

**NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH**  
**SUMMARY OF MEETING<sup>1</sup>**  
September 14, 2009

The Open Session of the National Advisory Council for Human Genome Research was convened for its fifty-seventh meeting at 8:35 A.M. on September 14, 2009 at the Fishers Lane Conference Center, Rockville, MD. Alan Guttmacher, Acting Director of the National Human Genome Research Institute, called the meeting to order.

The meeting was open to the public from 8:35 A.M. until 3:35 P.M. on September 14, 2009. In accordance with the provisions of Public law 92-463, the meeting was closed to the public from 12:30 P.M. on September 14, 2009 until adjournment for the review, discussion, and evaluation of grant applications.

Council members present:

Michael Boehnke  
Eric Boerwinkle  
Mark Chee  
Rex Chisholm  
Richard Cooper  
Jorge Contreras Jr.  
Richard Gibbs  
Geoffrey Ginsburg  
Caryn Lerman  
Patrice Milos  
Richard Myers  
Pearl O'Rourke  
Pilar Ossorio  
David Page (by teleconference)  
Paul Sternberg Jr.  
David Valle  
Richard Weinshilboum  
Claire Fraser-Liggett

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<sup>1</sup> 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".

Staff from the National Human Genome Research Institute:

Ajay, DER	Heather Junkins, OD
Sanja Basaric, OD	Rebecca Kolberg, OD
Tsegahiwot Belachew, DER	Rongling Li, OD
Vivien Bonazzi, DER	Carson Loomis, DER
Vence Bonham, OD	Teri Manolio, OD
Ebony Bookman, OD	Jean McEwen, DER
Joy Boyer, DER	Keith McKenney, DER
Lisa Brooks, DER	Lisa McNeil, OD
Comfort Browne, DER	Enrique Michelotti, DER
Joseph Campbell, DER	Janis Mullaney, OD
Debbie Chen, DER	Anita Nagwani, OD
Cheryl Chick, DER	Ken Nakamura, DER
Monika Christman, DER	Brad Ozenberger, DER
Priscilla Crockett, DER	Jane Peterson, DER
Christine Cutillo, DER	Rudy Pozzatti, DER
Camilla Day, DER	Ed Ramos, OD
Elise Feingold, DER	Jacqueline Reindl, DER
Adam Felsenfeld, DER	Cristen Robinson, DER
Barbara Fuller, OD	Laura Rodriguez, OD
William Gahl, OD	Jeff Schloss, DER
Jonathan Gitlin, OD	Geoff Spencer, OD
Mary Glynn, OD	Jeff Struewing, DER
Peter Good, DER	Larry Thompson, OD
Bettie Graham, DER	Elizabeth Thomson, DER
Eric Green, DIR	Susan Vasquez, DER
Alan Guttmacher, OD	Lu Wang, DER
Mark Guyer, DER	Christopher Wellington, DER
Linda Hall, DER	Kris Wetterstrand, DER
Sarah Harding, OD	Rosann Wise, OD
Lucia Hindorff, OD	Julia Zhang, DER
Christopher Juenger, DER	

Others present for all or a portion of the meeting:

Diane Baker, Genetic Alliance  
Judith Benkendorf, American College of Medical Genetics  
Joann Boughman, American Society of Human Genetics  
Karen DeLeon, NIA  
Dawayne Nutt, OS, DHHS  
Sharon Terry, Genetic Alliance  
Rhonda Schonberg, National Society of Genetic Counselors  
Mike Watson, American College of Medical Genetics

## **INTRODUCTION OF NEW MEMBERS AND STAFF, LIASONS AND GUESTS**

Dr. Guyer noted that the new Council slate has been approved, but that three of the new members are participating at this meeting as *ad hoc* Council Members: Michael Boehnke, Mark Chee, and Rex Chisholm.

Dr. Guyer introduced new NHGRI staff. Dillon Perry, Rebecca Lowdon, Assya Abdalla, Lin Gyi, and Corina Din-Lovinescu (Program Analysts, DER), and Evangeline Campbell (OD). Dr. Guyer welcomed members of the press and liaisons from professional societies:

## **APPROVAL OF MINUTES**

The minutes from the May 2009 Council meeting were approved as submitted.

