Center for Scientific Review
Center for Scientific Review Advisory Council Meeting
National Institutes of Health
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March 27, 2017

The Center for Scientific Review Advisory Council (CSRAC) convened at 8:30 a.m., Monday, March 27, 2017, at the Center for Scientific Review (CSR), 6107 Rockledge Drive, Bethesda, MD. The entire meeting was held in open session. Richard Nakamura, Ph.D., presided as chair.

Members Present

Alfred L. George, M.D. *(ad hoc)*
Paula Hammond, Ph.D.
Michael Hollingsworth, Ph.D.
Richard Nakamura, Ph.D.
José López, M.D. *(ad hoc)*
Julie C. Price, Ph.D. *(ad hoc)*
Stephan Targan, M.D.
Jennifer West, Ph.D.

Rene Etcheberrigaray, M.D., was the executive secretary for the meeting.

I. Welcome and Introductions

Dr. Nakamura, CSR Director, welcomed CSRAC members, CSR staff, and other attendees. He introduced the new members and thanked all members for their time and expertise. He asked for a motion to approve the minutes from the CSRAC September 26, 2016, meeting. CSRAC approved the minutes.

II. Research Commitment Index: A New Tool to Explore Investigator Bandwidth

Jon Lorsch, Ph.D., Director of the National Institute of General Medical Sciences (NIGMS), reported on the development of a measure to analyze scientific commitment and its impact on productivity. An analysis of NIH grants shows 10 percent of principal investigators (PIs) receive more than 40 percent of NIH funding. The measure revealed diminishing returns, if any, above a certain funding level. Many institutes and centers (ICs) see a leveling-off of publications, both in raw number and scientific impact, especially above the $500,000 level. Other agencies have also seen diminishing returns using a variety of metrics.

Development of the Research Commitment Index

NIGMS and the Office of Extramural Research (OER) developed the Research Commitment Index (RCI) to measure a PI's committed bandwidth. The RCI recognizes differences in grant mechanisms and the fact that some science, such as large clinical trials, is more expensive. The tool benchmarks a scale that begins by assigning 7 points to an R01. Most PIs are assigned a 7 (one R01) or 14 (two R01s); those with higher scores have more grants. The scores show an explosion in disparity since 1995, in which a small group of PIs accumulated a larger share of funding. Variables include the type of project, seniority of the PI, and relative citation ratio (RCR). Findings include a flattening of the RCR above a certain funding level. The analysis shows a similar effect among PIs who also receive Howard Hughes Medical Institute funding.

Funding over a certain level is also not correlated with mentorship, as measured by the number of early stage investigator (ESI) awardees trained per mentor.

Closing Thoughts and the R35 as a Possible Solution

Dr. Lorsch said the current system is unstable, with hyper-competition and a highly skewed funding distribution. It hurts early- to mid-career faculty the most. Limiting the total amount of funds to an individual PI could possibly allow for the funding of more investigators, with a resulting reduction in applicant burden, and greater returns for NIH's investment.

NIGMS is piloting the Maximizing Investigators' Research Award (MIRA, or R35), which provides a single grant to an investigator rather than to individual projects. An advantage for the review process is that the PI does not submit multiple R01 applications. The R35 is in the second round, with CSR reviewing ESI applications and NIGMS reviewing applications from established investigators.

