NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH
SUMMARY OF MEETING[1]
September 10, 2007

The open session of the National Advisory Council for Human Genome Research was convened for its fifty-first meeting at 8:33 A.M. on September 10, 2007 at the Fishers Lane Conference Center**,** Rockville, MD. Francis Collins, Director of the National Human Genome Research Institute, called the meeting to order.

The meeting was open to the public from 8:33 A.M. until 3:53 P.M. on September 10, 2007. In accordance with the provisions of Public Law 92-463, the meeting was closed to the public from 3:53 P.M. on September 10, 2007 until adjournment for the review, discussion, and evaluation of grant applications.

Council members present:

Eric Boerwinkle
Andrew Clark
Jorge Contreras, Jr.
Marilyn Coors
Geoffrey Duyk
Sean Eddy
Vanessa Northington Gamble
Richard Gibbs
Caryn Lerman
Patrice Milos
Jeffrey Murray
David Page
Stephen Prescott (participating via teleconference)
Harold Shapiro
Lincoln Stein
Paul Sternberg
Richard Weinshilboum

Council members absent:

Deirdre Meldrum

Ex Officio member absent:

Gerard Schellenberg

Staff from the National Human Genome Research Institute:

[1] For the record, it is noted that to avoid a conflict of interest, Council members absent themselves from the meeting when the Council discusses applications from their respective institutions or in which a conflict of interest may occur. Members are asked to sign a statement to this effect. This does not apply to "en bloc".

Mary Affeldt, OD
Ajay, DER
Glory Baldwin, DER
Catherine Bennet, DER
Vivien Bonazzi, DER
Vence Bonham, OD
Joy Boyer, DER
Pamela Bradley, OD
Lisa Brooks, DER
Comfort Browne, DER
Gloria Butler, OD
Ernsley Charles, DER
Debbie Chen, DER
Cheryl Chick, DER
Monika Christman, DER
Francis Collins, OD
Karen DeLeon, OD
Irene Dorsey, OD
Gwen Dudley, DER
Elise Feingold, DER
Adam Felsenfeld, DER
Colin Fletcher, DER
Peter Good, DER
Alan Guttmacher, OD
Mark Guyer, DER
Emily Harris, OD
M.K. Holohan, OD
Chris Juenger, DER
Mike Kabatt, DER
Carson Loomis, DER
Murugu Manickam, OD
Teri Manolio, OD
Jean McEwen, DER
Keith McKenney, DER
Lisa McNeil, DER
Anika Mirick, DER
Ken Nakamura, DER
Kenneth Ow, OD
Brad Ozenberger, DER
Tom Pearson, OD
Carmen Perera, OD
Jane Peterson, DER
Anne Pierson, DER
Erin Ramos, OD
Eddie Rivera, OD
Jerry Roberts, DER
Cristen Robinson, DER
Rudy Pozzatti, DER
Jeff Schloss, DER
Geoff Spencer, OD
Jeff Struewing, DER
Carolyn Taylor, DER
Gary Temple, DER
Elizabeth Thomson, DER
Larry Thompson, OD
Susan Vasquez, OD
Lu Wang, DER
Chris Wellington, DER
Kris Wetterstrand, DER
Diane Williams-Bey, DER

Others present for all or a portion of the meeting:

Anna Barker, NCI
Joann Boughman, American Society of Human Genetics
Daniela Gerhard, NCI
Perry Kirkham, Purdue University
Rachel Levinson, ASO - Biodesign
Roger Little, NIMH
Pilar Ossorio, University of Wisconsin
Jim Ostell, NCBI
Janis Mullaney, FNIH
Sharon Terry, Genetic Alliance
Wendy Uhlmann, National Society of Genetic Counselors

INTRODUCTION OF NEW MEMBERS AND STAFF, LIAISONS AND GUESTS

Dr. Guyer introduced new NHGRI staff: Pamela Bradley, Medical Genetics Fellow; Ephraim Johnson, Grants Management Specialist; Lisa McNeil, Program Analyst; Anika Mirick, Program Analyst; Tom Pearson, on sabbatical with Population Genomics; Anne Pierson, Program Analyst; Erin Ramos, Population Genetics Program Director; Chris Wellington, Program Analyst;

Dr. Guyer welcomed members of the press and liaisons from professional societies: Joann Boughman from the American Society of Human Genetics, Sharon Terry from the Genetic Alliance, and Wendy Uhlmann from the National Society of Genetic Counselors. Sharron Olsen from the International Society of Nurses in Genetics broke her ankle and was unable to attend Council.

APPROVAL OF MINUTES

The minutes from the May 2007 Council meeting were approved as submitted.

FUTURE MEETING DATES

The following dates were proposed for future meetings: February 11-12, 2008, May 19-20, 2008, September 8-9, 2008, February 9-10, 2009, May 18-19, 2009, and September 14-15, 2009

DIRECTOR'S REPORT

I. GENERAL ANNOUNCEMENTS

Dr. Collins presented certificates to the four members who will be rotating off Council after this round: Marilyn Coors, Geoff Duyk, Sean Eddy, and Jeff Murray.

In honor of the 25th anniversary of USA Today, the newspaper published its list of the most influential people of the last 25 years. Numbers four and five were Francis Collins and Craig Venter, respectively.

On July 9, 2007, Maynard Olson was named the winner for the 2007 Gruber Prize for Genetics. He will receive the Prize on October 24, 2007, at the American Society of Human Genetics annual meeting in San Diego, California. Dr. Olson is a former Council member and a current member of the NHGRI Board of Scientific Counselors.

On July 6, 2007, Marco Marra was elected to the Royal Society of Canada: The Academies of Arts, Humanities and Sciences of Canada. Dr. Marra, formally at Washington University, now heads the Vancouver Genome Center and is a leader of the full-length cDNA Mammalian Gene Collection project.

Dr. Aravinda Chakravarti has been announced as the ASHG President- Elect. Dr. Chakravarti is a former Council member and was a key member of the HapMap consortium. Dr. Wylie Burke is the current president of ASHG.

Dr. Vanessa Gamble, a current Council member, has moved from Tuskegee University to George Washington University where she has been named University Professor of Medical Humanities.

Dr, Stephen E. Straus, the first director of the National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH), died of brain cancer on May 14, 2007.

II. NEW NHGRI INITIATIVES

The ENCODE project has released one RFA, "A Data Analysis Center for the Encyclopedia of DNA Elements (ENCODE) Project." The application receipt date is September 20, 2007.