## **FUTURE MEETING DATES**

The following dates were proposed for future meetings: February 8-9, 2010; May 17-18, 2010; September 13-14, 2010; and February 7-8, 2011; May 16-17, 2011; Sept. 12-13, 2011

## **DIRECTOR'S REPORT**

### **I. GENERAL ANNOUNCEMENTS**

Francis Collins was sworn in as the sixteenth Director of NIH on August 17, 2009. Kathy Hudson, formerly of NHGRI, will serve as NIH Chief of Staff

Janet Rowley was awarded the Presidential Medal of Freedom. Dr. Rowley was honored for her work on cancer as a genetic disease, which has led the way to a deeper understanding of cancer biology and for more personalized approaches to cancer care. Dr. Rowley has been a longtime advisor to both the extramural and intramural programs of the NHGRI.

Ulrike Peters Ph.D., M.P.H., an investigator in the NHGRI PAGE program, has been selected for the Presidential Early Career Award for Scientists and Engineers. This award is the highest honor bestowed by the U.S. government on outstanding young scientists and engineers at the beginning of their independent careers. Dr. Peters was recognized for her research on selenium and the interaction of genetic variations and nutrition on cancer prevention.

### **II. NHGRI – EXTRAMURAL PROGRAM**

**Sequencing.** The Mouse Genome Sequencing Consortium published a finished, high quality assembly of the mouse genome that contains 1,259 mouse-specific genes that were previously missing from or misrepresented in the draft mouse sequence (<http://www.plosbiology.org/article/info:doi/10.1371/journal.pbio.1000112>).

The July meeting of the Research Network on Large-scale Sequencing addressed issues of next-generation sequencing, prospects for third-generation sequencing, progress on the large-scale projects (HMP, 1000 Genomes, medical sequencing, and cancer sequencing), and issues of data deposition and bioinformatics capacity. The meeting recommended that the Research Network and the centers should continue to choose ambitious projects that will drive technology forward, maintain synergistic center interactions, and serve as models for disease-specific sequencing projects. This meeting also noted the success of the sequencing program's earlier decision to devote a significant portion of the 2009 budget to implementation of 454, Solexa and SOLiD platforms, as all of the centers are now running the new technology at "production" levels. The friendly competition among them has generated benefits to throughput and cost.

A group at the University of Washington, led by Debbie Nickerson and Jay Shendure, published a paper demonstrating the value of whole exome sequencing (<http://genome.gov/pfv.cfm?pageID=27533187>). In their work, the authors analyzed DNA from 8 individuals, representing three populations, who had previously been studied in the International HapMap Project, and obtained high quality sequence data from just the exome part of the genome. They also applied the technique to DNA from 4 unrelated individuals who had been diagnosed with Freeman-Sheldon syndrome, a rare inherited disorder caused by mutations in the MYH3 gene, and demonstrated that sequencing whole exomes from a small number of unrelated individuals with a single-gene disorder can serve as a genome-wide scan for the causative gene. This work was done as part of The Exome Project, a collaborative effort of NHLBI and NHGRI (<http://www.nhlbi.nih.gov/resources/exome.htm>).

**1000 Genomes.** Data collection for the three 1000 Genomes project pilots has been completed, and the data are being cleaned and prepared for release and analysis. From 182 low-coverage samples, 17 million SNPs were seen, of which 9 million were novel. The two trios from the deep-coverage project added 1 million novel SNPs.

**Cancer Genome Sequencing.** The Cancer Genome Atlas ovarian cancer project is nearing completion. 6000 genes have been sequenced in 238 cases (tumor/normal pairs) and whole genome datasets have been obtained from another 12 cases; more than 8 terabases of DNA sequence were generated overall. While the TCGA pilot project formally ends in October, the lung squamous cell carcinoma component has not been completed and will be continued. Meanwhile, the scale-up for the next five years is being implemented. The NCI plans to fund a new round of Genome Characterization Centers to do the gene expression and methylation analyses, as well as low-scale sequencing activities. NCI will also fund a new set of Data Analysis Centers to manage the data and present integrated views to the community. NHGRI will continue to provide large-scale sequencing capacity for TCGA, while NCI will use ARRA funds to support additional large-scale sequencing