Discussion Highlights

- ***Accuracy of the RCI:*** Alfred George, M.D., noted many junior scientists go into industry and other fields, rather than academic research, given the saturated market. ESI awards may not be an accurate reflection of mentorship in a given lab. Michael Hollingsworth, Ph.D., noted the RCI does not take into account other outcomes. For example, clinical trials are expensive and may result in just one paper, but can greatly impact practice. Dr. Lorsch said other studies have seen diminishing returns above a certain point, including a review of the National Heart, Lung and Blood Institute (NHLBI) clinical trials portfolio.
- ***Cost of science:*** Dr. Hollingsworth asked whether a cost index is factored into the analysis, as the cost of science has increased since the mid-1990s. Julie Price, Ph.D., reinforced that some science costs more. Dr. Lorsch said the MIRA is a remedy to funding labs with multiple R01s. He also challenged the idea that success requires a large lab.
- ***MIRA review:*** Paula Hammond, Ph.D., asked whether components of the MIRA exacerbate disparity. Dr. Lorsch acknowledged concern because of the MIRA's focus on track record, and they have analyzed the outcomes of each round with this in mind. To date, ESI MIRA awardees have been two years younger than ESIs who received R01s.
- ***Team science:*** Dr. George asked about the relationship between the RCI and the modified Relative Citation Ratio. Larger grants are team science-oriented, which influences the number of publications and citations. Publication standards have also changed over the years. He cautioned against over-interpreting publication data.

III. CSR Update

Dr. Nakamura reviewed the CSR mission and highlighted new CSR hires and promotions since October 2016.

Employee Survey

He then reported on results from a 2016 employee survey, sharing NIH and CSR-specific data. The CSR data, which are generally positive, mask differences across Integrated Review Groups (IRGs) related to perceptions about leadership and management. CSR senior staff is discussing the findings for possible solutions.

Changes in Expectations

Applicants, reviewers, and scientific review officers (SROs) have had to respond to many changes in expectations. The system changes in some way in almost every round.

Rigor and Reproducibility

Rigor and reproducibility is an important overall issue for many reasons. It is important to communicate the need for NIH's initiative in this area and to ask review committees to pay more attention to it. The results are paying off.

CSR Approach to Measuring Review Output

CSR is trying to improve review quality by emphasizing evaluations by the scientific community; experiments in review; and evolutionary improvements of staff, organization, and processes. He asked Council for input on whether the review and award process can be sped up, and if CSR should consider directly reviewing papers.

He noted CSR has already undertaken and reported on quality activities, including studies of ranking and scoring procedures, with several others in process.

Fairness of Review

CSR is designing a large-scale anonymization experiment to understand the gap in review outcomes between black and white scientists. He reviewed the study's assumptions, aims, and design. The Center will do a preliminary study on 90 applications; a total of 2,400 are envisioned.

Future of Science and Technology

Dr. Nakamura reviewed appropriations and the numbers of NIH grant applications since 1998. Excluding a spike after the American Recovery and Reinvestment Act in 2009, applications are at record numbers.

IV. National Institute on Minority Health and Health Disparities Update

Eliseo J. Pérez-Stable, M.D., Director of the National Institute on Minority Health and Health Disparities (NIMHD) since September 2015, presented on the history, mission, and vision of the Institute.

Minority Health and Health Disparities Research at NIH

After providing background and definitions related to minority health and to health disparities, Dr. Pérez-Stable highlighted mechanisms that lead to health disparities. NIMHD has developed a research framework that looks at biological, behavioral, physical, sociocultural, and healthcare system determinants, from the individual to the societal level. They collect minority data based on nomenclature used by the Office of Management and Budget. They also consider rural populations and sexual gender minorities in health disparity research.

Priorities

NIMHD emphasizes the inclusion of diverse participants in biomedical research, not just research with a minority health or disparities focus. Dr. Pérez-Stable acknowledged the challenges in recruiting minorities but also expressed the need to end the myth that the barriers are insurmountable. The Institute also seeks ways to improve workforce diversity.

Dr. Pérez-Stable said the Institute promotes innovation from extramural scientists in funding R01 applications, as well as in collaborating with other ICs. In the October 2015-September 2016 Councils, CSR helped in the review of 228 Research Program Grant (RPG) applications. He reported on the study sections that reviewed these applications and how they fared. NIMHD has created functional extramural programs in clinical health services research, integrative biological and behavioral sciences, and community health and population science. NIMHD will also support several new research areas in FY 2017. In August 2016, NIMHD lead a Health Disparities Research Institute in Bethesda and cosponsored several workshops. NIMHD also is in the process of creating an intramural program, which will begin with the hiring of a scientific director.