The trans-NIH Genes, Environment, and Health Initiative (GEI) has released two RFAs – "Methods for Statistical Analysis of DNA Sequence Data for Studies related to Variation to Disease" (receipt date September 20, 2007); and "Genome-wide Association Studies in the Genes, Environment, and Health Initiative - Study Investigators" (receipt date October 18, 2007). The NHGRI population genomics program has also released two RFAs – "Epidemiologic Investigation of Putative Causal Genetic Variants—Study Investigators" (receipt date November 19, 2007); and Epidemiologic Investigation of Putative Causal Genetic Variants—Coordinating Center" (receipt date November 19, 2007). The latter two were issued in response to a discussion during the May 2007 Council meeting about doing rapid follow-up in prospective genetic association studies.

III. RECENT SCIENTIFIC ACCOMPLISHMENTS AND ISSUES

NHGRI - EXTRAMURAL PROGRAM

Large-scale sequencing: A summary of the traces in GenBank for all organisms that NHGRI is supporting is found in the NHGRI Sequencing Update table. The table includes listing of Q20 bases in the trace repository for all organisms.

In May 2007, Council approved a proposal that was submitted by the Annotating the Human Genome Working Group (AHG) to produce draft assemblies of several primate genomes (cynomolgus macaque, mouse lemur, bushbaby/galago, baboon, squirrel monkey, and tarsier). This was the last Council round that proposals from the Comparative Genome Evolution Working Group (CGE) were to be considered, as that working group has finished its work. Council approved a proposal to sequence the draft assembly of elephant shark as part of the Evolution of the Proteome project, as well as a proposal to construct draft sequences of five members of the ecdysozoan lineage (a crustacean arthropod, a centipede, a chelicerate, a tardigrade, and a priapulid worm). In addition, proposals for the comparative sequencing of Tetrahymena and Oxytricha were approved during the May 2007 Council round. Lastly, a proposal to sequence the reference genomes of 200 bacteria and archaea strains from human was approved as a pilot project of the Human Microbiome Project.

On September 6, 2007, an editorial in *Nature* expressed concern that NHGRI was turning its attention solely to human sequencing. However, NHGRI considers that to be incorrect. The table of deposited traces and the new approved sequencing targets, for instance, document NHGRI's commitment to continue to generate sequence data for comparative and evolutionary analyses.

NHGRI and NCBI held a meeting on July 27, 2007 to discuss the development of a Short Read Archive to store sequencing reads from new sequencing technologies. Representatives from the large-scale sequencing centers and the companies developing the technologies attended. The group discussed methods and specifications for submitting data to NCBI and data elements and formats for associated metadata. The target date for development of the Short Read Archive is October 1, 2007.

On August 1, 2007, the latest installment of sequencing technology development grant awards were made, and announced in a press release. Awards were made toward developing technologies in both the "$1000 genome" and the "$100,000 genome" categories. The RFAs will be reissued immediately.

CEGS program: The CEGS at Stanford (David Kingsley, Will Talbot and Rick Myers) has been renewed and a new CEGS award was made to Mark Vidal and his team at Dana Farber Cancer Institute. The current CEGS program announcement expires in October 2007 and will be reissued.

HapMap: The HapMap Phase II paper has been accepted for publication, pending a few revisions, and will describe the results of the analysis using additional samples at deeper coverage. HapMap Phase III will use samples from 7 additional populations. All samples for this phase, with the exception of the Maasai, are currently stored at Coriell as both DNA and cell lines.

GWAS: The Genetic Association Information Network (GAIN) has selected studies for ADHD, nephropathy in type 1 diabetes, psoriasis, major depressive disorder, schizophrenia, and bipolar disorder. The data from the ADHD study are complete and now available through the dbGaP database. It is also now possible to request access to the diabetic nephropathy data, although the dataset is not yet complete. To access these datasets, data requesters must fill out a web-based 'data access request' which is reviewed by the GAIN Data Access Committee (DAC). The DAC reviews the request to ensure that the intended data use agrees with any restrictions that may be on the use of the data. Fifteen requests have been approved: nine for access only to the ADHD dataset, four for access only to the diabetic nephropathy dataset; and two for access to both. Approvals include requests from GAIN PIs, their collaborators at other institutions, and other investigators from universities, the NIH, and the pharmaceutical industry. Two requests were disapproved: one for both datasets because the proposed use did not appear to be consistent with the data use limitations of the datasets, and one for the ADHD dataset because not enough information was provided. Both requestors were given the opportunity to address these issues, but the DAC has not received additional information from either.

NHGRI has discussed its data release and data access policies with the Wellcome Trust. While NHGRI releases GWAS data immediately with a 12 month embargo on publication by others, the Wellcome Trust Case/Control Consortium plans to make data from GWA studies available 6 months after the data are analyzed. Dr. Lincoln Stein reported that, at the Human Genome Variation meeting, the Europeans were considering setting a maximum 12-month embargo on access to GWA data.

A manuscript describing the design and implementation of the Genetic Association Information Network (GAIN), including approaches for project selection, data deposition and distribution, collaborative analysis, publication and protection from premature intellectual property claims is in press.

Cancer genomics: The NHGRI-supported large-scale sequencing centers have completed first-pass sequencing of ~900 genes in 188 samples of lung adenocarcinoma as part of the Tumor Sequencing Project (TSP). Putative mutations discovered in these data are undergoing validation. The tumor samples were also analyzed for copy number variations using high density SNP arrays. The consortium has submitted a paper on the SNP array findings and is preparing to report on the tumor sequencing results. Included in the latter paper will be a description of lessons learned in the course of applying large-scale genomic technologies to lung cancer. Dr. Anna Barker gave a presentation on TCGA later in the open session.

ENCODE/modENCODE: NHGRI has released RFA HG-07-010 which solicits applications to develop and implement a Data Analysis Center (DAC) as part of the ENCODE Project. The DAC will work with the ENCODE Analysis Working Group and the ENCODE Data Coordination Center to coordinate, support, and assist in the analysis of data produced by the ENCODE Consortium. Applications are due September 20, 2007 with funding anticipated in the spring of 2008.

A manuscript describing the findings of the ENCODE pilot project was published in *Nature* on June 14. A set of companion papers was published at the same time as an ENCODE special issue of *Genome Research*. The *Nature* paper reported on the generation and analysis of datasets produced on the ENCODE regions, which constitute 1% of the human genome, and contained integrative analyses carried out by members of the five ENCODE analysis groups.

Applications for the ENCODE Scaling RFA (HG-07-030), which solicited proposals for studies to find functional elements across the entire human genome or studies for new or continued pilot projects on the ENCODE regions, will be considered during the closed session of this Council meeting. Applications received in response to an RFA to support an ENCODE Data Coordination Center (DCC) (HG-07-031) will also be considered during the closed session.