While TCGA is the primary cancer genomics effort at NHGRI, the sequencing centers are also developing projects individually or in collaboration with each other, such as the Tumor Sequencing Project on lung adenocarcinoma. The centers are using these projects to explore improved methods in whole genome sequencing and analysis, transcriptome analysis, and analysis of disease processes such as A good example of the exemplary research coming from

NHGRI Centers is the recent report from the Washington University center led by Rick Wilson and Elaine Mardis describing the whole genome characterization of a second AML specimen and comparison with their first AML sample. The report shows that mutations discovered in these two genomes by entirely unbiased whole genome sequencing can reveal alterations of unanticipated genes and these genes can be subsequently implicated in the pathogenesis of the disease by screening additional samples of AML for recurrence of the mutations and implicate these genes in disease pathogenesis. (<http://content.nejm.org/cgi/content/full/361/11/1058>)

**Centers of Excellence in Genomic Science.** The CEGS program recently made four awards; two centers were renewed and two new centers were added. One of the new projects is designed to better understand transcriptional regulation through the development of a method that determines the proteins that are bound to a specific segment of DNA using novel capture and mass spectrometric approaches. Conceptually, it is the inverse of chromatin immunoprecipitation (ChIP), in that chromatin will be isolated by trapping specific DNA sequences and the bound proteins will be isolated by mass spectrometry. Thus, the method does not require specific protein affinity reagents or any prior knowledge of the potentially bound proteins.

### **ENCODE and modENCODE**

A marker paper describing the scope and plans of the modENCODE Consortium was published in the June 18 edition of *Nature* (<http://www.nature.com/nature/journal/v459/n7249/full/459927a.html>).

The ENCODE Analysis Working Group held a workshop in late July at the HudsonAlpha Biotechnology Institute in Huntsville, AL. The hands-on workshop focused on data integration, working towards an analysis paper that the group hopes to publish next year. The modENCODE Consortium is planning a similar workshop in early December to plan integrative analysis papers for the worm and fly.

ENCODE and modENCODE will gain substantial resources through ARRA funding, which will enhance the scope and utility of both projects.

### **III. NHGRI – INTRAMURAL PROGRAM**

**The Therapeutics for Rare and Neglected Diseases Program (TRND).** The NIH Office of Rare Diseases Research (ORDR) will oversee the program, and the laboratory operations will be administered by NHGRI, in close collaboration with the NIH Chemical Genomics Center (NCGC).

#### **Researchers Uncover Genetic Variants Linked to Blood Pressure in African-Americans.**

A team led by NHGRI's Charles Rotimi reported the discovery of five genetic variants related to blood pressure in African-Americans, findings that may provide new clues to treating and preventing hypertension. (<http://genome.gov/pfv.cfm?pageID=27532579> and <http://www.plosgenetics.org/article/info:doi/10.1371/journal.pgen.1000564>). The researchers

analyzed more than 800,000 SNPs using DNA samples from 1,017 participants in the Howard University Family Study, a multigenerational study of families from the Washington, D.C. metropolitan area. The investigators found five genetic variants that were present significantly more often in people with hypertension than in those without the condition. The variants were associated with high systolic blood pressure, but not with diastolic blood pressure or combined systolic/diastolic blood pressure.

**Researchers Discover the Genetic Event Underlying the Short Legs of Dachshunds and Other Short-legged Dogs.** Dr. Elaine Ostrander and colleagues published results that demonstrate that a single evolutionary event appears to explain the short, curved legs that characterize dachshunds, corgis, basset hounds and at least 16 other breeds of dogs. In addition to what it reveals about short-legged dogs, the discovery provides new clues about how physical differences may arise within species and suggests new approaches to understanding a form of human dwarfism. Both papers appeared in early online editions of the journal *Science*. (<http://www.sciencemag.org/cgi/content/full/325/5943/995> and <http://www.sciencemag.org/cgi/content/abstract/1177808>). In the past month, Dr. Ostrander's team also reported that variants in just three genes, acting in different combinations, account for the wide range of coat textures seen in dogs, from the poodle's tight curls to the beagle's stick-straight fur.

