states that if they are isolated or technically produced, they can be patented, even if they are structurally identical to a natural element (i.e., genomic sequences). The Directive also states that a DNA sequence without an indication of a function is not a patentable invention. Dr. Straus stated that there is no grace period in Europe. It was his opinion that the United States should make strong efforts to influence Europeans in the direction of a grace period similar to that found in approximately 30 countries around the world.

He noted that a major difference in patentability between the U.S. and Europe is the issue of relevant prior art. In Europe, if a substance is already part of the prior art, it can be patented as a substance, not as a use, and the substance patent covers all subsequent medical, therapeutic, or diagnostic uses, whether claimed or not. This is not the case in the U.S.; there is a much more narrow interpretation of prior art. Oral disclosures and public use of substances outside of the country are not considered prior art and patents can be obtained on them. In Europe, these situations constitute prior art and patents are not allowed.

Another important requirement for patentability in Europe is inventiveness or “non-obviousness.” The European Patent Office applies a “could/would” test, meaning that the question posed is whether an average expert in the art would have done it (not could have done it) with a reasonable expectation of success. “Industrial applicability” is strictly applied in Europe; DNA claimed for the production of a protein or part of a protein can only meet this patentability requirement if the protein or partial protein and its function were disclosed from the beginning.

Addressing patentability under U.S. law, Dr. Straus noted that, “anything man-made under the sun” can be patented. The non-obviousness requirement, as applied by the Federal circuit, has a low yardstick.

A partial amino acid sequence does not make the DNA sequence obvious. He stated that the U.S. examination guidelines on utility require that the genomic invention be specific, substantial, and credible.

Under U.S. law, there are no specific rules for patent protection, and there is no statutory research exemption. The European Directive is much more specific, and has a provision stating that protection for products containing or consisting of genetic information extends to all materials except the human body. Europe has a statutory research exemption that covers all further developments and improvements to a patented invention, even for commercial purposes. This has created a situation in which patent owners are unable or unwilling to try to prosecute someone for performing research with their inventions. However, the research exemption does not cover the use of research tools for the purpose for which they have been patented.

Europe has a specific provision concerning multi-functionality of genes and alternative splicing. It addresses situations in which patented genes overlap only in part, and states that if the overlap is not essential for the respective invention, the patents are independent. To date, there has been no case law to test this provision in practice.

Dr. Straus displayed a graph showing that Europe has a rising curve of patent applications, however, the number of gene patents granted has been always much lower in Europe than in the United States. This is partly due to the obstacle of non-obviousness, which is much stricter in Europe.

Dr. Straus discussed the Myriad Genetics situation, stating that the company had four patents granted by the EPO for methods to diagnose a predisposition for breast and ovarian cancers. The first patent was issued in 2001 and revoked in opposition, because the co-inventor from the U.K. testified that it was simple to file in view of the prior art. The revocation was based on non-obviousness. The other three Myriad patents still had appeals pending. Dr. Straus explained that even after the appeal, actions could be filed in all the designated member states of the EPO.

There were strong reactions to the Myriad Genetics patents by Greenpeace, the German Federal Chamber of Medical Doctors, patient organizations, and the European Parliament. The main concern in Europe was that the patents would create an obstacle to accessing the secrets of the human genome, would result in high testing costs, and would negatively affect improvements in diagnostic methods. However, there were no requests for compulsory licenses in Europe, which would have been possible in all countries, and no court cases were pending. Dr. Straus said it seemed that Myriad Genetics and its opponents were not actively fighting each other.

Dr. Straus's Institute had conducted interviews in 25 institutions, such as large pharmaceutical companies, research institutes, and clinics. They did not find evidence of public concerns. The majority of those interviewed were in favor of product patents on DNA sequences. A number of those interviewed pointed out that when they found out that a gene was patented, they stopped searching for further functions because they did not want to become dependent on the patent owner. Dr. Straus noted that the results of this survey could not be viewed as representative because there were few products on the market.

Dr. Straus summarized by stating that the U.S. has filed for and been issued many more applications for gene patents than Europe. He said that it was not known whether the patents would be valid after official decisions were made. There has not been excessive litigation in either the U.S. or Europe and it was not clear whether there would be a negative impact on research and development.