The modENCODE project has begun monthly conference calls. It is likely that the data from the projects will start to appear soon.

Informatics: The NHGRI has formed the Genome Research Informatics Network (GRIN) to coordinate activities of the NHGRI Informatics Portfolio, including the model organism databases. One of the goals of the GRIN is better interoperability of the genome databases and improved efficiencies of these projects. An initial conference call was held on August 27, 2007. Peter Good and Vivien Bonazzi are overseeing the GRIN.

The NIGMS Center for Bioinformatics and Computational Biology announced the appointment of a new center director, Karin Remington. Dr. Remington will be chair of the Biomedical Information Science and Technology Initiative Consortium (BISTIC) responsible for trans-NIH extramural computational biology programs.

The NIH has formed a new Trans-NIH Bioinformatics Coordinating Committee chaired by Dr. Donald Lindberg, Director of the NLM. The Committee has a two-year charter to perform several tasks, including representing NIH in external forums on biomedical informatics, preparing reports appropriate as important events occur, maintaining an inventory of informatics initiatives including NIH programs with other agencies, ensuring dissemination of relevant informatics developments across the NIH, establishing a community of common interest to facilitate coordination of biomedical informatics efforts across the NIH, and advising the NIH Director as well as the Directors of all ICs on biomedical informatics developments.

Mouse knockouts: The KOMP repository grant (Kent Lloyd, P.I.), which was discussed by the NCRR Council in May, was awarded at the University of California, Davis (UC Davis); it includes a subcontract to Pieter de Jong at Children's Hospital Oakland Research Institute (CHORI). The repository will archive, maintain, and distribute up to 8,500 strains of embryonic stem cell clones, live mouse lines, frozen embryos and sperm, and vectors.

In March several NIH Institutes and the Knockout Mouse Project (KOMP) announced (NOT-HG-07-011) the opportunity for investigators to apply for administrative supplements to have mouse knockouts made from existing mutant ES cell resources. Twelve applications were

received and reviewed, nine were approved for funding. These awards are now being processed. The KOMP working group is discussing whether to re-issue the notice later this year.

EUCOMM and NORCOMM became collaborators at the March 2007 meeting of the International Knockout Mouse Consortium (IKMC). TIGM has also joined the IKMC. TIGM has now completed the deposition of more than 275,000 nucleotide sequence tags into the Genome Survey Sequences division of GenBank. The tags identify transposon insertion sites in TIGM's library of C57BL/6 mouse embryonic stem cells.

Mammalian Gene Collection: The MGC library currently contains non-redundant, full-length CDS cDNA clones for approximately 15,808 human genes and 14,782 mouse genes. MGC also contains full-length CDS clones for 5113 rat genes and 7080 cattle genes. MGC continues to provide infrastructure support for the cloning and characterization of Danio (zebrafish), *X. laevis*, and *X. tropicalis* cDNAs, which now have full-length clones, respectively, for 9575, 9455, and 4965 total unique genes.

The project has essentially exhausted the potential of the PCR rescue approach to complete the full-length cDNA library. In December 2006, following review of proposals submitted in response to an RFP, MGC awarded a contract to GeneArt for synthesis of cDNA clones for a maximum of ~3000 genes. Since then, a lower-than-expected yield from PCR rescue has raised the number of genes that are candidates for synthesis to nearly 4000. Because GeneArt is now at maximum capacity, MGC initiated a second contract with Codon Devices, which was ranked second in the RFP technical review, to synthesize nearly all the remaining genes. GeneArt and Codon Devices are beginning to produce data. The final meeting of the MGC is scheduled for January 2008.

NIH Roadmap: There will be separate presentations on two new Roadmap initiatives, the Human Microbiome Project and the Epigenomics Project, later in the Open Session.

The Molecular Libraries Screening Center Network began its third and final year of the pilot phase with the data from over 140 screened assays already deposited in PubChem. Many of the screens were successful in identifying probe candidates, many of which are now undergoing structure optimization. Four centers have produced a total of nine new probes to date. The pipeline from assay to probe takes 18 to 24 months.

The pilot phase of the MLSCN will end in July 2008 when the production phase of the initiative begins. The production phase will include only three types of centers; it is anticipated 2-4 high-throughput Comprehensive Centers, 2-3 high-value target, lower-throughput Specialized Screening Centers and 2-3 Specialized Chemistry Centers will comprise the new Molecular Libraries Probe Production Center Network (MLPCN). Investigators applying for the production phase will use a two-phase process, beginning with an X02 pre-application. The X02 is a relatively brief application that will be peer reviewed to identify the most competitive applicants, who will then be invited to submit full U54 applications. The U54 receipt date is expected to be January 4, 2008 and the applications will be reviewed at the NIMH May 2008 Council.

The centers have recently contributed a number of important publications, which can be found in the Council members' table folders.

NHGRI – INTRAMURAL PROGRAM

Based on clues provided by a study with transgenic mice, a research group at NHGRI has developed a strategy that will be tested as the first treatment for people with hereditary inclusion body myopathy (HIBM), a rare, degenerative muscle disease. The scientists, led by Marjan Huizing, Ph.D., an associate investigator in NHGRI's Medical Genetics Branch, reported their findings in the June issue of the *Journal of Clinical Investigation*.

NHGRI and NCI have teamed with Group Health Cooperative in Seattle and Henry Ford Health System in Detroit to launch a study to investigate the interest level of healthy, young adults in receiving genetic testing for eight common conditions. Called the Multiplex Initiative, the study will also look at how people who decide to take the tests will interpret and use the results in making their own health care decisions in the future. A total of 1,000 participants who meet the study's eligibility requirements will be offered free multiplex genetic testing. ABC World News Tonight recently featured Dr. Colleen McBride and the Multiplex project.

In last week's online edition of the *Proceedings of the National Academy of Sciences*, researchers from NHGRI; the University of California, Los Angeles; and Peking University in Beijing, China, reported developing a technology to knockout zebrafish genes in a stable, targeted manner.

NHGRI OFFICE OF THE DIRECTOR

Dr. Collins gave a presentation to patent examiners about the patenting of results from genome-wide association studies. His presentation detailed the NHGRI data access procedures and the NIH opinion that the GWAS data should be considered pre-competitive and not subject to patenting and license.