**Study Reveals New Genetic Culprit in Deadly Skin Cancer.** Researchers from NHGRI, NCI, and Johns Hopkins have identified a new group of genetic mutations involved in the deadliest form of skin cancer, melanoma. Mutations were found in nearly one-fifth of melanoma cases in a gene already targeted by a drug approved for certain types of breast cancer (<http://www.nature.com/ng/journal/v41/n10/abs/ng.438.html>).

#### **IV. ROADMAP PROGRAMS**

**MLPCN (Molecular Libraries Probe Production Centers Network).** The MLPCN completed the first year of its production phase in June 2009. The Network processed 117 probe projects and generated 46 potent and selective probes. Many of the probes have properties that suggest them as the basis for potential clinical benefit. For example, one probe blocks tau aggregation in an Alzheimer's disease model, while another is a ligand for a muscarinic acetylcholine receptor (<http://pubs.acs.org/doi/abs/10.1021/bi9006435>).

**Human Microbiome Project (HMP).** The first HMP Research Network meeting was held in Gaithersburg June 9th-10<sup>th</sup>, 2009. The meeting brought together the sequencing centers, demonstration projects, technology and computational tools development projects, and ELSI grantees; a total of 160 people attended. All currently funded researchers made presentations, either oral or poster. 282 of the planned 900 reference bacterial genome sequences from organisms associated with the human body have been completed thus far. The HMP website ([www.hmpdacc.org](http://www.hmpdacc.org)) now includes the strain catalog. Clinical sampling of the normal volunteers at Baylor and Washington University in St. Louis is continuing well. 177 of the planned 250 have been sampled already, and second visits have begun for some.

At the May 2009 Advisory Council meeting, the Council considered the second round of applications for the HMP Roadmap Technology Development RFAs; five awards were subsequently made. These new projects address the development of cell-sorting based on ribosomal RNA gene content, physical and functional characteristics, and surface-protein complement, and enhanced capabilities for cultivation and recovery of previously uncharacterized isolates. The awards total \$1.8M in FY2009 (Roadmap funds). Applications for the third and final RFA are due today; they will be presented at the May 2010 Council meeting.

**GTEx.** The Laboratory, Data Analysis & Coordinating Center (LDACC) for GTEx will be funded through a single contract with an anticipated award date of May 2010. The grantees receiving awards through the Statistical Methods RFA will be encouraged to use GTEx data, once they are available. Tissue procurement for GTEx is to be accomplished in collaboration with caHUB, which will award sub-contracts to rapid autopsy and/or transplant groups. The project is expected to have tissue samples available in early summer of 2010.

## **V. NHGRI OFFICE OF THE DIRECTOR**

**Population Genomics.** The Office of Population Genomics recently received very positive assessments from the External Scientific Panels of its two largest programs, the Gene-Environment Association Studies (GENEVA) and Electronic Medical Records and Genomics (eMERGE) Network. The GENEVA ESP was very favorably impressed by the genotype cleaning methods being developed and encouraged expansion of the consortium to include more GWA studies that could benefit from and contribute to these evolving methods. The eMERGE ESP was positive about phenotype and exposure measures being defined by electronic medical records (EMR), particularly their high predictive values and transferability across EMR systems. They encouraged development of additional EMR definitions and wide dissemination of these measures for use in genomic research.

The Consensus Measures for Phenotypes and eXposures (PhenX) Toolkit initiative has finalized four of its proposed 20 domains, in demographics, cardiovascular, anthropometry, and tobacco/alcohol use; it has working groups actively developing measures in nine other domains.

As of the second quarter of 2008, the NHGRI GWA catalogue includes nearly 400 publications and more than 1,700 variants. It is heavily used by the scientific community for research and more recently for development of the new Illumina GWA platform. Research using the catalog has included a comprehensive, genome-wide analysis of GWA-defined loci that demonstrated that the vast majority, nearly 90%, of trait-associated SNPs are intronic or intergenic. This raises questions about strategies focusing heavily on exons in looking for functional variants, although trait SNPs are significantly enriched for non-synonymous sites and 5kb promoter regions (<http://www.pnas.org/content/106/23/9362.full>).

