Center for Scientific Review
Peer Review Advisory Committee Meeting
National Institutes of Health
U.S. Department of Health and Human Services

April 19, 2007

The first 2007 meeting of the Peer Review Advisory Committee (PRAC) convened at 8:30 a.m. on Thursday, April 19, 2007, in the Natcher Conference Center, National Institutes of Health, Bethesda, Maryland. The entire meeting was held in open session. Dr. Antonio Scarpa and Dr. Jeremy Berg presided as Co-Chairs.

Members

Jeremy Berg, Ph.D., Co-Chair
Antonio Scarpa, M.D., Ph.D., Co-Chair
Dean E. Brenner, M.D.
Joe Martinez, Jr., Ph.D.
Craig McClain, M.D.
Daria Mochly-Rosen, Ph.D.
Edward Pugh, Jr., Ph.D.
Louise Ramm, Ph.D.
Beverly Torok-Storb, Ph.D.

Ad Hoc Members

R. Lorraine Collins, Ph.D.
Andrew Murray, Ph.D.

Dr. Matt Winkler, Ph.D., was not present. Dr. Norka Ruiz Bravo, Ph.D., attended ex officio. Dr. Cheryl Kitt, Ph.D., was the Executive Secretary for the meeting.

Welcome, Upcoming Meetings, and Approval of the December 2006 PRAC Minutes

Executive Secretary Dr. Cheryl Kitt welcomed PRAC members and said the slate of potential members for PRAC has been submitted, based on nominations from throughout NIH and from outside committees. She expressed hope that new members would join PRAC by the end of 2007. She announced PRAC's next meeting dates: August 27 and December 3, 2007, and April 7, August 4, and December 8, 2008. Dr. Kitt asked for approval of the minutes of the December 2006 meeting. The minutes from the December 2006 PRAC meeting were amended to reflect attendance by Dr. Beverly Torok-Storb and then approved.

Improving Peer Review: CSR Initiatives

Dr. Scarpa welcomed PRAC members and NIH staff and colleagues. He introduced new staff members Ms. Melanie Keller, CSR Executive Officer, and Ms. Kristin McNamara, program analyst. He said he would summarize data about CSR peer review, highlight recent activities, discuss organizational issues for which he seeks PRAC input, and share his vision for peer review.

CSR Data

For the past three years, NIH has received almost 80,000 applications annually, of which about 52,000 are reviewed by CSR. In 2006, this process required about 18,000 reviewers, 250

scientific review administrators (SRAs), and 1,800 review meetings. Applications have increased by 50 percent from five years ago, and the question remains whether this rate of increase will continue. Some work has been done on modeling to predict the rate of growth, which will be discussed later.

SRAs are urged whenever possible to hold meetings on the West Coast to ease the burden on reviewers from those states. Reviewers averaged 11.6 applications each 10 years ago, compared to 6 applications now, in part because they now have to spend more time writing their own applications. Dr. Scarpa is looking for ways to increase the number of grants per reviewer to reduce the total number of reviewers necessary. Meetings with too many reviewers, he said, hamper discussion.

Recent Activities

Increased communication and transparency: A new internal advisory committee has been created. Dr. Scarpa meets weekly with division directors and twice monthly with chiefs of the Integrated Review Groups (IRGs). He now also meets monthly with two groups of SRAs, as well as with Management Services. Finally, he meets monthly with a crosscutting group of CSR staff.

Increased uniformity: The appeal advisory committee chaired by Dr. Don Schneider, Director of the CSR Division of Molecular and Cellular Mechanisms, responds to issues related to deadlines, study section assignment, and other processes. Rather than many individuals making decisions on these issues, the committee sees all of them and thus is more consistent. In addition, a best practices committee, chaired by Dr. Kitt, is looking at the best ways to conduct meetings, structure summary statements, and other concerns.

Increased efficiency: The big change, which occurred successfully, is electronic submission of applications. Although it alone does not save time, electronic submission will allow for more efficient distribution of grant applications to review groups, as will be reported later in the meeting. New text fingerprinting software for application referrals will save three weeks in the review process.

Improved study section alignment and performance: When the payline is low, complaints rise about how study sections review applications. Two approaches help ensure sections have a manageable load and reflect changing science. First, a retreat is held each month to focus on one IRG. By September, all IRGs will have been reviewed once; then, the cycle begins again. As a result of the retreats, changes have been made to several study sections with the assistance of the scientific community. Second, CSR is hosting six open houses in 2007, each involving three to five IRGs, for leaders of scientific societies and others to talk about whether their discipline is properly evaluated and, if not, suggest alternatives. The first event took place in March. Twenty-six of the 28 study section chairs registered, as did 52 leaders from 26 professional societies. NIH review and program staff and two PRAC members also participated. While some adjustments will be made in upcoming open houses, feedback was positive. Collected comments and a meeting summary have been posted on the Web site.