The ELSI Assessment Panel (EAP) convened for its first meeting on September 9, 2007. The EAP members on Council are: Harold Shapiro (Chair), Vanessa Gamble, and Caryn Lerman. Other members are Jeff Murray, Jonathan Moreno, Tom Murray, Pearl O'Rourke, Pilar Ossorio, Sharon Terry, and David Valle. The EAP is charged with addressing the question of whether ELSI activities in NHGRI's Division of Extramural Research and Office of the Director are structured and performing in a maximally effective way that will help realize the Institute's goals. The EAP is planning to meet three times and will report to Council in May 2008. The EAP is particularly interested in reaching out to organizations, as well as young and established investigators. This outreach will be done both by conference call and via a face-to-face meeting in Washington, DC.

William W. Lowrance, a consultant in health research policy and ethics, and Dr. Collins co-authored a Policy Forum article entitled *Identifiability in Genomic Research*, in the latest issue of *Science*. The article addresses how unique, individual genomic data should be managed with care to maintain public trust. The article was based on the deliberations of an NHGRI-sponsored

workshop in October 2006 on identifiability and on the white paper, *Privacy, Confidentiality, and Identifiability in Genomic Research*.

The 2007 NHGRI "Current Topics in Genomic Research" Short Course marked the 10th anniversary of this course, which is given for faculty and students at colleges and universities with substantial enrollment of under-represented minority, rural and/or disadvantaged students. Attendee evaluations indicated that the course was extremely well-received and valuable. Most of the graduates use what they learn to develop curricula in genetic research and to provide summer research opportunities for students interested in genomic research.

The 2007 Community Genetics Forum, will be held on October 12. Each year this forum is focused on a different part of the country. This year, the forum will be led by the University of Michigan, which has organized 5 Forums to be held concurrently in 5 states (Flint, Michigan; Minneapolis, Minnesota; Chicago, Illinois; Des Moines, Iowa; and Portageville, Missouri). NHGRI researchers and staff will travel to the individual forums to participate. The program will be integrated across the five states using video-conferencing technology.

The NHGRI, in conjunction with NICHD, ORD, CDC and HRSA, is sponsoring a two-day workshop on carrier screening on February 6-7, 2008. The workshop will examine emerging issues in carrier screening for genetic disorders in light of advances in genomic technologies. Advocates for spinal muscular atrophy (SMA) pushed hard for this workshop because they are concerned that the NIH has not moved forward fast enough in the effort to offer SMA carrier screening.

The NHGRI and the Office of Medical Applications of Research's Consensus Development Program are co-sponsoring an NIH-wide State of the Science conference (date TBD) on the use of family history as a screening tool in the primary care setting. The primary goal of the conference is to generate a report and promote research on the clinical applications of family history by identifying gaps in the knowledge base.

On November 5, the NHGRI will host a genomics roundtable during the American Public Health Association meeting in Washington DC. Leaders in the field of public health, representatives of state health departments, and academic centers involved in public health genetics will meet with NHGRI leadership to discuss topics relevant to public health genetics, and to explore new relationships and opportunities between the NHGRI and attending organizations. Dr. Gamble reported that there is now a public health genomics interest group as a part of the APHA which will have its first meeting at the November APHA meeting.

NHGRI – POLICY

There will be a separate presentation on GWAS policy later in the Open Session. Dr. Collins thanked the American Society of Human Genetics for its efforts in getting the word out about the opportunity for public comment on the GWAS polices.

The FY 2008 President's Budget was submitted to Congress on February 5, 2007. The total requested is $28,858 million, a decrease of $328 million from the FY 2007 Joint Resolution, which passed after the budget was submitted. The 2008 President's budget request for the National Human Genome Research Institute (NHGRI) included $484,436,000, a $2 million decrease from FY 2007. The House Appropriations committee recommended $29,649,887,000 for the NIH, which would be $750,000,000 above the FY 2007 appropriation and $1,028,646,000 above the President's request. The House bill includes $493,996,000 for NHGRI. The Senate bill, S. 1710 would provide NIH with $1 billion over the FY 2007-enacted level or $29,899,887,000 ($1.3 billion over the FY 2008 PB). The Senate version includes $497,031,000 for NHGRI. The President has said he will veto any appropriations bills that exceed his budget request, and every bill passed by the House and Senate appropriators so far exceeds the President's Budget.

The Genetic Non-Discrimination Act (H.R. 493, S. 358), passed the House on April 25 by a vote of 420-3. The Senate and House staff negotiated the bill all summer and seemed to be in agreement, but when Senators Kennedy and Enzi attempted to bring the bill to the Senate floor for a vote by unanimous consent in late July, there were two anonymous "holds" placed on the bill that prevented the vote, one of which was quickly dropped. Senator Coburn (R-OK) has stated that he put a hold on the bill because he objects to some of the technical details dealing with business issues. The Coalition for Genetic Fairness has done a good job of asking people to call Coburn's office in an effort to get the bill moving.

The Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) met for its summer session on July 10th. A 33-member SACGHS Task Force on the Oversight of Genetic Testing met most recently on September 6th with the charge of developing a "comprehensive map of the steps needed for evidence development and oversight for genetic and genomic tests, with improvement of health quality as the primary goal". The Task Force is slated to present a report to the SACGHS on November 9th.

PROJECT UPDATE: The Cancer Genome Atlas (TCGA)

Dr. Collins welcomed Dr. Anna Barker to give a project update on TCGA. Dr. Barker is Deputy Director, Advanced Technology and Strategic Partnerships, NCI.

NCI and NHGRI will each contribute $50 million over three years to support the TCGA pilot. The TCGA pilot is intended to determine the feasibility of applying large-scale genomic analysis to a disease state. It is expected that the TCGA will identify genetic changes that are important in cancer but have are not yet been identified. The initiative approaches this goal systematically, by using a variety of genomic technologies to analyze a set common samples; providing all participating researchers with high quality biomolecules will allow results to be compared across platforms. The hope is that this approach will allow a much better definition of relevant cancer genes and lead to a molecular taxonomy of cancer this will lead to new treatment approaches and better tailoring of treatment strategies to individual patients.

Another goal of the TCGA pilot phase is to develop new collaborative relationship among clinicians, basic scientists, informatics and sequencers. While there have been some inevitable clashes of operational culture among the groups, the participants in the interdisciplinary network are beginning to work well together. The pilot project has selected three cancer types of high importance for its initial study: glioblastoma multiforme, ovarian cancer, and squamous cell lung cancer.

The Biospecimen Core Repository (BCR) was the first component of the network to be established. The BCR currently collects and quality assures samples, re-verifies sample pathology, extracts the DNA and RNA analytes, distributes them to the characterization and sequencing centers, and enters de-identified clinical data into database.