Discussion Highlights

- ***Workforce diversity:*** In answer to a question from Dr. George, Dr. Pérez-Stable said NIMHD is involved in supporting diversity through training grants, working closely with Hannah Valentine, M.D., Chief Officer for Scientific Workforce Diversity, and others. The plan is for NIMHD to invest in training, perhaps through a K program.
- ***Academic institutions:*** Dr. Pérez-Stable explained that NIMHD has retooled the Research Centers for Minority Institutions program. A new Funding Opportunity Announcement (FOA) was published in December 2016. A variety of institutions responded.
- ***COBRE program:*** Dr. Hollingsworth suggested collaborating with the Centers of Biomedical Research Excellence (COBRE) program, which expands research capacity. Dr. Pérez-Stable said he would look into possible NIMHD involvement.

V. Incorporating Preprints and Other Interim Products into NIH Review

Neil Thakur, Ph.D., Special Assistant to the NIH Deputy Director for Extramural Research, reported on a recent Request for Information: Reporting Preprints and Other Interim Research Products, related to the use of preprints and preregistered protocols in the review process.

Background

HHMI, the Wellcome Trust, and other funding institutions accept these products in an application. NIH wanted to issue clear guidance since its rules were confusing. NIH's interest is to support stable rules that advance science and to prevent bad practices from taking root.

The Request for Information resulted in 351 responses and rich feedback. Most were very positive. Many respondents said interim products speed up scientific dissemination and allow for comments that can improve the product and develop collaborations. A minority did not support the change because preprints are not peer-reviewed.

Updated Instructions

Updated instructions apply to May 2017 and thereafter. They call for citation standards in including preprints in applications, including a permanent identifier, clear identification of the product as interim, and acknowledgment of funding. Repository best practices are also recommended to make the content findable, accessible, interoperable, and reusable.

Applicants, especially ESIs, have expressed interest in including preprints for peer review. Reviewers, however, are not required to read them.

Discussion Highlights

- ***Space saver:*** In response to a question from Stephen Targan, M.D., Dr. Thakur said the application must still make the case in the allotted pages, with the citations as a reference.
- ***Bias concerns:*** Dr. Price expressed concern that access to negative results in interim products could bias a review. Dr. Thakur said applicants will need to consider this potential impact.
- ***Accessibility via search:*** In response to a question from Dr. Hollingsworth, Dr. Thakur said PubMed does not include interim products, but Google Scholar indexes them. Jose López, M.D., asked, as a journal editor, whether preprints bias the novelty of findings. Dr. Thakur said the journals are also discussing this. Some are not open to preprints while others encourage them. Dr. Nakamura noted the physics, math, and economic communities use this process, and it will take some adjustment for the biomedical community.
- ***Use in review:*** A member of the audience asked about post-submission materials in an appendix. Dr. Thakur stressed the use of preprints is an option and not required for applicants to submit or for reviewers to read. Dr. López said it will increase burden on reviewers as many will feel obligated to read them, especially if they know other reviewers have. He noted that preprint citations are not allowed to be submitted post submission: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-050.html

VI. Proposed Formation of a New Chartered Study Section in the Interdisciplinary Molecular Science and Technology IRG

Noni Byrnes, Ph.D., Director of the CSR Division of Basic and Integrative Biological Sciences, presented on the need to establish a new study section called Cellular and Molecular Technologies (CMT) within the Interdisciplinary Molecular Sciences and Training (IMST) IRG.

Background

In 2004, the Panel on Scientific Boundaries in Review (PSBR) recommended and CSR implemented the formation of the Microscopic Imaging (MI) and Enabling Bioanalytical and Biophysical Technologies (EBT) study sections. In 2010, CSR convened another external working group, which recommended the merger of MI and EBT, forming the Enabling BioAnalytical and Imaging Technologies (EBIT) study section. By 2014, EBIT had grown quite large and the MI-like applications were moved to a recurring "overflow" special emphasis panel (termed EBIT-SEP). In 2015, the scope and boundaries of EBIT and EBIT-SEP were considered by a broad, external bioengineering working group, which recommended that EBIT-SEP either be dissolved or expanded in scope and converted to a chartered study section. It also recommended that CSR identify a review locus for "microphysiological systems."

