## NATIONAL ADVISORY COUNCIL FOR HUMAN GENOME RESEARCH MEETING SUMMARY

May 19-20, 2014

The Open Session of the 71<sup>st</sup> meeting of the National Advisory Council for Human Genome Research (NACHGR) was convened at 10:00 AM on May 19, 2014, at the Fishers Lane Terrace Level Conference Center in Rockville, MD. Dr. Eric Green, Director of the National Human Genome Research Institute (NHGRI), called the meeting to order.

The meeting was open to the public from 10:00 AM until 4:30 PM on May 19, 2014. In accordance with the provisions of Public Law 92-463, the meeting was closed to the public from 8:00 AM to 10:00 AM and 4:30 PM to 6:00 PM on May 19, 2014, and from 8:00 AM until adjournment on May 20, 2014, for the review, discussion, and evaluation of grant applications.

Council members present: Eric Boerwinkle, ad hoc Joseph Ecker, ad hoc James Evans Chanita Hughes-Halbert, ad hoc Martin Kreitman, ad hoc Howard McLeod Deidre Meldrum Jill Mesirov Anthony Monaco Lucila Ohno-Machado David Page, ad hoc

Council members absent: Carlos Bustamante Lon Cardon, ad hoc Howard Jacob Amy McGuire Robert Nussbaum

#### Staff from the National Human Genome Research Institute

Nonie Arora, DPCE Alice Bailey, DPCE Jessica Barry, ERP Shannon Biello, ERP Vivien Bonazzi, ERP Vence Bonham, DPCE Lawrence Brody, ERP Fave Brown, DPCE Comfort Browne, ERP Christine Chang, ERP Cheryl Chick, ERP Monika Christman, ERP Deborah Colantuoni, ERP Catherine Crawford, ERP Chris Darby, ERP Christina Daulton, DPCE Camilla Day, ERP Nicholas Digiacomo, ERP Elise Feingold, ERP Adam Felsenfeld, ERP Leigh Finnegan, ERP Ann Fitzpatrick, DM Brandon Floyd, ERP Tina Gatlin, ERP Jonathan Gitlin, DPCE Bettie Graham, ERP Linda Hall, ERP Joe Henke, DM Lucia Hindorff, ERP Heather Junkins, ERP David Kaufman, ERP

Manjit Kaur, DPCE Destiny Lancaster, ERP Ronalina Li. ERP Nicole Lockhart, ERP Mark Lucano, DM Ebony Madden, ERP Allison Mandich, IOD Teri Manolio, ERP Jean McEwen, ERP Keith McKenney, ERP Jeannine Mjoseth, DPCE Preetha Nandi, ERP Jacqueline Odgis, ERP Vivian Ota Wang, ERP Michael Pazin, ERP Ajay Pillai, ERP David Robinson Laura Rodriguez, DPCE Kate Saylor, DPCE Jeffery Schloss, ERP Michael Smith, ERP Jeff Struewing, ERP Kathie Sun, ERP Jennifer Troyer, ERP Simona Volpi, ERP Lu Wang, ERP Chris Wellington, ERP Kris Wetterstrand, IOD Ken Wiley, ERP Sherry Zhou, ERP

#### Others present for all or a portion of the meeting:

Raeka Aiyar, Genetics Society of America Adam Berger, IOM Natasha Bonhomme, Genetic Alliance Bob Cook-Deegan, Duke University Jaclyn Karasik, Duke University Jon Lorsch, NIGMS Joseph McInerney, ASHG Leah Miller, NIH/OD Nicole Mizell, NIAID David Robinson Rhonda Schonberg, NSGC

## INTRODUCTION OF NEW NHGRI STAFF, LIAISONS, AND GUESTS

## APPROVAL OF MINUTES FOR THE FEBRUARY, 2014 MEETING

### **DIRECTOR'S REPORT**

Dr. Eric Green presented the Director's Report to Council.

### PRESENTATION FROM NIGMS DIRECTOR by Jon Lorsch

Dr. Jon Lorsch gave a presentation about the National Institute of General Medical Sciences (NIGMS).