The project has set very stringent criteria for sample accession. For example, the pilot requires 0.2g samples that consist of at least 80% tumor cells and are accompanied by a normal sample from the same individual. Many retrospectively collected tissue samples have been found not qualify for TCGA because they don't meet the quality criteria. Only 30% of collected glioblastoma samples meet the qualifications. This has led to a much slower rate of sample acquisition than originally planned, but it is expected that TCGA will get about 200 brain tumor samples this year from retrospective studies (compared to the 500 expected at the beginning of the project). To increase the flow of glioblastoma samples, TCGA wants to reconsent all living donors of samples in the existing retrospective collections and will also start prospective collection of new samples. TCGA has also changed its sample collection strategy and is beginning to collect samples for both lung and ovarian cancer at the same time as the glioblastoma collection is being completed. Lung samples may pose a problem because they are often contaminated with other tissues. Prospective sample collections for these two cancer types should begin in October. Elizabeth Thomson and Brad Ozenberger have been working on the TCGA human subjects and reconsent policies. Dr. Barker reiterated the importance of working with survivor groups in order to increase education about donating samples to studies like TCGA.

Another component of the TCGA pilot is the Cancer Genome Characterization Centers (CGCCs), which are funded by NCI at the level of $12-15 million a year to analyze the TCGA samples for chromosomal copy number changes, gene expression profiles, and epigenomics composition. The epigenomics project is being done as a pilot within TCGA and is progressing quickly. The initial data generated by the CGCCs is of high quality and is reproducible across the different CGCCs. The centers are now starting to integrate the expression data with the epigenomic copy number data. The selection of the next set of sequencing targets will be the first selected on the basis of TCGA-generated data. The selection process is underway and the output should be sent to the Sequencing Centers within 2 to 3 weeks. TCGA data will be available online at http://cancergenome.nih.gov.

The Genome Sequencing Centers (GSCs) are currently sequencing an initial set of 600 genes in the glioblastoma samples; these sequencing targets were identified by literature analysis and with advice from experienced investigators. As noted, the second set of sequencing targets will come

from the initial analysis of data extracted by the CGCCs from TCGA samples. There does not seem to be much overlap between the two target lists.

caBIG is being used by TCGA for data management. The portal for data access is in development and the data will be stored in two tiers: open access and controlled access. The quality and analysis of data that are being produced by TCGA is unprecedented. TCGA will have an impact on everyone working on cancer today.

The NHGRI/NCI TCGA project team meets every other Thursday for 2 hours. The TCGA Steering Committee, made up of the project PIs, meets by teleconference on the alternate Thursdays. The TCGA Network also has working groups to address specific aspects of the project, including the Biospecimen and Production, Analysis, and Publication working groups. In addition, there are three Disease Working Groups, one for each of the three tumor types being studied by the pilot. The Steering Committee met in person in July 2007 and will meet again in December 2007.

The institutes will have to decide by the autumn of 2008 if they want to scale TCGA up. The identification of new cancer genes and the ability to identify cancer subtypes would justify a scale up. NCI would like to use this approach to look at 50 to 70 cancer types. The NHGRI and NCI hope that other countries will have interest in using the TCGA model to study different types of cancer and have joined the Wellcome Trust, Genome Canada, and the Ontario Institute for Cancer Research to organize a meeting on October 1-2, 2007 to discuss the establishment of an International Cancer Genomics Consortium.

Until compelling TCGA data are released, the initiative will have its critics. However, the success of the TSP project will help blunt some of these criticisms. Similarly, the initial data from the TCGA glioblastoma samples indicate that the results will be powerful if enough samples can be made available. It will be important to ensure that the cancer community and the genomics community stay connected.

Council member Dr. Geoffrey Duyk is a co-chair of the TCGA External Scientific Committee. He stated how impressed he was with the robustness of data that were presented at the July 2007 TCGA meeting. He also noted the importance of securing an acceptable flow of samples and to making sure that there is not a mismatch between the sample supply and the project's analytical capacity. He supported the suggestion that the investigators should start broadly collecting prospective samples across all tumor types. He also asked if there would be any advantage to recruiting study participants from the US armed services. These cohorts could be carefully followed for many years. Dr. Collins reported that TCGA has recently begun to explore a relationship with the Veteran's Affairs (VA) that would allow TCGA to advantage of the extensive VA electronic medical records, particularly for lung cancer and prostate cancer initiatives. Dr. Collins serves on the new Genomic Medicine Advisory Committee of the VA. He reported that the VA would be a great resource for prospective sample collection. TCGA could also take a lesson from countries such as UK, Singapore, and Japan which have successfully created population-based biobanks for molecular medical research.

NIH Peer Review Project

Dr. Lawrence Tabak, Director of NIDCR was scheduled to present a status report on the NIH project to assess the peer review process. Unfortunately, at the last minute Dr. Tabak could not be present at Council. His slide presentation was distributed to Council members, NHGRI staff, and the others in attendance.

Roadmap 1.5: Human Microbiome Project (Dr. Jane Peterson)

The goal of the Human Microbiome Project (HMP) is to characterize the microbes and microbial communities that inhabit the human body. The HMP has been approved for $115 million over five years as a trans-NIH project involving 22 participating ICs. A number of cooperative agreements and grants to effect the HMP will be awarded in FY08 and others in subsequent years. Intramural investigators will be allowed to apply for HMP funding.

All data and resources from the HMP will be released to the public. Concept clearances will not be brought to the NACHGR. However, the first HMP initiatives will come to the September 2008 Council meeting for consideration.

There are seven initiatives within the NIH HMP. These are (1) to generate a reference set of the genomes from 1000 isolated human commensal organisms, and use 16S rDNA sequencing to characterize the microbiomes at five sites (GI tract, vagina, oral cavity, skin, and nasal passages) from healthy normal individuals who will be recruited and consented specifically to donate samples for this project; (2) a set of demonstration projects designed to determine the relationship between the microbiota at a specific body site and health and disease; (3) development of new technologies needed for microbiomic studies, such as methods to sequence the genomes of unculturable organisms; (4) development of new informatics tools for the analysis of complex metagenomic datasets; 5) a data analysis and coordination center; 6) a repository to collect microbes, DNA, and metagenomic samples that have been sequenced; and 7) a program to address relevant ELSI issues.

To address the many questions about sampling strategies for metagenomic analysis and the HMP, NIH held a workshop on July 25, 2007, chaired by David Relman of Stanford University. Attendees included microbiologists, sample collection experts, informaticians, statisticians, ELSI experts, and sequencing experts. The workshop recommended that there should be three nested levels of sampling. The first level should include non-invasive sampling from all five body sites from considerably more than 100 donors. A subset of 100 of these donors would make up the second sampling level, at which individuals will undergo somewhat more invasive sampling. A third, quite small subset (perhaps 10 individuals) would then be recruited to undergo even more invasive sampling (e.g., GI tract sampling via colonoscopy). The workshop further recommended that all of the first-tier donors should be consented for sampling from all sites. Other recommendations included defining the appropriate metadata that should be collected

before sampling begins, the value of collecting host DNA, and the need to archive DNA and RNA from both the host and the microbes rather than raw samples. In the Council discussion, Dr. Duyk suggested also collecting serum from donors to facilitate studies looking at immune responses to microbes.