CMT Formation
To address the recommendations of the bioengineering working group, CMT was envisioned to handle the microscopic imaging applications currently assigned to the EBIT-SEP, to include additional cell-based technologies currently reviewed in other study sections largely within the Bioengineering Sciences and Technologies (BST) IRG, and to become the locus of review for microphysiological systems. A mock sort of applications indicate that this would result in a chartered study section with a healthy 70-80 applications, while at the same time helping to alleviate some oversubscribed chartered panels in BST.

Council Approval
CSRAC moved, seconded, and approved a motion to establish the CMT study section.

VII. Intra IRG Ranking Study

Amy Rubinstein, Ph.D., Chief of the Oncology 1-Basic Translational (OBT) IRG, reported on a study to determine if sets of applications reviewed in different study sections are of similar quality overall, as judged by the likely impact of the applications on the field of science. To test the null hypothesis that the average rank of applications from different study sections is the same, experienced reviewers rank-ordered applications chosen at random from among the top 20 percent from all study review groups (SRGs) within the same IRG.

Dr. Rubinstein explained the study design and noted the scoring differences between study sections within an IRG were modest, if any.

One factor that might account for differences in average rank across all IRGs is reviewers' familiarity with a topic. Familiarity was associated with how well an application was ranked. Another factor explored, but not found to affect score differences, was type of science (basic, applied or clinical). The study team will continue its analysis.

Discussion Highlights

- ***Familiarity:*** Dr. Targan asked about assigning applications across all study sections, when familiarity is an issue. Dr. Rubinstein suggested SROs should consider this issue in assigning applications. In response to a question from Dr. George, she said the familiarity-related differences were small but statistically significant. She also clarified that in this study, no two reviewers received the same applications to review; the intent was not to test if two people would rank-order the same grants differently.

VIII. NIH SBIR/STTR Program Update

Mathew Portnoy, Ph.D., SBIR/STTR Program Coordinator in OER, explained how NIH implements the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. SBIR and STTR are set-aside programs to support small-business research with potential for commercialization. NIH is one of 11 agencies involved in the congressionally mandated program, with NIH receiving about $814 million in SBIR and $114 million in STTR funding. CSR reviews about 80 percent of these grant applications.

Dr. Portnoy explained the goals of the programs. For SBIR, goals include to stimulate technological innovation, use small business to meet federal R&D needs, encourage participation by minorities and disadvantaged persons in technological innovation, and increase private-sector commercialization derived from federal R&D. STTR seeks to stimulate innovation and technology transfer between small business concerns and research institutions. Eligibility criteria include a business must have 500 or fewer employees and operate as a for-profit company. NIH funds Phase I and two stages of Phase II awards. Success rates average about 14 to 15% (higher for Phase II, which consist of Phase I awardees) and audits show NIH is meeting the required set-aside spending.

An analysis by the National Academy of Sciences (NAS) indicated NIH was successful in meeting most of the SBIR/STTR goals. NIH has had less success in meeting the goal to encourage participation by minorities and disadvantaged persons, but has made progress. NAS recommended the inclusion of commercialization considerations into review of SBIR/STTR applications, in addition to scientific merit. A working group is considering how to move forward. He also reported the timeline for SBIR/STTR applications from receipt to award has improved.

Discussion Highlights

- ***Industry involvement:*** In response to a question from Dr. George, Dr. Portnoy said most reviewers from industry are company PIs, with a goal that they constitute 25 to 50 percent of an SBIR/STTR panel. They receive training, although most are familiar with the program.
- ***Minimum size:*** Dr. Targan noted the ceiling and asked about a floor in business size. Dr. Portnoy said the program does not require a minimum level of revenue or employees and very early start-ups have received funding. About one-third are new to NIH each year.
- ***Key elements to change:*** In response to a question from Dr. Hammond, Dr. Portnoy said they are looking at how other agencies assess commercialization.
- ***Funding:*** Dr. Hollingsworth asked about the payline for SBIR/STTR grants. Dr. Portnoy said the scores vary from the 10s into the 20s and 30s. He noted ICs with tough paylines for R01s tend to have tough paylines for SBIR/STTR grants.