Council was interested to hear about NIGMS's idea of supporting investigators' full research programs rather than individual research projects (similar to the Howard Hughes Medical Institute model), and wondered how NIGMS is thinking of implementing this since many investigators have projects funded by multiple NIH institutes/centers (ICs). Dr. Lorsch replied that the initial program will target PIs with multiple NIGMS grants, and if this proves to be successful, then expansion of the program could be considered more broadly to include investigators whose research interests and sources of funding involve multiple ICs. If an investigator has a large basic research portfolio that is NIGMS funded, and would like to expand in a translational way to study a particular disease, then disease-specific ICs could pick up these related projects. Council noted that many disease-specific ICs also fund basic computational research.

Council asked how NIGMS plans to monitor the long-term expense associated with an increasing number of databases, the inevitable increase in the scope of many databases as the capacity to produce data rapidly increases, and how NIGMS and NHGRI plan to get other stakeholders to contribute funding to support these databases. Dr. Lorsch agreed that as databases become more important, it is necessary to continue to support them while devising efficient ways to manage unbridled increases in their costs. The cost increase issue validates the decision of Dr. Francis Collins to create a new leadership position at the trans-NIH level to address the problem. The first Associate Director for Data Science, Dr. Philip Bourne, is starting to look into ways to increase efficiency and decrease costs, such as forging stronger connections among the databases. Dr. Green noted that the Moore Foundation held a meeting recently that focused upon the issue of the growth of databases. It is becoming clear that the solutions to the problem will not be simple or short-term, and organizations beyond NIH, including the private sector, will have to be involved in developing long-term solutions to this looming problem.

One of the key areas addressed during the NHGRI-NIGMS retreat on December 2, 2013, was technology development. One conclusion from that retreat is that additional retreats involving the two Institutes should be planned, and one of them will focus on technology development. Currently, one branch of NIGMS is focused entirely on technology development. NIGMS hopes to tap into the experience gained at NHGRI from the massive expansion of genome sequencing technologies into the broader research community. An important question at NIGMS is how to determine the most cost-effective ways to support the broad range of technology development programs that need to be done at many different scales. Currently, NIGMS supports P41 Centers and individual investigator R21 grants, with very little else in between.

Council noted that, in the pharmaceutical and biotechnology space, many cellular assays are being used to develop therapeutics. A question was raised about how NIGMS plans to interact with industry, and what standards should be set regarding cell lines to help address the problem of reproducibility in research results. Dr. Lorsch noted that the driver of recent reproducibility discussions came largely from pre-clinical research results that were found not to be reproducible and therefore were not translatable. NIGMS includes industry representatives on its Council, and plans to engage and consult additional industry representatives and stakeholder organizations to gain the necessary expertise and advice to guide the research standards that will be established.

In responses to Dr. Lorsch's presentation of the 15-year NIGMS funding trend of investigatorinitiated research vs. targeted supported of specific areas of research, Council asked what NIGMS perceived to be the appropriate level of funding for investigator-initiated research. Dr. Page also inquired if other ICs at NIH were reconsidering the proportion of their funds that would go to investigator-initiated research, and what kind of resistance NIGMS anticipates it will encounter to the decision to increase support of investigator-initiated research and reduce the amount of funding for targeted research. Dr. Lorsch responded that NIGMS is in the middle of a strategic planning process for the next 5 years, and determining the optimum level of support for investigator-initiated research will be decided through the strategic planning process. He did acknowledge that a substantial increase likely will occur. Regarding the discussion of this issue more broadly across NIH, Dr. Lorsch noted that each IC has its own mission and must determine what mechanisms are best suited to help them achieve their research goals. He noted that the origins of the shift of research funding from investigator-initiated to targeted research programs can be found in the doubling of the NIH budget that began in the late 1990's. and now that the NIH budget has been flat or reduced for the past several years many ICs are looking very carefully at how their funding should be distributed. But there has not been broad discussion of this topic collectively among the IC Directors. Finally, Dr. Lorsch noted that, for the most part, feedback from NIGMS stakeholders has been very positive about the plan to increase support of investigator-initiated research.

Council agreed that contaminated or mislabeled cell lines are critical factors affecting the reproducibility of research findings, but they noted that a reproducibility problem also exists in bioinformatics, where poorly documented software often makes coding unusable to other investigators. Since this is still regarded as a relatively young field of study, it is appropriate to address this problem now. Council advised not to underestimate the ability of NIH to change the behavior of scientists in many different aspects of biomedical research. Dr. Lorsch noted that NIGMS's FOA to develop transportable training modules is, in part, an attempt to induce a cultural shift in attitudes about sharing outcomes and resources related to training.