Following the workshop, HMP convened a set of expert working groups to define Standard Operating Procedures for sample collection. These working groups will also help define the environmental variables that should be considered and controlled in the sampling process.

In the discussion, Council members posed several question: How are environmental factors going to be taken into consideration? Will the HMP look at longitudinal variables? How is the HMP going to look at change in the microbiome over time? In response to these questions, Dr. Peterson noted that a number of these questions were raised at the workshop but not answered definitively. For example, to address the issue of longitudinal variables, some workshop participants suggested sampling the donors repeatedly at frequent time points. Dr. Peterson also stated that the primary objective of the Roadmap HMP effort, as only a five-year effort, is limited and is specifically to demonstrate the feasibility of the metagenomic approach to study the relationship between the human microbiome and human health. She noted that the real objective is to create a new approach to the study of human health and to have many of the complex questions raised by Council members pursued by individual ICs subsequent to a successful demonstration of the value of that approach by the Roadmap effort.

Dr. Eddy expressed concern that sampling microbial DNA from different areas of the body will produce variable amounts of DNA. He asked whether a whole genome amplification step had been considered. Dr. Peterson stated that DNA would likely be pooled either from multiple individuals or multiple sites on the same individual.

Dr. Duyk suggested sampling burn victims, people with colitis, transplant patients, or patients undergoing lung biopsies because these conditions all require significant infectious disease surveillance. Dr. Murray suggested sampling people in close contact, such as sexual partners or mothers and babies, who would be likely to share microorganisms between them. Dr. Peterson stated that such projects could be done as demonstration projects.

Roadmap 1.5: Epigenomics (Dr. Elise Feingold)

Epigenomics is the genome-wide analysis of epigenetic marks and their effects on biology. Many human health outcomes appear to be due to epigenetic effects. This is another area that the IC Directors decided was appropriate for inclusion within the Roadmap as it may lead to a transformation in our understanding of disease and treatment.

The Epigenomics Roadmap Project is run by an implementation working group led by three institute directors: Dr. Jim Battey, Dr. Nora Volkow, and Dr. Samuel Wilson. The implementation working group held a workshop in March that set out the following goals

for the project: (1) to create an international consortium; (2) to create a reference epigenome; (3) to standardize sequencing platforms, procedures, and reagents; (4) to develop demonstration projects; (5) to advance new technologies; and (6) to develop a public data resource.

U01s will be used to fund Reference Epigenome Mapping Centers. The U01 mechanism will also be used to fund Epigenome Data Analysis and Coordination Centers to analyze data and coordinate with NCBI about the transport, storage, and access to data. The R01 and R21 mechanisms will be used to fund technology development grants and grants looking for novel epigenetic marks in mammalian cells. The RFAs for all of the initiatives will be released shortly for funding next summer.

The Epigenomics Project will also begin a number of initiatives to study the relationship between epigenomic changes and specific diseases and conditions. These initiatives will receive half their funding from Roadmap and half from individual ICs. These RFAs will be released each year and funding will begin in the summer of 2009.

The overlap between the Roadmap Epigenomics Project and ENCODE will be discussed in closed session. NHGRI will encourage coordination between the two projects to minimize overlap between them. The Epigenomics Roadmap project will be able to recruit projects that are not covered by ENCODE.

Process for identifying new ELSI Initiatives (Dr. Jean McEwen)

The ELSI Advisory Panel (EAP) has been charged with reviewing the NHGRI ELSI program. It will deliver its findings and recommendations at the May 2008 Council meeting. In the intervening period, the ELSI program would like to implement a process for identifying new areas of interest and communicating these to the ELSI research community. Dr. McEwen presented for Council consideration a proposal for a three-step process.

First, a staff working group of OD and DER staff would meet three times a year to develop a list of emerging ELSI issues. A Council working group, made up of four or five Council members and possibly some outside participants, will review the staff working group reports three times a year via conference call and will identify those priority areas that might require RFAs (for the next year, it might be logical to have members of the ELSI review panel (EAP) serve as the Council working group). The working group recommendations would be presented to Council for review and modification, and approval of necessary concept clearances. ELSI staff will then implement research initiatives in the approved priority areas. The list of emerging priority issues will be posted on the ELSI website rapidly, and the community will be notified of changes in the priority list through a listserv. Seven other ICs have expressed interest in working with NHGRI on this, although these ICs have not been asked to commit funds yet.

Dr. Shapiro stated that NHGRI should be cautious about making long-term commitments via this process before the EAP can analyze the state of ELSI. Dr. McEwen stated that

staff recognized that any recommendations from the EAP relevant to this issue would override anything different that the staff might have implemented before May 2008.

CONCEPT CLEARANCE: ELSI Analysis of Natural Selection in the Human Genome (Dr. Jean McEwen)

Positive natural selection leads to the increase in advantageous traits in a population over time. The process of positive selection in humans has been strongly supported by analyzing the relationship between differences in phenotype (e.g., lactose tolerance, sickle cell trait) and the frequencies of certain alleles in different populations. The Wellcome Trust Case/Control Consortium has identified 13 regions within the human genome that show evidence of advantageous positive, natural selection. The existence of demonstrable positive natural selection in humans raises a number of issues with potential social implications. NHGRI ELSI staff have proposed an RFA that would solicit studies in this area.

Examples of research questions include: What are the ELSI implications of scientific research on positive natural selection? How will the implications of this research vary depending on whether the trait varies between or within populations or both? Is the trait of interest seen as advantageous in all environments or just in people with certain genotypes or in certain environments? Is the trait still under selection in some geographic areas but not in others? Does this create issues of stigma and discrimination? Other responsive studies would look at how the design of these studies involves ELSI considerations, or how the results of finding of positive selection effects are communicated to the public, or how the results of these studies can contribute to the public's understanding of differences between racial and ethnic groups.

This RFA would advance the mission of NHGRI because the institute's many sequencing initiatives have identified, and will continue to identify, variants undergoing positive selection. For example, using HapMap data, investigators have been able to use a variety of algorithms to identify about 800 segments of the genome that show statistical evidence of recent geographic selection. The driving forces behind these differences remain undefined but potentially will bring many ELSI issues to light.