Bhaven Sampat, Ph.D.
Assistant Professor of Health Policy and Management
International Center for Health Outcomes and Innovation Research
Columbia University School of Public Health

Dr. Sampat's research centers on the economics of biomedical innovation, the law, and the economics of the patent system and science policy. He was the principal investigator on a Ford Foundation project examining patent system reform in developing countries, and he created the first freely searchable database of post-TRIPS Indian patents and applications.

Dr. Sampat presented data on DNA-related patenting in India and the political economy of patent system reform in developing countries. He stated that the 1995 TRIPS agreement required developing countries, including India, to modernize their patent systems. TRIPS led to an upward harmonization of international patent laws, meaning that countries were compelled to change the laws to make them look more like those of developed countries, especially the United States. Changes in India included enacting a minimum patent term of 20 years and not allowing countries to discriminate across fields. This decision was somewhat controversial, as there was concern that granting product patents on pharmaceuticals would lead to an increase in drug prices. Also, based on economic theory, it might make sense for developing countries to have less stringent intellectual property rights than developed countries.

Despite the general trend toward harmonization, Dr. Sampat stated that there was considerable flexibility under TRIPS that would allow developing countries to design their patent laws to maximize benefits and minimize costs. Areas of flexibility included the definition of "inventive step" in utility, the possibility of research exemptions, and restrictions on patentable subject matter. For example, in India, Section 3 of patent law excludes from patentability scientific principles, abstract theories, products of nature, new forms of old substances without increased efficacy, and processes for medicinal and diagnostic treatment of human beings. However, the extent to which these laws would hold up was not clear, either in India or other developing countries.

Dr. Sampat collected data on the approximately 60,000 applications filed at the Indian Patent Office in the post-TRIPS era. The distribution of applications across the top 10 international patent classes (IPCs) showed that the pharmaceutical classes A61K and C07D were at the top of the list. Also well represented were C12N (microorganisms or enzymes) and pictorial communication patents. The largest applicant in India was CSIR, a system of publicly funded laboratories that conduct research in a range of fields. The second largest was Hindustan Lever, a consumer products company involved in chemicals work. Multinational pharmaceutical companies were also prominent in the list of top 20 applicants.

Dr. Sampat said it was hard to identify DNA-related patents in India, as they do not use U.S. patent classes and it is impossible to obtain data on claims of Indian patents in a large sample. Dr. Sampat looked at patenting in the set of IPCs characterized by Verbeure et al. as corresponding to DNA-related patents in an article in the *European Journal of Human Genetics*. Based on the data Dr. Sampat collected on the 60,000 patent applications filed in India since 1995, about 4 percent were in DNA-related IPCs. The top 25 patent holders in these classes accounted for one third of the patents, including multinational pharmaceutical companies, CSIR, and the University of California. Dr. Sampat also analyzed data on priority DNA patent applications in the U.S. in 2000 and 2005 using the search algorithm developed by Dr. Cook-Deegan and colleagues for the Duke DNA Patent Database (DDPD). There were 3,800 U.S. patents issued in 2000. He mapped them to Indian patent applications, and found that in 2000, 41 of the 3,800 U.S. patents had corresponding Indian applications, or about 1 percent. By 2005, the number

increased to 2.5 percent. Overall, a small percentage of DNA patents in the U.S. had corresponding applications in India. Multinational pharmaceuticals were highly represented as applicants. Dr. Sampat also looked at the extent to which academic owners of DNA-related patents in the U.S. were likely to file corresponding applications in India. He found that non-academic owners of DNA-related patents in the U.S. file for corresponding Indian patents for 2.8 percent of their inventions, while academic owners of such patents in the U.S. file for 1.45 percent of their inventions.
Dr. Sampat noted that several movements in India were pushing for Bayh-Dole-type legislation. He said TRIPS is silent on the matter and there was a dramatic growth of interest in patenting, licensing, and entrepreneurship in India. He believed legislation was imminent and was an important development to monitor. He stated that academic institutions were increasingly filing patent applications.