IX. Proposal to Convert the Societal and Ethical Issues in Research (SEIR) from a Study Section to a Recurring Special Emphasis Panel (SEP)

Valerie Durrant, Ph.D., Director of the CSR Division of AIDS, Behavioral, and Population Sciences, highlighted the history of the Societal and Ethical Research (SEIR) study section, which formed in 2011 with the expectation that application numbers would increase. It now averages 23 applications per round and has nine members. It is difficult to maintain a quorum, there is often a mismatch between the expertise of the small panel and the needs of the applications, and the low number of R01s leads to significant fluctuations and gaps in the percentiles.

Normally, CSR prefers standing study sections to SEPs. However the size and nature of the science seems better suited to a SEP, she said. Input from the extramural community and from IC

program staff support the change. Some expressed concern about the perception of the science if the study section becomes a SEP, but they remained supportive.

If approved, the change would begin for the January 2018 Council. CSR would communicate with current and recent applicants and otherwise spread the word. If application numbers increase, CSR would suggest chartering the SEP as a study section in the future.

Discussion Highlights

- ***Identity:*** Dr. Hammond suggested keeping a name for the SEP, not just a number. Dr. Durant noted it will be assigned a number but recognition will remain that it is an "ethics panel."
- ***Percentiling:*** In answer to a question from Dr. Hollingsworth, Dr. Durant said the group will percentile using the CSR All base. Currently, about half of the applications are related to genomics.

Council Approval

CSRAC moved, seconded, and approved a motion to convert the SEIR study section to a SEP.

X. Council Discussion and Closing Remarks

A Review Paradigm

Dr. Nakamura asked Dr. Hollingsworth to discuss a review system at his institution. Dr. Hollingsworth explained that a call for applications for seed money resulted in 41 applications, which meant there was insufficient expertise left to review them. He put together a review panel of the applicants themselves. Each reviewed three grants and stepped out during discussion and scoring of their own grant. Before each discussion, four senior scientists presented short initial summaries of the science in the application. In addition, nobody knew who was reviewing what until the day of the review. A survey acclaimed the system as open and transparent, with a good distribution of scores. Participants also expressed support for use of the scientific summaries in introducing each application for consideration.

Discussion Highlights

- ***Younger investigators:*** Dr. Nakamura asked about special provisions for younger investigators. Dr. Hollingsworth said senior and junior investigators fared equally. He has received requests to repeat the process.
- ***Use in CSR:*** A member of the audience asked Dr. Nakamura whether CSR would need a special waiver to use a similar process. From the audience, Dr. Byrnes said the Challenge grants under ARRA used a similar method. The large number of applicants had an impact on identifying reviewers who had not submitted an application before. NIH granted a waiver with the justification.
- ***Collusion:*** Another audience member asked whether the process would lead to deal-making. Dr. Hollingsworth said while that could occur, he did not see it. He would expect reviewer integrity but the process could also be monitored.
- ***Orphan applications:*** In response to another audience member, Dr. Hollingsworth said orphan applications were not a problem in this process.

Closing Comments

Dr. Nakamura asked CSRAC for ideas for future meeting topics. He thanked them for their participation and closed the meeting.

We do hereby certify that, to the best of our knowledge, the foregoing minutes of the March 27, 2017, meeting of CSRAC are accurate and complete. The minutes will be considered at the next meeting of the Advisory Council, and any corrections or comments will be made at that time.

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Rene Etcheberrigaray, M.D.
Executive Secretary
Center for Scientific Review Advisory Council

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Richard Nakamura, Ph.D.
Chair
Center for Scientific Review Advisory Council