Council questioned what positive or negative incentives were being considered to induce PIs to comply with data sharing policies and put their data in the public domain. Laura Rodriguez described progress on the most recent version of an NIH genomic data sharing policy. She noted there has been lots of discussion about what incentives could be implemented to increase compliance with the policy. The new policy has been approved internally, and it is expected to be published in 4-6 weeks, with implementation planned for applications received in 2015 that would be funded in Fiscal Year 2016.

Council asked how NIGMS sets boundaries for its clinical research program; specifically, how does NIGMS determine when a clinical study has become "too clinical"? Dr. Lorsch noted NIGMS is responsible for certain clinical areas of research (for example, trauma, anesthesia, emergency care, burns, sepsis, etc.). Within these areas, NIGMS looks for clinical advances

that will increase our fundamental understanding of the underlying processes that led to the clinical advances. Thus, even in the more clinical aspects of their research portfolio, NIGMS attempts to retain the over-riding goal of their mission – to achieve fundamental advances in all of the research sponsored by NIGMS.

### CONCEPT CLEARANCE, eMERGE PHASE III by Teri Manolio

Dr. Teri Manolio presented a concept clearance for eMERGE Phase III.

Council commended the productivity of the eMERGE network, citing 332 publications across the wide spectrum of studies coming from this network. Council noted the unique nature of this network. One example is that it is doing applied ELSI research, the products of which are more easily and readily utilized by hospitals than typical academic research findings, and it has helped hospitals and health care systems make decisions about how and when to implement genetic and genomic technologies. Council commented that eMERGE should emphasize the fundamental discoveries that have been made not just about a particular disease, but a class of diseases that affect a particular organ. The example cited was *FOXE1* and its association with hyperthyroidism; but several other thyroid diseases have also been shown to be associated with *FOXE1* as a result of conducting a phenome-wide association study (Phe-WAS). Council also commented on the large amounts of data that are now publicly available via dbGaP as a result of the eMERGE program, and this is an impressive asset to a broad community of biomedical investigators.

Regarding the question of how much of eMERGE III should be focused on discovery versus implementation research, Council noted that arguments could be made for either goal. But the most appropriate course is to let the balance between the two goals be determined by the data that are collected from the projects funded by this RFA.

Some Council members raised concerns that the plan to limit the scope of the research to a select set of candidate genes represented a much too narrow goal. They noted that NHGRI should always promote genomic approaches in research, and limiting the research scope to a set of approximately 100 candidate genes is not very forward-looking. Council acknowledged there are cost and return of results issues to overcome in setting a broader scope for this RFA, but the solution to those problems will only be found by taking them on directly. NHGRI should anticipate future cost reductions for whole-exome and whole-genome sequencing, and plan to take advantage of those technology improvements. Other Council members acknowledged there is a need to do whole-genome sequencing on a much larger number of subjects, but it's not clear if that sequencing work needs to be done in a clinical context or in the context of a research project outside of the eMERGE program.

Council noted that the tremendous increase in the use of electronic medical records brings unprecedented opportunities, and that eMERGE is well-positioned to mine data necessary to identify the association of genotypes and phenotypes and answer other types of research questions, such as determining the penetrance of disease genes. NHGRI should give high priority to research activities that focus attention on the interface with the electronic medical records.

Some Council members encouraged greater focus on implementation, and noted that eMERGE is uniquely positioned to address how to translate genomic information into patient care and to understand the positive and negative consequences of that implementation step. Furthermore,

eMERGE should continue to address a diversity of clinical issues that are relatively rare overall, but more prevalent in some populations. Finally, eMERGE should help to resolve discrepancies between the interpretations about genomic of variants among different laboratories. Dr. Manolio noted that one way that eMERGE can help do this is to delve into the wealth of information in electronic medical records and study the associations (or lack thereof) of variants with phenotypes.

One Council member noted that it is easy to underappreciate the difficulty of doing phenotyping as a stand-alone activity. Extracting information from the narrative format of clinical notes is a difficult task, so the recipes for phenotyping and the natural language processing work that has been done in eMERGE are other great values of this program.

For the discovery part of this RFA, to achieve full power to detect variants that may be associated with an observed phenotype, one Council member recommended doing wholeexome sequencing, the increased cost of which could be covered by reducing the number awards. Another Council member noted that if implementation is to be prioritized, then targeted sequencing of a limited number of genes is the logical goal for this RFA because at this point in time, there is a relatively small set of targeted genes for which we have clinically relevant information.