**GWAS Policy Update.** The NIH GWAS Policy includes a 12-month publication embargo period, which applies to the submission of any work analyzing data from dbGaP, including publications, posters, oral remarks, etc. Recently, a violation of this policy was by the PI for a

dataset managed by the NHGRI DAC was identified. The DAC met within 24 hours and is following up with the institution and investigators involved. The NIH response process has worked very well and the journal (PNAS) has taken the situation very seriously. PNAS will publish an editorial regarding the publication policy with commentary from the NIH.

The Council discussed how such breaches of the policy might be prevented in the future. NIH is putting sanctions in place, while attempting to be careful not to be overly stringent in the case of an initial violation. The NIH also continues to explore better ways to make the policy clear to researchers; suggestions included making the check-boxes more visible or integrating it into the journal check-off system, with the reviewers becoming involved by screening for adherence to the policy. This would have broader implications for non-genomic data.

Meanwhile, with respect to wider data release issues, a follow-up to the May 2009 Toronto meeting is planned that will bring together international funding agency representatives and journal editors for further discussion about putting appropriate and implementable data release policies in place. The involvement of journal editors is an important aspect of the upcoming meeting. An upcoming Nature publication will highlight data release issues. The Nature website will feature a forum, moderated by the co-chairs of the May Toronto meeting, for discussion of data release.

**Summer workshop in genomics: Short Course.** The Education and Community Involvement Branch hosted the 6th NHGRI Summer Workshop in Genomics, otherwise known as the 'Short Course.' A record number of applications from undergraduate instructors were received this year for the course's 17 slots. Each faculty applicant selected picked his/her a promising student to accompany him/her for the week-long course. The participants were largely from institutions serving underrepresented minorities from 13 different states, Puerto Rico and Guam (news that made the local Guamanian newspaper!). This year, ECIB worked with the Society for Advancement of Chicanos and Native Americans in Science (SACNAS) in outreach and solicitation of applications. ECIB also partnered with the Director of Education of the American Society of Human Genetics, Mike Dougherty, throughout the course. Dr. Dougherty played a significant role in assisting faculty in curriculum development based on the information presented during the workshop. The Short Course included over 20 speakers from NHGRI, who discussed the exciting research carried out at the institute. The students (dubbed "Genome Scholars") also had an opportunity to shadow members of NHGRI labs and core facilities.

**"Blueprint" Meeting June 8-9, 2009.** A meeting entitled "Developing a Blueprint for Primary Care Physician Education in Genomic Medicine" was held June 8-9, 2009. The meeting, sponsored by NHGRI, several other IC's, CDC, and HRSA, convened leaders from a number of medical specialties, including internal medicine, family medicine, pediatrics, obstetrics and gynecology and preventive medicine, to create a blueprint for genomics education for primary care physicians for the next five years. A meeting report is being prepared for publication in a peer-reviewed journal. Attendees agreed to meet periodically to move this topic further along.

The Council suggested the inclusion of oncologists in genomics training and requested further discussion at future Council meetings about the size of genomics training efforts for physicians.



**Family History State of the Science Conference.** The Family History State of the Science Conference was held on Aug 24-26, 2009. The conference, co-sponsored by NHGRI and the Office of Medical Applications of Research (OMAR), was the culmination of a two-year planning effort. The panel found that there was only weak direct evidence supporting the use of family history as a screening tool for common complex conditions in primary care. The panel suggested an extensive research agenda relevant to personalized medicine and genomics and, along with a webcast, and the evidence report, drafted a companion statement that is expected to be published alongside the AHRQ evidence report in "Annals of Internal Medicine" soon.

## **VI. NHGRI POLICY**

### **Appropriations Update**

In contrast to the last several years, we anticipate that a final appropriation will be passed in advance of the start of the upcoming fiscal year. The House mark for NIH is approximately \$31.3 billion. The Senate mark more closely mirrors the Administration's request at \$30.8 billion, which is about \$400 million, or 1.5%, above the FY09 enacted level [*\$30.3 billion*]. The increase for the NHGRI programs is targeted at respectively 3.6% and 1.7% in the two bills.