Dr. Sampat stated that, overall, there was very little DNA-related patenting in India, and that most existing tests would likely remain unpatented. He said that although patents might serve as a barrier to access to drugs in India, other barriers, such as a poor medical infrastructure and poverty, are also important factors. Even if genetic tests were patented, he was not sure that prices for them would be as high or access as low as for pharmaceuticals. Price discrimination would probably blunt the costs of genetic tests. Dr. Sampat stated that there was very little evidence that DNA-related patents in India impeded research or any clinical applications. He discussed policy options that could limit future costs in India, but would have little downside risk. He said that it was not patents per se that were problematic, but overly broad patents. He noted that patent quality control by technically competent examiners was very important, however, patent examiners were underpaid in India and the infrastructure for searching through prior art was very weak. This could lead to the issue of some bad patents.

Dr. Sampat explained that India has a pre-grant opposition process, as well as post-grant opposition, which can be filed by any interested party within 12 months after a patent is issued. Some of the grounds on which patents can be opposed include obviousness, non-patentable subject matter, anticipation, and wrongful obtainment. A number of applications were filed in India that were not granted because of patient advocacy groups that teamed up with generic companies and mounted campaigns to oppose patents they thought would impose hard costs. The pharmaceutical industry argued that this was an "unholy alliance" because these groups file serial oppositions to the same patents to shorten patent life, which begins at the filing date. The industry was therefore trying to limit oppositions in India to the post-grant period, which Dr. Sampat did not agree with. He suggested alternatives, stating that conditional and surviving opposition lets applicants retrieve any patent life lost through opposition, or patents that have survived the opposition process could be "gold-plated."

Concerning public sector innovations, Dr. Sampat said Bayh-Dole was imminent in India and licensing was more important than patenting. He proposed that India and other developing countries resist the temptation to mimic Bayh-Dole as is, but instead, balance technology transfer and the need to generate revenue with other goals. Research exemptions could be built into licensing contracts, or there could be a rebuttable presumption of non-exclusive licensing. Academic patents could be opened up to peer review, both in India and in the U.S.

Dr. Evans opened up the floor to questions from both presenters.

Q&A

Dr. Tuckson asked whether the absence of patents in other countries stifles innovation. Dr. Sampat stated that companies generally will not invest money or try to innovate without being relatively sure that there

will be protection for their research results. He added, however, that there is a 50-year empirical legacy in economics on the impact of patents on innovation that indicates that in most industries, patents are not extremely important for innovation, except in the pharmaceutical industry. He said it is not known what the effect would be if the patent rules were changed. He added that there is no evidence that exclusive licenses are needed to facilitate technology transfer.

Dr. Williams asked Dr. Straus to reconcile two statements that seemed contradictory. Dr. Straus had said that in the interviews he conducted, he had not detected any negative impact of patents on research and development. Later, he said that if a gene was patented, other companies would not pursue additional functional aspects of that gene. Dr. Straus clarified that it was not the companies, but the universities and institutes that made those statements, and he said it was not clear whether that indicated a real negative impact. He stated that finding a further function of a gene does not automatically mean that something is commercially viable. His overall impression and the clear statement of those interviewed was that patents were not seen as an obstacle to innovation.

Dr. FitzGerald asked Dr. Sampat whether the unique status of health care in society is taken into consideration when economic analyses are conducted, including areas in which DNA or biological patents might be important. Dr. Sampat said that economists are good at making value judgments in monetary matters, but not at making moral or value judgments about the outputs of different industries, including health care.

International Reports and Recommendations Regarding Gene Patents, Licensing Strategies, and Genetic Tests

Dr. Evans stated that the last portion of the roundtable would focus on recent international reports that addressed gene patents, licensing, and genetic technologies, and how intellectual property affects genetic testing.

John Barton, J.D.
George E. Osborne Professor of Law, Emeritus
Stanford Law School

Professor Barton specializes in international and high technology issues and served as a member of the Nuffield Council's study of gene patenting. He was chairman of the U.K. Commission on Intellectual Property Rights and Developing Countries.

Mr. Barton presented information from several sources: a report by the Nuffield Council on Bioethics, some unpublished work on diagnostic gene patents, and several recent Supreme Court cases that affect patent law. He noted that gene patent claims are for a particular gene sequence, meaning various constructs embodying that sequence, proteins coded for by the sequence, or the research use for the sequence (e.g., an assay). He said it is important to make these distinctions because they affect the scope of the patent.