Council raised a number of additional questions about this RFA including: What is the rationale for requiring existing GWAS data? (This requirement creates a barrier for new investigators to compete.) How have the achievements from the first two phases of the eMERGE program informed the goals set for Phase III? What timeline is envisioned to evaluate the impact on cost-effectiveness and health outcomes? (Will this have to be a 5-year or 10-year study in order to effectively assess outcomes in those areas?). These questions originated from the perspective of some Council members that every concept clearance approved by the Council means that other research programs, including RFAs and unsolicited applications, will not be able to go forward. Therefore, for every RFA, the Council and NHGRI staff should rigorously ask two questions. (1) If NHGRI does not pursue this research what would be the impact on biomedical research? (2) Can NHGRI make a truly unique contribution that is unlikely to be substantially filled by other entities?

Council took note of the fact that while many private hospitals may be working on clinical protocols that are similar to the eMERGE III goals, their outcomes are likely to be suitable for the unique structure and features of the hospitals in which they were developed. If eMERGE is successful, it will drive investigators to develop programs that are highly translatable and broadly adoptable.

Regarding the rationale for requiring existing GWAS data, Council suggested decreasing the required number of samples to reduce the barrier of entry for new sites. When asked if a specific number of samples should be set as a requirement for applications, Council responded that applicants should provide a power calculation for their sample set(s), and peer review will determine the feasibility of the study design.

A goal of eMERGE has been to stress the importance of making broad programs applicable to many institutions. There is an expectation that the tools and approaches developed by eMERGE investigators will be taken up broadly by the community. One example is the eMERGE consent form, which is currently widely used. Staff also commented that aspects of ELSI research are integrated throughout the program, and this was another successful achievement of eMERGE in phases I and II.

Council noted that the goals of the eMERGE concept clearances have been lofty and broad, so in 4-5 years it may be difficult to assess whether eMERGE has made a difference and can be considered a success. One Council member offered the opinion that the number of publications produced by consortium members is not a good metric to determine the value of a program. Dr. Green noted that he often hears eMERGE discussed in other venues. Specifically, In scientific discussions about genomics and the implementation of electronic medical records, research accomplishments from eMERGE are frequently referenced, and investigators of the eMERGE Consortium are widely recognized for their expertise.

Council suggested that the RFA could stipulate that the applicants should define concrete metrics and milestones by which the success of the program should be judged. Another suggestion from Council was to use an objective baseline measurement of how many health care organizations make use of electronic medical records and genetics/genomics data at the present time and then five years from now when eMERGE III has been concluded.

In the language of the concept clearance, eMERGE's goals were framed in terms of health outcomes and cost effectiveness. Council stated that eMERGE should be judged against these metrics as well. They also noted the critical importance of health outcomes, and it would be very valuable to include in the RFA a requirement to describe a plan to effectively and easily measure changes in health outcomes.

Council voted to approve the eMERGE Phase III concept clearance, with 10 votes for approval, 1 vote opposed and 1 vote to abstain.

# PRESENTATION ON THE CLINICAL SEQUENCING EXPLORATORY RESEARCH PROGRAM by James Evans

Dr. James Evans gave a presentation on the Clinical Sequencing Exploratory Research (CSER) Program on behalf of the CSER principal investigators.

Council asked Dr. Evans how he defined the term "possible causal (genomic) variant" as he used it in his presentation. He noted that this is difficult to define, but there are three scenarios where a variant could be classified as a possible causal variant. First, a new variant is found in a gene that has been previously been shown to be associated with a specific disease. Second, an obvious gene disruption is found in one chromosome of a patient with a recessive trait, but no mutation is found in the second homologous chromosome. Third, a variant is found in a gene whose function does not seem consistent with the phenotype observed in the patient. A further complication is that different labs have different standards for interpreting and reporting such variants.

One Council member noted that 5 - 6% of CSER cases having incidental findings seemed high. Dr. Evans explained that this percentage is defined by what percentage of people have what appears to be a pathogenic variant in a gene that falls into the "medically actionable" category; thus, the number of patients defined as having incidental findings depends on various definitions of actionability.