Council had a number of comments. Mr. Contreras suggested that it would be important to solicit studies looking at legal issues such as privacy. Dr. Gamble stated that the phrasing of the research questions within the RFA will determine who applies. It is important to define terms such as 'recent history' and 'advantageous trait.' Dr. Stein suggested drafting an RFA that would address issues surrounding race directly, and not use 'natural selection' as a proxy for race. In response, Dr. McEwen noted that NHGRI has previously issued an RFA that solicited applications that looked extensively at racial issues and evolution, and that it is important to remember that differences in allele frequencies affect more than race. The RFA under discussion should be careful to link the effects of these differences to human health and community health. Dr. Murray suggested that the RFA look into the gene frequencies that are being selected for today

and will be selected for in the future as a result of socioeconomic disparities in and outside the United States.

Council members also noted that it may be important for NHGRI to prioritize which ethical, legal, and social questions to address with this RFA. There was also some question about whether this RFA was attempting to solicit research about the best methodology for studying the effects of research results reporting advantageous positive selection or whether the RFA was soliciting the studies themselves. Some Council members felt that the methodological question should be a priority. Finally, Council members were concerned that the RFA mechanism may do too little and take too long. There was enthusiasm on the part of the Council to take a different approach and to convene a working group to write a white paper outlining community standards studying positive selection.

DATA ACCESS

NIH GWAS Policy (Dr. Laura Rodriguez)

The GWAS policies were developed in response to an increasing number of requests for access to data from genome-wide association studies and the NIH's desire to have rapid and broad data release. Leadership from many ICs have been involved in the development of these policies. The GWAS policies provide guidance for three elements of data sharing: data management, scientific publication, and intellectual property.

All GWAS studies begin with investigators collecting DNA samples from participants who have been properly consented. These samples are then subjected to genome-wide association analysis and the resulting data are de-identified and deposited in a data repository at dbGaP. The contributing investigator's institution needs to provide certification to the NIH that the data to be entered in the repository have been appropriately stripped of all identifiers. Based on 2004 OHRP guidelines, the data repository will not be engaging in human subjects research because the key to the code linking data to specific study participants will never be shared with the NIH. Additionally, OHRP determined that secondary data users will not be conducting human subjects research because they will not have access to identifiers within the datasets

For access to the data, investigators will have to submit a Data Access Request (DAR) for review by a Data Access Committee (DAC) made up of NIH staff with appropriate scientific and ethical expertise. The same DAR can be used to request access to multiple data sets. As part of the DAR, a requester will have to agree to the terms and conditions for data access as outlined in the Data Use Certification (DUC) that must be cosigned by his/her institution. The DAC assigned to each dataset will review the DAR for consistency with any data use restrictions put on the dataset. The NIH is working to ensure that all DACs function in a consistent way.

Data requesters must also agree to inform the NIH of any breaches in security concerning the data and how these breaches have been handled. Data users must also renew their

requests for data access, including submission of annual progress reports to the DAC. Requesters who have violated any of the stipulations of the DUC will have their passwords for data access deactivated.

Dr. Duyk stated that the NIH must be careful about the chain of custody of GWAS data. Education of lab technicians and others working with the requesting PIs will be important.

dbGaP will also have an open-access tier that will not require DAC approval for access. Information available in this tier will include: study protocols, summary-level data, and genetic associations for studies in the controlled-access database that have passed the embargo date.

All data in the open and controlled-access dbGaP database are considered government records. However, the NIH has obtained an agreement that the release of individual-level, raw data would be a breach of privacy and therefore, these data will not be subject to FOIA requests.

All GWAS data in dbGaP are considered to be pre-competitive by NIH, and should be available in the public domain without being patented. While data will be made available as soon as possible, there will be a maximum 12-month embargo on publications and other dissemination of analysis of GWAS data by any investigator other than the sample supplier. dbGaP has been educating journal editors to recognize manuscripts that make use of GWAS data and are submitted before the 12-month embargo period has expired. Using GWAS data as preliminary data in grant applications may be difficult under the publication embargo because applications can become public information

Dr. Rodriguez reiterated that the GWAS policies do not supersede institutional IRB rules. Some investigators may need to get IRB sign-off before data are submitted to dbGaP. Much of the confusion on the part of IRBs with the data submission process comes from questions over what is meant by ‘de-identified’ vs. ‘coded’ data.

dbGaP demo (Dr. Jim Ostell)

Dr. Collins welcomed Jim Ostell from NCBI to demonstrate dbGaP.

dbGaP can be accessed through PubMed. Dr. Ostell used the AERDs study on macular degeneration as an example. All data columns have two version numbers: one, the V number, refers to the content of the data column while the other, the P number, refers to a specific patient. This allows patients to withdraw their data. Each ‘V’ version of the data may have a different number of patients. Data requesters will only be able to see summary data from past versions. Contributing investigators must include protocols for data collection as well as a summary of the data and a description of data use restrictions with their submitted data.

The dbGaP site allows approved data requesters to search variables across different studies. Currently this functionality uses a word search and there is no standardized language between studies.

dbGaP works with vendors to calculate QC values and version genotypes. Users will be able to go back and look at previous versions of the genotypes.

By the end of 2008, there will be data from approximately 100,000 individuals and hundreds of thousands of variables in dbGaP. NCBI expects that once the trans-NIH GWAS policies go into effect, many groups will ask to put their data in dbGaP.

dbGaP regulates data access using the NIH eRA commons system to validate the identity of data requesters. eRA allows for international requesters and the system has agreed to create accounts for companies and other entities that did not previously qualify for eRA accounts. Once users are authorized, they can log in and pick which data sets they wish to access. Requests for data access are reviewed by the DAC responsible for managing access to that specific dataset. DACs are able to view the other datasets requested by the requester. Once approved, data requesters then choose which data elements they wish to download. Each downloaded file requires a password that is unique to that file. Downloaded data is grouped by consents and each PI must agree to the consent stipulations before unpacking the data.

To date, the GAIN DAC has granted 15 requests for data access. On average, the DAC has taken about 15 days to review a request for data access once the SO has signed off.

A committee chaired by Michael Gottesman will bring together the chairs of DACs across the NIH to share lessons learned and provide oversight to ensure that the data access system is working well. A working group of Dr. Zerhouni's advisors has also been established to monitor the data access system.

Dr. Duyk reported that McKinsey and insurance firms may want access to dbGaP data for consulting purposes and asked how the database would account for this. Dr. Collins stated that insurance companies would likely not qualify for data access without a clear statement of their intended purpose. There was some concern that insurance companies may ask intermediaries to access data and research particular questions for the company, but transfer of GWAS data to third parties in prohibited by current policies.