Mr. Barton discussed a report by the Nuffield Council, which he co-authored in 2002. He noted that the Nuffield Council is an academic group that does not include representatives from the diagnostic industry, which was important to recognize when evaluating the report’s conclusions. The report addressed three key policy issues: protecting the patentability of a therapeutic protein based on a natural protein; avoiding

restriction of the scientific use of a gene sequence and limiting the impact on science; and the question of expanding or broadening patentability of a diagnostic test and its impact on diagnostic testing.

The Nuffield Council Report applied legal principles (e.g., non-obviousness to restrict problems associated with genomic patents) firmly. To the extent possible, it distinguished the DNA sequence as information (which the Council wanted to keep in the public domain and broadly useable), from the embodied sequence as a chemical (which would be legitimately patentable). If those approaches did not work, the report recommended defining various restrictions/licenses to achieve the same result with respect to scientific research and diagnostics. The report had a strong bias towards public access to tests. The feedback on the report in the British community was quite positive.

Mr. Barton then discussed a real world experiment he conducted at NIH several years previously. It evaluated patents as incentives in the diagnostic context. Instead of examining the patents and diagnostic tests for which there had been complaints or concerns, he chose an unbiased sample of diagnostic tests provided by GeneTests. He used their 10 most commonly chosen tests and their 10 most common gene review access tests. Because of some overlap, he arrived at a sample of 17 gene tests and attempted to look at the kinds of patents that covered them. It was very difficult to determine who owned the patents. Mr. Barton looked at secondary literature and conducted searches by disease names and on author names from key scientific articles. He found patents on technological methods, relevant proteins, gene mutations, and consensus sequences. Although the number of patents was divided evenly between the private sector and the public sector, there were significant differences in focus. The private emphasis was heavily on hereditary hemochromatosis, the BRCA1 and BRCA2 genes, and spinomuscular atrophy, and almost every other patent was in the public sector. The obvious implication was that patents and diagnostics encourage private sector innovation for the most popular, big-market kinds of tests. However, the incentive effect is limited to the most common genetic diseases. For the others, there is an assumption that it is an easy leap from detecting a gene sequence to having an effective diagnostic test. However, this depends on FDA's actions concerning the regulation of diagnostic tests. If FDA makes it difficult to bring a diagnostic test to market, a patent might be needed. A period of exclusivity is necessary to justify investing in clinical trials and the elaborate tests required to bring a product to market. Therefore, there is an interplay between the value of gene patents and the regulatory standards applied to them.

Mr. Barton summarized several emerging issues in the field of pharmacogenetics. They included intellectual property (IP) rights on a pharmaceutical product versus a company that has IP rights on the associated diagnostic test (e.g., Herceptin); IP rights on relevant metabolic agents (e.g., P450); IP rights on correlations derived from large pharmacogenetic studies; and arrays, where many different diagnostic tests can be on one chip.

Mr. Barton explained how the law has changed since 2005. He stated that the Supreme Court did not like the direction the Court of Appeals for the Federal Circuit took concerning patent law. He described several cases that made major changes in patent law within the previous several years and that were reversed by the Supreme Court. Merck v. Integra allowed the pharmaceutical industry to infringe on many biotechnology industry patents, as long as it was done as part of a regulatory process. This opened up research possibilities for pharmaceutical firms. eBay v. Mercantile Exchange reinstated the traditional equity test for injunction and could have the effect of restricting the ability to enforce a patent on a scientific research tool. The KSR International v. Teleflex case radically changed and tightened the standards of non-obviousness in the U.S. and could form the basis for striking down some genomic patents. In the case of Laboratory Corporation of America v. Metabolite, a patent on a correlation was questioned by the Supreme Court on subject matter grounds. The Court reached out for the case and then

retreated over dissent by three justices. If successful, the case could strike down sequence-based diagnostic patents. Mr. Barton said the net result is that money that could be obtained as a royalty for a diagnostic patent shrunk dramatically and the enforceability of diagnostic patents was in question. The business implication was that diagnostic gene patents might remain in an ambiguous situation for a long time. He said there is a very good chance that the Supreme Court changed the law in exactly the direction recommended by the Nuffield Council report.