Another Council member noted the distinction between erroneous versus premature implementation. He thought that there is little harm relative to the gain that could be realized by pushing genomic technologies broadly into the translational setting. Dr. Evans thought

otherwise – that research on the whole genome should be expansive, but implementation should be conservative and limited in scope, and only be done if better outcomes can be achieved. He thought the proper approach would be to constantly "skim" the most clinically robust findings into implementation as our knowledge about genomic variants rises to a level where there is much less chance of harmful outcomes to patients and family members. It was clarified that while discovery does happen in CSER, implementation is a critical and more important focus, and whole-genome sequencing costs versus benefits must be weighed at many points in time.

Council noted that is important to be careful about estimating penetrance from clinical-based samples. The population-based epidemiological studies have much better and much deeper phenotyped samples, and ascertainment bias is less of a concern with these samples.

Council asked what CSER hopes to change regarding genetic heterogeneity in intellectual disabilities. Dr. Evans noted that making the right genomic diagnosis can, in some cases, have a tremendous impact on treatment. In some cases, diagnosis helps with prognosis, and issues such as family planning, even if it is not usually a game-changing event. Better diagnostic modalities are at least helpful in mitigating the personal "diagnostic odyssey" of some patients as they go through multiple rounds of unnecessary doctor visits and testing. In this area, CSER investigators could document whether their research efforts are making a difference economically as one metric of success.

Council asked how CSER plans to address the need for collection of other –omics datasets. Dr. Evans responded that tumor genome sequencing might be the best setting to test the impact of adding expression data, by performing RNA-Seq to inform whether a particular mutation is going to cause increased susceptibility to different possible therapeutic drugs.

# PRESENTATION ON THE CENTERS FOR MENDELIAN GENOMICS PROGRAM by Richard Lifton

Dr. Richard Lifton gave a presentation on the Centers for Mendelian Genomics (CMG) Program on behalf of the CMG principal investigators.

Council asked Dr. Lifton if there are data suggesting that causal mutations for Mendelian diseases may reside in non-protein-coding regions of the genome. Dr. Lifton responded that there are several examples of patients that lack detectable mutations in the exome portion of their genomes and the CMGs are at a transition point where it is becoming practical and affordable to consider doing whole-genome sequencing on these unsolved cases. In OMIM there are a very small number of cases where linkage has been found, and the trait has been mapped to a specific region of the genome, but mutations in protein-coding regions have not been identified. This indicates that whole-genome sequencing should be selectively deployed in the characterization of Mendelian traits, and the CMG investigators are enthusiastic to begin applying whole-genome sequencing in their Centers.

Council questioned if it is realistic to expect there will be at least one Mendelian trait associated with each of the 21,000 protein-coding genes in the human genome. Dr. Lifton noted that we can expect that mutations in 15 - 30% of genes will be embryonic lethals; therefore, these mutations will not be observed in the human population. But his expectation is that the vast majority of genes are being maintained in the human population due to selection; therefore, the genes must have important functions, and we can expect a consequence to their inactivation.

Many phenotypes will only be displayed in the right environment, and it will be difficult to assign a phenotype to otherwise healthy individuals. The preferred approach would be to sequence individuals that have a significant medical illness, without an obvious diagnosis; this could lead to the identification of new traits or diseases that are associated with mutations in genes that have not been previously characterized.

Council asked Dr. Lifton about the challenges associated with interpretability of genomic variants that are discovered, noting there is likely a "publication bias" that results in investigators selecting for variants that are more easily interpretable and for which there is some information that helps to link the variant to the phenotype being studied. Council noted that while the CMG investigators have been spectacularly successful, it is also evident that there are many more variants that have been identified but not yet published. The reason for this is that the interpretation of these variants has been more difficult, and the CMG investigators lack the time and resources to get deeply involved in functional studies. Regrettably, this prevents broad dissemination of the full set of research results from the CMGs. Dr. Lifton acknowledged that the interests of the CMG investigators often end up contrasted against the interest of the broader public. NHGRI and the scientific community would like to have the variant results made available as quickly as possible, but the investigators are motivated (and now required) to perform functional studies that will enable them to attain publications in high profile journals. Maintaining a proper balance between these two outcomes requires careful attention.

Council stated that during the CMG concept clearance and in the very early stages of the program, they heard about large international efforts in studying Mendelian diseases, and asked how the CMG's interactions have played out with international investigators. Dr. Lifton responded that most collaborations are built on personal relationships that investigators in the CMG network have all over the world. Over 400 collaborators contribute to the CMG pipelines, but most studies are largely the result of chance ascertainment, coupled with existing relationships that CMG investigators have established with researchers around the world going back many years. By nature, the work is not coherently well-organized across the CMG network. Groups are generally happy to collaborate and pool data when both are studying the same mutation. However, Dr. Lifton cautioned that immediate, open access of data might hinder motivation and would likely discourage the amount of international collaboration the CMGs have enjoyed to date.