### **Genetic Information Non-Discrimination Update**

The provisions of Genetic Information Non-discrimination Act (GINA) for health insurance (Title I) went into effect on May 21st of this year under the statutorily mandated timeframe. The regulations for this section, and those for the Title II employment provisions, have been under development since GINA was signed into law, and there has been a very strong effort to coordinate among all jurisdictions. The effective date for Title II is November 21st of this year.

Although this process has taken longer than hoped, the Title I regulations interpreting the bill's requirements in health insurance are expected any time. These regulations had to traverse a particularly complex clearance process because they involved components requiring the Department of Treasury, the Department of Labor, and two entities within the Department of Health and Human Services to draft regulatory provisions in a non-conflicting and harmonized fashion. The Equal Employment Opportunity Commission has been working on the employment sections of the law during this time.

### **Peer Review Update**

Several aspects of the new peer review system are now in place. These include the use of a 1-9 point scoring system, revised review criteria with criterion sub-scores provided by each assigned reviewer, and use of a new bullet-style format that is intended to make reviewer comments more succinct. The reviewers will also review applications in best to worst order of the preliminary scores.

Anecdotal observations indicate that reviewers are comfortable with the new scoring system. It seems to be easier for them to work with the fewer numbers in the scoring system, although there reportedly were difficulties distinguishing between scores 2 and 3. Some reviewers continue to write lengthy paragraphs instead of bullet points.

Applicants have showed some confusion about the alignment of the sub-scores with the overall impact scores. There is a level of ambiguity, a lack of information in the new summary statement format that is causing further confusing. Attention needs be given to relaying the proper information to applicants to enable them to better understand their score and the reasoning behind it.

The peer review changes are still in the evaluation stage. The changes that have been implemented on reviews done during the summer 2009 will be evaluated by the Office of the Director. An online survey of applicants and reviewers will bring in some feedback about the new review process, which will be evaluated by a contractor with results expected in October, 2009.

In discussion, Council members noted that the summary statement is an important means for applicants to receive feedback to improve their grant applications, and expressed concern that the bulleted style of the reviews might be problematic for providing sufficient feedback in proper context for the applicant. One of the reasons for conducting the online survey is to get this kind of feedback from more participants in the review process.

Council also expressed concern about the effect of the order of review on scores. NIH staff are currently considering a more dynamic and fluctuating order for reviews. However, this is a dynamic calibration and its utility will need to go through testing for its contribution toward improved review.

Council commented that NIH should seriously consider who the real customers of the summary statement are. CSR has stated that Council and the staff who make funding decisions are the main customers of the summary statement. The original intent, according to these statements, was primarily not for the summary statements to be used by applicants to help them be more informed about the evaluation of their grant application. Council members strongly stated, however, that researchers have used summary statements for a long time as important learning material, and that program officers varied widely in their practice and ability to provide information about reviews to applicants. Feedback to applicants continues to be a very important part of researchers' learning process for writing grants and their subsequent career development. Council noted that the importance of NIH finding a proper balance between the tutorial role of the summary statement and the sustainability of the review system. If the summary statement is no longer going to be expected to provide sufficient information about the review, program officers will have increased responsibility to attend the reviews and provide the information to applicants. At the least, summary statements should contain enough information, such as important weaknesses, to be useful to applicants in improving future applications. The guiding principle when it comes to summary statement has always been to make it clear why the researcher received a specific score.

#### **Program on Therapeutics and Neglected Diseases (TRND) – Chris Austin**

TRND is a new NIH program that is designed to bridge the space between basic research and drug development, with a goal to get drugs to the markets. Even with the productivity of genomics, translating the genome into biological insights and therapeutics remains an unsolved

problem. Currently, the drug development process has a number of problems. For example, not only are a small percentage of diseases and genome-encoded targets being considered for drug development, these are mostly diseases that are highly prevalent in the developed world. Rare and neglected diseases, which either have a very low prevalence rate within the USA, or are mostly infectious and subsequently found mostly in improvised countries, are not major foci for drug development in the private sector. TRND is a trans-NIH initiative to build an integrated drug development pipeline for rare and neglected diseases by providing capabilities that most academic drug research programs cannot take new molecular targets or chemicals that may have therapeutic potential and conduct the many types of studies need to develop a new drug. The program recognizes that the failure rate of the drug development pipeline is very high and expensive. 20% of the effort of TRND will be allocated toward improving success rates.