Christina Sampogna, LL.M.
Administrator
Organisation for Economic Cooperation and Development (OECD)

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Ms. Sampogna manages OECD's initiatives pertaining to the life sciences, including intellectual property, research and development, innovation, human genetics and genomics, and counterfeiting. Ms. Sampogna managed the unit that developed the Canadian government's patent policy for the field of biotechnology, which required legislative reform, and she provided legal and policy advice to governments and expert committees on a broad range of topics.

Ms. Sampogna was invited to present on the OECD's guidelines for the licensing of genetic inventions. She stated that the point of the OECD guidelines was to address the stifling of innovation, research, and access to technologies, especially concerning therapeutics and diagnostics. They offer a set of principles and best practices that foster research and delivery and accessibility of products and commercialization. The guidelines attempt to balance competing interests in the marketplace, i.e., research versus the need to commercialize technologies and the interests of the private and public sectors.

Ms. Sampogna displayed two graphs indicating that investment in research and development (R&D) was increasing. One chart came from an FDA report, "Innovation or Stagnation: Challenge and Opportunity on the Critical Path to New Medical Products," and the other came from PhRMA's annual report for 2006. While investment in R&D increased over a 10-year period, the FDA found that the number of new products brought to market decreased and the costs of doing so increased. Although a great deal of money was being invested in the life sciences, Ms. Sampogna suggested that society may not be obtaining enough value for these investments.

She said the main purpose of the OECD guidelines is to address issues pertaining to the licensing and technology transfer of genetic inventions with the aim of fostering R&D, stimulating innovation, and increasing access and diffusion. They provide guidance to the marketplace that encourages access for the delivery of health care products and services, research, and commercialization. The guidelines were developed with the input of over 200 stakeholders through public consultations around the world, including developing countries. They were adopted by the OECD Council, which is its highest decisionmaking body. OECD members include the 30 most industrialized countries in the world. The guidelines are intended to be forward-looking in terms of future developments and innovations.

The guidelines are divided into five sections. The first section addresses licensing, and it sets the tone for the rest of the document. The first statements on licensing present the key objectives: licensing practices (LP) should foster innovation in the development of new genetic inventions related to human health care and should ensure that therapeutics, diagnostics, and other products and services employing genetic inventions are made readily available on a reasonable basis. LP should encourage rapid dissemination of information concerning genetic inventions.

The second section of the guidelines addresses health care and genetic inventions. This section balances access and choice, stating that LP should not be used to restrict the choice of other products or services. They also entreat licensees and licensors to make product and services available to both patients and health care providers. Another important point in this section encourages licensees and licensors to use the highest applicable standards of privacy, safety, and good laboratory methods.

Freedom to conduct research is addressed in the third part of the guidelines, advocating access and the sharing of information, with clear, well defined confidentiality clauses. The balance sought is the need for academics and researchers to publish, versus the needs of the private sector to delay or to restrict the publishing of some information. A key point is that commercial considerations should not unduly hinder academic freedom or education.

The fourth section covers commercial development, to identify practices in the marketplace that, while not illegal, should be avoided in the context of biotechnology and genetic inventions because they result in detrimental effects. Examples are royalty stacking, multiple patents and licenses, reach-through rights, and exclusive licensing.

The final section of the guidelines discusses competition and competition law. It encourages licensees and licensors to comply with competition law, and discourages behaviors such as tied selling, noncompete clauses, and not expanding the breadth of exclusive rights beyond the scope of rights. The section also states that fundamental genetic inventions (e.g., PCR, research tools) should be licensed non-exclusively.

Ms. Sampogna stated that the guidelines were adopted in 2006 and many countries were in the process of implementing and otherwise supporting them. The Czech and Polish governments distributed the guidelines to a large segment of the government, the private sector, and the public sector. This type of dissemination communicates to market participants the government's view of good corporate behavior. In the biotechnology licensing field, the guidelines can be used to generate corporate social licensing, which retains a return on investment, but does not stifle innovation. Other governments have translated the guidelines into French, Japanese, Italian, and German. Some governments have made them available on their websites.