CSR Organization Initiatives

Dr. Scarpa is proposing to supplement the existing CSR structure with crosscutting areas in

knowledge management, career development, recruitment, and other areas. They are more proactive about recruiting SRAs by placing ads in *Science* and other publications, rather than responding when a resignation occurs and having a gap of as long as one year.

CSR has had four review divisions for many years. With the retirement of the director of the Division of Biologic Basis of Disease, Dr. Scarpa asked for PRAC input about whether the divisions should be adjusted. He pointed out the IRGs are of uneven size and questioned whether four review divisions is still the correct number. No decision has been made or even planned, but he welcomes input.

CSR Budget
The budget for CSR operations was $60 million last year, with an additional $40 million for reviewer travel and honoraria. It is a lot of money, but it represents great value. Review costs, including travel for 18,000 reviewers, is less than 0.2 percent of the budget requested in the applications reviewed. Airfare costs have decreased through an initiative to purchase nonrefundable air tickets, as previously reported to PRAC, although higher hotel costs have reduced the savings.

A Vision for Peer Review
Peer review in the broader context of NIH portfolio management is a high priority for NIH Director Dr. Elias Zerhouni. Dr. Zerhouni formed an advisory committee, co-chaired by Dr. Berg and Dr. Larry Tabak, Director of the National Institute of Dental and Craniofacial Research, to look at peer review. PRAC members will be involved.

Dr. Scarpa highlighted progress on efforts to shorten the review cycle, recruit and retain more high-quality reviewers, and decrease the burden on reviewers and applicants.

Shortening the review cycle: The goal is to provide applicants with a review and score within three months so they can re-apply and have as many as three reviews of their application within one year. Posting of summary statements within a month (new investigators within 10 days) has been the foundation of this effort. A pilot study enabled 2,000 new investigators in 40 study sections to choose to revise and resubmit their R01applications in the very next review cycle. About 13 percent resubmitted in the next round. Thirty percent of the re-submitters in the pilot scored within the 15th percentile range, compared to 16 percent of non-pilot new principal investigators (PIs).

The opportunity was extended to 3,000 new investigators in February and will expand further to between 7,000 and 8,000 in June. By November 2007, he foresaw that all new investigators, about 12,000 people, would have the opportunity to resubmit in the next round.

Reviewer recruitment and retention: Reviews are as good as the reviewers who conduct them, which makes recruiting and retaining the best reviewers very important. As many as 18,000 reviewers are used, compared with 8,000 to 9,000 five years ago. Most reviewers are ad hoc, rather than permanent members of study sections. This is partly because the science is much broader and requires the expertise of ad hoc reviewers, but also because of the decrease in the load from an average of 11.6 to 6 applications per reviewer.

A near-term solution is to require less travel by providing additional review platforms: telephone- and video-enhanced discussions, as well as asynchronous electronic discussions. The goal is to have 10 percent of all reviews electronic by the end of 2007. While the face-to-face aspect is lacking in asynchronous discussions, even reviewers who were initially reluctant have found the discussions are deeper. Dr. Scarpa emphasized flexibility in the use of new review modes. For example, a study section could meet in person once a year and then meet electronically the rest of the year. An evaluation of the various platforms is under way. Electronic reviews are particularly useful for clinical reviewers, physicists, and reviewers from other countries.

A second near-term solution to reviewer recruitment and retention is to shorten in-person meetings to one day, in order to lessen time away from work. Finally, a shortened review application is a potential way to increase the number of applications per reviewer. NIH and extramural support for a shortened application has been strong, although not uniform. (The findings from a trans-NIH committee on a shortened application are discussed later on the agenda.) A shortened application would represent a major cultural change. He urged caution in making changes and asked for advice from PRAC.

A topic in very initial discussions is a rolling review with no deadlines, which might ease the burden of applicants, their institutions' offices of research, and CSR. A pilot is being considered, perhaps looking at fellowships or small business applications. Another pilot being discussed is one to provide an incentive to reviewers by giving them a rolling deadline or by extending the period of their funding for an additional three to six months to cover the time they spend reviewing applications.

Dr. Scarpa concluded his remarks with praise for the dedicated CSR staff.

Discussion

Identifying reviewers: Dr. Edward Pugh praised the many experiments taking place. Over the course of a few years, much will be learned about what works best. Interesting reviewers to serve is probably the single most important aspect of enhancing peer review. He termed service on a study section as an induction into the system, but suggested a "permanent reserve" with emeritus status who can serve as needed, and a database to capture information about them. Dr. Scarpa said a database is kept of reviewer service, but it cannot characterize their service. In addition, professional societies have been helpful in suggesting potential reviewers. Every study section has its own history and way of doing things, so bringing someone in who served five years ago does take some adjustment. However, bringing reviewers back in has generally worked well.