One of the major areas of research at the NIH Chemical Genomics Center (NCGC) is novel targets for rare or neglected diseases. NCGC, which is an intramural NIH program, also collaborates extensively with scientists in the extramural community. NCGC will be a principal collaborator in TRND, allowing the program to take advantage of both of these features. TRND will work closely with disease-specific experts on selected projects, leveraging both the in-house scientific capabilities needed to carry out much of the preclinical development work, and contracting out other parts, as scientific opportunities dictate. This work is expected to enable the mission of all the institutes of the NIH, as there are 6000-7000 diseases that qualify as rare and neglected. Since TRND will only be able to work on a very small number at a time (plans are to start with 5), it will be very important to determine milestones that will allow the program to know when to stop working on specific diseases and when to continue. The non-profit community, including organizations such as the Genetic Alliance, is considering contributing to this initiative as well.

Council inquired about the program working with previously approved compounds. Dr. Austin noted that such an effort is currently ongoing, with the NCGC having already collected about 500 approved compounds. Council was very encouraging and looked forward to the impact that improvements in technology will have on the work of the program.

#### **American Recovery and Reinvestment Act (ARRA)**

As expected, the NIH received an extraordinarily large number of applications for the ARRA Challenge Grant (RC1) and Grand Opportunities Grant (RC2) programs. To handle this number of applications, the Center for Scientific Review (CSR) established a two-level editorial review process which involved an initial triage, after which 20% of the submitted applications went to study section review. For example, NHGRI received 210 Challenge Grant applications; 30 of these were reviewed and 13 were proposed for funding. In total, NHGRI considered 472 applications for RC1, RC2, competitive supplements, administrative supplements, and additional R01s beyond the payline. 122 were proposed for funding. NHGRI has spent \$113.6M (of the \$127M appropriated) of its ARRA funds to date. The remainder were held back for award early in 2010, as the Institute had announced a receipt date of December 1, 2009 for additional administrative supplement requests.

ARRA awards were made in all of the areas that the Institute had announced as priority areas. Sequencing technology (NHGRI's Signature Project), and genomic function received the most funding, along with a new program for Medical Sequencing Discovery projects to mid-size sequencing laboratories, as had been recommended by the March 2009 Sequencing Workshop. Funding in the ELSI area went entirely to Challenge Grants.

The following points were made during discussion with Council members. ARRA activities will be handled with a very high level of transparency and involve extensive tracking and reporting. Congress will use the number of people hired as one measure for success; the tracking of these statistics will be done centrally by NIH. ARRA could provide the opportunity to look at the value of short-term very directed funding.

### **COUNCIL-INITIATED DISCUSSION**

Council members suggested an usually large number of potential agenda items for the September 2009 Council:

1. An update on the search for a new NHGRI Director
2. Status of the current planning process.
3. Further discussion on genomics training for primary-care physicians.
4. Data release policy implementation and an update from the Toronto data release workshop
5. Discussion with the new NIH Director, Dr. Collins
6. Family history and the future of risk calculation using genetic data.
7. ClinSeq
8. Patenting
9. An update on third-generation sequencing technologies
10. An update on plans the ENCODE and modENCODE midcourse review Update
11. An update on the follow up of the ELSI review
12. An Updates about informed consent issues
13. Global health and the NIH Director's plans
14. Sequence data management and report from the Cloud Computing Workshop

### **ANNOUNCEMENTS AND ITEMS OF INTEREST**

Dr. Guyer directed Council to the Council folders containing items of interest, reports from liaisons, and information on the FY 2010 budget.

### **CONFLICT OF INTEREST**

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

## REVIEW OF APPLICATIONS

In closed session, the Council reviewed 396 applications, requesting \$231,591,929. The applications included 68 research projects, 84 ELSI grants, 3 research center grant, 2 conference grants, 1 career transition award, 13 SBIR Phase I grant, 4 SBIR Phase II grants, 1 STTR Phase 1 grant, 4 individual training grants, 2 continuing education training award, and 8 resource access awards. A total of 157 applications totaling \$73,416,940 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

\_\_\_\_\_  
Alan Guttmacher, M.D.  
Chairman  
National Advisory Council for Human Genome Research