Ms. Sampogna noted that the NIH guidelines, *Best Practices for the Licensing of Genomic Inventions* in 2005, were developed in parallel with the OECD guidelines, with communication and collaboration taking place between the organizations. She said other funding agencies, whether public or private, and government research centers could adopt similar sets of guidelines, which would have a large impact. Organizations such as BIO could distribute the guidelines (or an adapted version) directly to their members to use as guiding principles. Ms. Sampogna stated that a number of best practices and principles in the guidelines could be implemented directly by universities in their technology transfer practices, and could be adopted at a higher level as guiding principles.

In closing, Ms. Sampogna mentioned the "Collaborative Mechanisms for IP" project, which addresses the uncertainties of numerous patents and attempts to use various mechanisms to leverage IP. These mechanisms have been used in other industries, but generally, not in the life sciences. The scope of the project is to see how these mechanisms, such as a patent clearinghouse, could be used in the life sciences to avoid having to negotiate with numerous patent holders. A report on different mechanisms for consideration was scheduled for release later in the year.

Patents Discussion/Next Steps

Dr. Evans opened up the floor for questions for Mr. Barton and Ms. Sampogna.

Dr. Julio Licinio asked for more information about a clearinghouse for the life sciences. Ms. Sampogna said there was a great deal of interest and enthusiasm for the idea, although it would be very complicated and not easy to set up. It took many years to set these up in the IT field. A number of government reports and industry players had recommended the development of a life sciences clearinghouse and were interested in working with OECD to develop the initiative.

Dr. Evans asked what types of incentives could be implemented to encourage the formation of patent pools or clearinghouses. Ms. Sampogna said this issue was being investigated. Some of the pools formed were compulsory because of government intervention, and others were voluntary. She noted some key challenges, one of which was incentives. Another was a standards issue, as many pools have been formed around the development of a standard, but she said this is difficult to develop in the life sciences. Competition law issues are also complex. Ms. Sampogna said it was encouraging; however, that the United States, the European Commission, and Japan had all issued general guidelines on patent pools and standard setting. In addition, the U.S. Federal Trade Commission (FTC) and the U.S. Department of Justice (DOJ) have been proactive in working with the developers of patent pools to ensure that they meet competition law and address anti-trust issues.

Dr. Winn-Deen said that something more powerful than best practices was needed, because best practices would not have prevented the actions of Myriad Genetics or the issues surrounding Canavan disease testing. She said there was a disconnect between the goals of university technology transfer offices (TTOs) and the ideas that were being presented. Although many companies and universities act in the interest of patient health, there are always some bad actors that must be forced to do the right thing. Ms. Sampogna agreed that it was difficult to incentivize TTOs because they are interested in short-term, high-return situations. She said that an enforcement element might be needed in addition to the guidelines.

Dr. Evans asked all the international speakers to join the panel. He displayed several question relating to the gene patents report for discussion with SACGHS and the panelists. The first question asked, “How should pending U.S. patent reform initiatives be addressed as we develop recommendations?” He suggested that the Committee receive an update on the status of pending legislation and recent court decisions at the next session. It was agreed that the Task Force would monitor developments and report back to the full Committee as necessary.

The next questions were, “Are there approaches utilized by other countries or international advisory groups that could be adapted to the U.S. system? Which approaches should be used as models to apply to the U.S. system?” Dr. Williams noted that the Committee should recommend actions that fall within the purview of the Secretary of HHS. Dr. Leonard asked Dr. Alan Guttmacher of NHGRI whether NIH has the power to march in and take over the rights to patents. Dr. Guttmacher was not familiar with all of NIH’s rights in this area, but noted that such actions would have repercussions beyond NIH. Before considering them, the agency would need legal counsel and other advice, because it is not clear whether NIH has free reign in this area. Dr. Guttmacher suggested calling upon the Secretary to ask NIH and other Federal agencies to examine their abilities concerning march-in rights and to consider the criteria under which they might use them.