Dr. Beverly Torok-Storb said institutions that receive NIH dollars should be required to field a pool of qualified reviewers. She also found the idea of rewards for reviewers appealing, although their performance would need to be evaluated as it is in other career development steps.
Dr. Norka Ruiz-Bravo said a database with evaluations of reviewers would have to be open through the Freedom of Information Act.
High priority of peer review: Dr. Berg elaborated on the committee looking at peer review. Peer review emerged as the highest priority at the IC Directors' retreats. Two committees emerged in the past few weeks. One is a working group of the Advisory Committee of the NIH Director. The

second is a working group of the Steering Committee, mentioned by Dr. Scarpa, and co-chaired by Dr. Tabak and Dr. Berg. There is an aggressive time frame to look at fundamental aspects of peer review, particularly the integration of peer review and program, and the second-level review of Counsils. A representative of the steering committee is planning to present at the next PRAC meeting.

Dr. Dean Brenner said he agreed that a look at the divisions and IRG assignments is needed. It would take some time, but the result could be better reviews. Dr. Scarpa suggested forming a PRAC subcommittee to advise CSR in terms of organization.

Reviewer incentives: Dr. Brenner also said researchers in the translational clinical environment in which he works value stability of funding. Having a longer funding term with at least minimum resources to support a lab is very important, and providing such support to long-term groups may be a way to attract and retain reviewers. Dr. Scarpa said Dr. Zerhouni favors an extension, although he stressed it would cover just a few months, assuming a reviewer spent six weeks per year reviewing grants over a period of four years. Reviewer fatigue is not exclusive to the United States, but it must be addressed. Abolishing the deadline to submit applications, as occurs for those whose applications are reviewed in Special Emphasis Panels (SEPs), may also be a valuable incentive to offer a permanent study section member.

Dr. Andrew Murray, new ad hoc PRAC member, drew a parallel between reviewing and teaching. They can be viewed as either burdensome or tremendously enriching. Having good reviewers find other good reviewers helps make meetings educational and entertaining. With funding less secure now, people must be persuaded that serving as a reviewer is a worthwhile experience. Some kind of incentive, tied to attendance, is critical.

Dr. Louise Ramm said an increase in grants to support the time spent in reviews would be difficult in a time of tight budgets. The IC Directors would have to look at the idea closely. Dr. Berg said the argument could be made that getting the highest quality of reviewers is worth the cost, but all the consequences would have to be carefully looked at.

Dr. Ramm asked if electronic reviews attract people who would not normally serve as reviewers. Some asynchronous reviews over the summer are for the shared instrumentation program, which involves people not already involved in electronic reviews, so their experience will be interesting. Dr. Brenner commented on clinical reviews he has chaired. He insists reviewers attend the whole meeting for the sake of the study section dynamic. More flexibility in review platforms could increase the quality of reviewers, but there is a tradeoff in terms of that dynamic. Dr. Scarpa said he would share the evaluations to date, which have been positive.

Dr. Craig McClain said a rolling deadline would benefit institutional grants management, which right now is very cyclical. An incentive for translational and clinical reviewers would also be good because of the complexity of their financial structure. Dr. Joe Martinez agreed some kind of reward would bring some people back to reviewing.

NIH infrastructure: Dr. Martinez asked whether the CSR infrastructure has increased in parallel with the large increase in the number of applications. Increasing infrastructure would be an

important investment. Dr. Scarpa said staff size has increased, but not commensurate with the increase in applications. Three years ago, 59 additional people were recruited. Dr. Ruiz Bravo agreed about the importance of supporting CSR. She noted that, while the NIH budget doubled, the funds that went to RM&S (Research Management & Services) did not. The ICs are tapped to support CSR and other functions. They have been generous in a time when their own budgets have not been increasing. Dr. Kitt said it is a tribute to SRAs and other staff that they continue to get things done even as the workload has doubled.

Dr. Lorraine Collins said, just as the goal is to attract and retain quality reviewers, a quality staff at CSR is necessary. She supported Dr. Martinez's comments to raise the question whether CSR needs more staff or support, given the changing number and nature of applications. She said the scientific community would support this.

Study section meetings: Dr. Daria Mochly-Rosen said locations in the west, east, and center of the country could mean that reviewers attend one meeting and telecast into others. She preferred that option to meeting only electronically or over the phone. She suggested rotating the meeting location and also exploring the possibility of sub-locations where a meeting could be telecast. Dr. Scarpa said a study section would ideally meet one time in person and twice electronically. Turning to the shortened review cycle, Dr. Mochly-Rosen questioned whether the relatively low number of people who resubmitted immediately might be misleading. When she asked whether CSR is prepared for a larger number, Dr. Scarpa said the total number of applications will be the same, but distributed differently. She noted figuring out how study section service went from being considered stimulating to a burden is the challenge of PRAC. The biggest component, she said, is that researchers have to write many more grants themselves.