How to Access Cancer Genomics Data (Dr. Brad Ozenberger)

Data from the Tumor Sequencing Project (TSP) are not available through dbGaP, but are housed at the National Cancer Institute Center for Bioinformatics (NCICB). Data requesters can access open-access data through the NHGRI webpage at www.genome.gov/cancersequencing. For access to controlled-access data, requesters must fill out a DAR to be reviewed by the NHGRI Medical Sequencing DAC.

The data portal to access TCGA data is now available through the TCGA website. A TCGA DAC made up of NHGRI and NCI staff reviews requests for access to controlled-access data which includes most clinical data, SNP calls, and linking tables.

CONCEPT CLEARANCE: X01-based solicitation to provide access to large-scale sequencing capacity for association studies (Dr. Lisa Brooks)

Dr. Guyer described the X01 mechanism for solicitation of requests for access to an NIH resource. X01s were established to allow the use of the NIH electronic application tracking systems and to allow initial peer review. However, since no funds are awarded, X01s do not require Council second-level review. NHGRI staff is bringing a concept for Council clearance to use the X01 mechanism to solicit and evaluate requests for the use of NHGRI-supported large-scale sequencing capacity to sequence regions under association peaks.

Dr. Brooks explained that GWAS genotyping studies have been successful at finding regions of the genome that are associated with disease. Once these results have been replicated and validated, they usually need to be followed up to find the responsible variant within the association peak. Sequencing is one way that researchers can take a detailed look at regions under association peaks in order to assess variation in SNPs, structural elements, LD relationships, frequency of variants, and the association of variants with particular phenotypes. Furthermore, sequencing will allow researchers to prioritize SNPs to look at via functional studies. Any part of the project beyond sequencing that requires money (i.e. data analysis, reconsent of study participants, distribution of clones with regions of interest) will not be supported by this X01 mechanism.

NHGRI estimates that it may initially receive approximately 15 X01 requests under this RFA, but that this number likely will increase as technology improves. NHGRI will review all applications for the strength of the evidence for association and will choose projects based on scientific merit, balance of disease portfolio, and minority representation. Dr. Eddy asked if NHGRI had considered allowing the sequencing centers to do the review; Dr. Brooks said staff had not. Dr. Duyk asked if NHGRI would publish its research priorities for the community (yes, it would) and how the institute would deal with applications that were scientifically meritorious but did not fit within this list of priorities (requests for high priority projects would be granted first).

The proposed timeline for releasing the X01 is as follows: in September 2007, a notice would be posted in the NIH guide; in December 2007, a program announcement would be released; and in May 2008, NHGRI hopes to report to Council on the first set of sequencing projects accepted under the X01 mechanism. Data from all projects supported by this mechanism will be deposited in dbGaP and GenBank.

Dr. Gibbs expressed concern that this concept clearance was premature because the sequencing centers are still in the process of introducing the new technologies into their

pipelines. He said he is wary of creating expectations among investigators that are not in line with the capabilities of the sequencing centers to use the new technologies efficiently yet. Furthermore, he felt that existing projects may cover the goals of this concept clearance to provide the sequencing centers with development projects.

Dr. Felsenfeld agreed that the NHGRI medical sequencing program (MSP) has technically similar pilot projects in the sequencing pipeline. These projects will be useful in clarifying some of the technical issues. The allelic spectrum projects may serve as pilot projects for association studies by producing preliminary data that could direct the course of this project.

NHGRI would not plan to institute a publication embargo on data from these projects. It is not clear that a nine-month embargo on publication by others would significantly protect the investigator (1) because it is not yet well understood how the data will be analyzed and how much time will be required for the analyses, and (2) because the sequence data will be released immediately allowing other investigators to begin analysis right away. Dr. Boerwinkle argued that PIs should have protected time to execute the analysis plan that they will have to submit in order to be awarded an X01 in the first place. Furthermore, PIs are more willing to release data in the public domain if they are protected for publication. Others felt that a publication embargo was inappropriate because investigators were getting sequencing and genotyping done for free. The goal of these projects is to find disease genes to improve health, not to get recognition for publishing a paper.

Dr. Eddy expressed the opinion that if NHGRI is planning to only pay for the sequencing under a particular association peak once, regardless of how many groups are interested in sequencing that region, then the sequence data should be considered a community resource and should not be subject to a publication embargo. However, if NHGRI will pay for the sequencing of a particular region for each interested investigator, then the investigators are competing and a publication embargo should be implemented. Many Council members felt strongly that this RFA should be a Ft. Lauderdale-regulated initiative with no formal publication embargo.

The Council decided that there were too many issues that needed to be addressed and that a program announcement could not be ready for release in December 2007. The Council will revisit this concept clearance at the February 2008 Council meeting in light of the entire NHGRI medical sequencing program. The Council will address questions of data access and restricted publication at that time. The chairs of the Medical Sequencing Working Group (MSWG) will be invited to attend the February 2008 Council meeting.

COUNCIL-INITIATED DISCUSSION

The February 2008 Council meeting will include a short presentation on technologies to set the context for a discussion on the medical sequencing program. A more detailed presentation on new technologies will be given at the May 2008 Council meeting.

The Council would like to hear more about GRIN and other bioinformatics resources. This discussion will include a brief overview of the Secretary's advisory document on pharmacogenoimcs.

During the May 2008 Council meeting, staff will make a presentation on the Molecular Libraries Project.

Dr. Collins suggested that Council revisit the 'Future of Genome Research' document which was originally written in 2003.

ANNOUNCEMENTS AND ITEMS OF INTEREST

Dr. Guyer directed Council to the Council folders containing items of interest.

CONFLICT OF INTEREST

Dr. Guyer read the Conflict of Interest policy to Council and asked the members to sign the forms provided.

REVIEW OF APPLICATIONS

In closed session, the Council reviewed 149 applications, requesting $99,548,179. The applications included 26 regular research grants, 22 pilot projects, 0 program projects, 23 ELSI grants, 49 RFA grants, 1 area grant, 1 center grant, 3 conference grants, 1 training grant, 0 continuing education training program grants, 9 SBIR Phase I grants, 5 SBIR Phase II grants, 4 fellowship grants and 4 STTR phase 1 grants. A total of 96 applications totaling $75,905,958 were recommended.

I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.

_____ _____

Date Mark Guyer, Ph.D.
Executive Secretary
National Advisory Council for Human Genome Research

_____ _____

Date Francis S. Collins, M.D., Ph.D.
Chairman
National Advisory Council for Human Genome Research