Dr. Michael Amos stated that more information was needed from industry. Dr. Evans said that a representative of Perlegen had addressed the Committee in an earlier exploratory session, but he agreed that it was important to balance industry and economic considerations with social considerations. He noted that the SACGHS Task Force on Gene Patenting and Licensing Practices and Patient Access to Genetic Tests included Emily Winn-Deen and Mara Aspinall, who were both industry representatives. Dr. Teutsch stated that the Committee needed to hear from someone with expertise on the relationship between innovation and increasing health care costs.
Dr. Evans posed the last discussion question: "Did the international roundtable session provide sufficient information regarding approaches of other countries and international organizations, and what other information might be critical for our information-gathering process?" Dr. Gurvaneet Randhawa said he was not clear about the utility of patents in promoting innovation. Dr. Evans explained that data on this issue was a focus of the case studies underway by Dr. Cook-Deegan's team at Duke University. He said that much of the data would be in the form of temporal associations, e.g., passage of the Bayh-Dole Act followed by an increase in patent applications by universities. The Task Force hoped to obtain some data that showed causation. Ms. Sampogna added that Wesley Cohen and John Walsh at Duke University were studying patents and innovation at a higher level than was Dr. Cook-Deegan's group. She recommended that the Task Force look into their work.

Dr. FitzGerald asked if the Committee needed more information on the role of the WTO, and Mr. Barton stated that the work of the Patent Office at WIPO was more relevant because they were conducting patent harmonization discussions.

Dr. Straus commented on the possibility of NIH using its power to influence forms of licensing. He stated that for some technologies (e.g., Cohen-Boyer technology or monoclonal antibodies), reasonable licensees will only offer non-exclusive licenses. However, in other cases, the risks involved will require exclusive licenses. He said that making publicly funded discoveries available to everyone does not work, and he urged the Committee not to take a rigid position.

Dr. Straus also made a counterpoint about the international organizations and agreements. He said he did not think there would be any substantial development progress at WIPO, because developing countries believe that the WTO is the more powerful organization. The WTO has the ability to pressure the Americans, Europeans and Japanese. He stated that the TRIPS and the General Agreement on Tariffs and Trade (GATT) work well for developing countries, including India, China and many others. Statistics indicate that there is significant technology transfer and direct foreign investment that would not have occurred without the TRIPS and GATT. He made this point because he said that some in the U.S. were of the opinion that the TRIPS was working against the interests of developing countries and this was not the case.

Dr. Straus then acknowledged the difficulty of balancing the economic interests of health care and pharmaceuticals. He said it was clear at the international level that the health care systems in the U.S., Japan, and Europe were subsidizing the costs of other countries' (e.g., Australia and Canada) access to pharmaceuticals. Mr. Barton responded by stating that Dr. Straus's point about who was paying for innovation was crucial. He agreed that the United States, Europe, and other developed nations were paying for the cost of pharmaceutical innovation and some others were getting a "free ride." However, he was not convinced that the TRIPS was good for developing countries, although he believed GATT was beneficial. Dr. Straus commented that the two could not be separated. Mr. Barton said the extent to which foreign direct investment was encouraged and IP systems were strengthened by the TRIPS was a matter of debate.

Dr. Evans summarized the session by stating that the Task Force received further confirmation of the need for a distinction between diagnostic testing and drug development products. He stated that the Nuffield Council report emphasized the theme that, to the extent possible, it is important to make the distinction between the sequence, which is unpatentable, from the embodied sequence as a chemical, which is patentable. He asked the Committee to think along those lines. Dr. Evans concluded by stating that the Task Force planned to present a draft report to SACGHS in the fall of 2008. He thanked the speakers and staff members that provided support.

Session on Direct-to-Consumer Marketing of Genetic Tests

Public Health Surveillance of Awareness and Use of Direct-to-Consumer Genetic Testing
Katrina A.B. Goddard, Ph.D.
Fellow, National Office of Public Health Genomics, CDC
Associate Professor, Epidemiology and Biostatistics
Case Western Reserve University

Dr. Tuckson introduced a presentation by Dr. Katrina Goddard on the public's awareness and use of direct-to-consumer (DTC) genetic testing. Dr. Goddard is a geneticist from Case Western University and she was serving in a fellowship at the National Office of Public Health Genomics at the CDC.