Given that so many CMG projects involve international collaborations, Dr. Lifton was asked if there are global issues in IRB standards, ethics, or data sharing that U.S. investigator should be studying more carefully. Dr. Lifton stated that international IRB standards are very different from what has evolved in the U.S., in part because insurability and employability issues drove the standards and practices in the U.S. and they are unique to the U.S. versus countries with national healthcare systems. With regard to data sharing, we can be hopeful that many other countries will decide to implement the policies that U.S. scientists have put in place. One benefit of international collaboration is that, since many singleton mutations are discovered, there are often other groups around the world that may also be studying the same genes and may have found other examples of singleton mutations. GeneMatcher, an algorithm developed at Hopkins, allows investigators around the world to put genes being studied in a database (without any phenotypic information). GeneMatcher has the potential to offer a path forward to turn singleton mutations into solved cases by connecting investigators who discover that they have a common interest and data that are valuable to both groups.

One Council member asked how we might systematically get a handle on the role of somatic mutation in human tissue and disease, especially when phenotypes aren't clearly visible. Dr.

Lifton noted that, aside from cancer cases, investigators and physicians rarely get tissue biopsies, and this is a major limitation to the study of somatic mutations and their role in disease development.

In response to a question of what is keeping us from completing the catalog and defining all Mendelian diseases, Dr. Lifton replied that ascertainment, scaling up the collection of patients, and funding are the main roadblocks. However, costs are coming down with the next generation of DNA sequencing instruments. The CMGs initially underestimated the cost and challenge of case ascertainment due to the lack of patients coming through the joint sample solicitation web portal. This caused each Center to ramp-up their individual ascertainment activities. At this time, the overall program is doing well with respect to recruitment.

## COUNCIL-INITIATED DISCUSSION

Council asked for a presentation on the R01 portfolio to put it into proper context relative to the other research initiatives of NHGRI. This information was included in Dr. Schloss' closed session presentation earlier in the day, and he will revisit this part of his presentation to make sure it is highlighted in sufficient detail at future Council meetings.

Council would like to hear an update from Dr. Schloss about what technology development is currently happening and what is still needed in genomics. They would like to know what is next for the \$1000 genome program, and what the needs of the field are. At the February 2014 Council meeting, there was some discussion about the need for more functional assays, and this might integrate into a broader discussion about NHGRI's overall plans for technology development.

Council suggested that the new director of the Division of Genomics and Society, Dr. Larry Brody, give a presentation on his vision of the research goals for this new Division. Dr. Brody will give a presentation in connection to the update that will be given by the NACHGR Genomics and Society Working Group at the September 2014 Council meeting.

Looking at initiatives across the board, Council asked if it was possible to get examples where genome sequencing or other genomic technologies have made a difference in clinical outcomes. Council has heard about CSER, IGNITE, and eMERGE, and would like to see case studies or something similar to highlight the value of these programs.

### ANNOUNCEMENTS AND ITEMS OF INTEREST

Dr. Rudy Pozzatti drew Council's attention to three items of interest:

- 1) National Society of Genetic Counselors (NSGC) February 2014 Report to Council
- 2) American Society of Human Genetics Report to Council
- 3) Genetic Alliance Report to Council

## CONFIDENTIALITY AND CONFLICT OF INTEREST

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

### **REVIEW OF APPLICATIONS<sup>1</sup>**

In closed session, the Council reviewed 306 applications, requesting \$465,434,935 (total cost). The applications included: 129 research project grants, 11 ELSI applications, 120 research center applications, 1 conference application, 5 career transition award applications, 26 SBIR Phase I applications, 6 SBIR Phase II applications, 4 STTR Phase 1 applications, 1 STTR Phase 2 application and 3 education project award applications. A total of 161 applications totaling \$156,680,735 were recommended.

09/8/2014 Date

Rudy Pozzati Rudy Pozzatti, Ph.D. **Executive Secretary** National Advisory Council for Human Genome Research

09/8/2014 Date

Eric Green

Eric Green, M.D, Ph.D. Chairman National Advisory Council for Human Genome Research

<sup>&</sup>lt;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" votes.