Dr. Goddard stated that DTC genetic tests had recently exploded onto the market. In 2003, 14 companies offered DTC health-related genetic tests. In 2006, the CDC identified 27 companies offering DTC tests, including non-health-related genetic tests, such as paternity testing and ancestry testing; and health-related tests, such as nutrigenetics, predictions of fetal gender, BRCA1 and BRCA2 testing, and hereditary hemochromatosis and cystic fibrosis carrier testing. She said the Internet gives immediate access to these tests.

A 2006 Government Accountability Office report on nutrigenetic testing raised concerns that the tests might be misleading, unsubstantiated, and make ambiguous predictions. The CDC initiated studies to look at surveillance of DTC tests, with the goals of providing baseline information about public demand and interest in nutrigenomic tests and provider knowledge and experience with DTC genetic tests. As the data are collected over time, the CDC plans to assess the impact of changes in policies and public or provider education programs and the evolution of the availability and demand for these tests.

Dr. Goddard said two national surveys were conducted in the previous year. The Healthstyles Survey included 5,250 consumers from around the Nation and the online DocStyles Survey of physicians included 1,250 respondents. In addition, several CDC-sponsored State programs in public health genomics, including those in Oregon, Michigan, and Utah, added questions about DTC genetic testing to their Behavioral Risk Factors Surveillance System (BRFSS) surveys. These are considered representative of the general population. The Oregon and Utah questions and the national surveys specifically used the words "genetic" and "DNA," while the Michigan survey used simpler language (e.g., "a sample from the inside of your cheek," which would exclude genetic tests not taken from a cheek swab). All the surveys mentioned that the test could be ordered directly, but the national survey did not mention that health care providers were not involved in the testing. The Michigan survey restricted the time period to the previous 12 months, while the other surveys were more general.

Dr. Goddard summarized the results from these surveys, stating that the highest rate of awareness of DTC genetic tests was in Oregon (24.4 percent) and the lowest rate was in Michigan (7.6 percent). All the

surveys reported a very low rate of use, i.e., less than 1 percent. All the surveys identified the same characteristics of age, household income, and education level as important predictors of awareness of DTC genetic tests. The rate of awareness increased as age increased, with the exception of the oldest age category, in which there was a drop in awareness. Those with the highest household incomes and the highest levels of education were the most likely to be aware of DTC genetic tests. Consumers were most likely to find out about the tests through television, magazines and newspapers (the media); but 60 percent of respondents who had used a DTC genetic test heard about it from a health professional.

Slightly less than half of the physicians were aware of DTC genetic tests, with males more likely to have this awareness. Of the physicians that were aware of DTC genetic tests, about 75 percent said less than 1 percent of their patients had asked them questions about these tests, and more than 90 percent of physicians had fewer than I percent of their patients discuss results of a DTC test with them. Physicians were asked to identify up to five of their most trusted sources of information on patient health-related topics. Journal articles were the most trusted source, followed by Government agencies, then other physicians. However, the media was cited as the most trusted source concerning information on DTC genetic tests.

Overall, Dr. Goddard said the CDC found that only a small percentage of the U.S. population was aware of or had used DTC genetic tests, and that the media is the most frequent source of information for both consumers and physicians. These findings suggested that other venues, such as professional organizations and Government agencies, might be useful for providing education about these tests. Since only a small number of respondents had actually used a DTC genetic test, it was not possible to characterize that population well. Health outcomes following testing done were not assessed.

Next Steps and Closing Remarks

Dr. Tuckson summarized and discussed next steps, stating that the following meeting would focus primarily on pharmacogenomics and oversight. A response to the CMS letter on the coverage and reimbursement report was to be developed by Dr. Williams, who was asked to serve as the lead SACGHS member for coverage and reimbursement issues, since former Task Force Chair Debra Leonard rotated off the Committee.

The Committee agreed that all issues under discussion had been adequately addressed and Dr. Tuckson adjourned the meeting.

We certify that, to the best of our knowledge, the foregoing meeting minutes of the Secretary's Advisory Committee, Genetics, Hea , and Society are accurate and correct.

Reed Tuckson, M.D.
SACGHS Chair

Sarah Carr
SACGHS Executive Secretary