Dr. Murray suggested a once-yearly face-to-face meeting could include a short segment in which participants explain their work, which could make the meetings more stimulating. Dr. Scarpa said the number of reviewers in the room is a major impediment for discussion. Dr. Murray said the goal should be to involve reviewers who are smart, critical, and knowledgeable, so that perhaps 20 reviewers would be necessary, with an ad hoc only needed for specific expertise. Dr. Scarpa said a smaller number would mean that each would have to review more applications. Dr. Torok-Storb said applicants and recipients must do their part as reviewers. She expressed concern about SRAs. SRAs can enhance a meeting experience, but not if they are overworked.

Dr. Kitt thanked PRAC for the rich discussion. CSR will follow up on the issues that came up.

Update on Electronic Submission

Ms. Megan Columbus, Program Manager for Electronic Receipt of Grant Applications, reported on the recent transition to electronic submission of R01 applications. She said the applicant community deserves kudos for the smooth transition. Things were quiet, with business as usual, albeit in a different way. Earlier, concern was expressed about whether Grants.gov and NIH's eRA systems could handle the volume. The eRA system had no problem. Grants.gov had no problem in February but slowed a bit in March because of a larger number of receipt dates at other agencies.

In February, nearly 4,000 were submitted via Grants.gov, with 70 percent error-free on the first submission and 94 percent error-free by the second submission. In March, nearly 5,000 were submitted. Slower processing times by Grants.gov meant the percentage successfully submitted in the first and second submission were not as high as in February, although most were processed well within 48 hours. NIH extended the error-correction window to accommodate the delay. Grants.gov is adding servers and bolstering capacity to handle the volume. The eRA processing times were consistent. Application file sizes were not as large as expected, with an average of 5 megabytes.

About 15 percent of applications used system-to-system transmission, in which data elements are submitted directly to Grants.gov from an institution or service provider. The implication is that every change made by Grants.gov ripples to institutions and service providers, so all changes must be made with this ripple effect in mind.

Mac users did not seem to have difficulty with the new IBM PureEdge Viewer or Citrix solution, although Mac applicants are looking forward to Grants.gov's new Adobe form solution.

In response to applicant feedback, Ms. Columbus and others are refining NIH error and warning messages, editing the application guide for clarity, conveying applicant feedback on form functionality to Grants.gov, and looking for ways to simplify the process and improve the application image. For example, they are exploring how to remove extra white space in the application, although any changes must go through Grants.gov and are not easy to make.

Grants.gov is scheduled to move to Adobe eForms later this year, so NIH will need to determine its transition strategy to these forms. Because applicants use the same form from one round to another, changes must avoid disruption to applicants. Transition dates for fellowship (F), training (T), and career development (K) applications will be set once necessary software is in place, while handling complex mechanisms is still under discussion with Grants.gov.

Discussion

Feedback: Dr. Berg congratulated the effort. When he asked investigators for comments, he received just one "benign" response. Dr. Brenner said his own experience in electronic submission worked well, although he and his colleagues had feedback. Ms. Columbus said they review all comments sent through the Web site. If a change makes sense for the community at large, they try to address it. Dr. Brenner said electronic submission required a longer lead time than with paper forms at his institution, which Ms. Columbus said seems to be the norm.

Dr. Ruiz Bravo thanked Ms. Columbus and recognized the team effort of several hundred people who have helped in various ways, including Dr. Suzanne Fisher, Director of the CSR Division of Receipt and Referral. She and Ms. Columbus meet every two weeks to go over issues that have arisen, such as feedback about error messages. She welcomed Dr. Brenner's and others' feedback. Dr. Martinez asked about the impact on smaller institutions, as reported in a recent article in the Chronicle of Higher Education. Ms. Columbus said she is in contact with the author and is working on issues that might arise for small institutions without a central research office or small businesses. The ICs have slides explaining the process to use at scientific meetings.

Dr. Martinez asked how rolling deadlines would affect electronic submission. Ms. Columbus said the whole system would have to be looked at. Dr. Kitt said success of the system is a tribute not only to the Office of Extramural Research (OER) staff, but also to academic institutions. A lot of communication and outreach took place all along the way.

Lessons learned: Dr. Pugh said the switch to electronic submission is an example of good government. The PSBR (Panel on Scientific Boundaries for Review) process serves as another example. In both, there was open communication and an opportunity for all stakeholders to communicate. There needs to be a way to digest and learn from the processes for future changes. The open houses are another good way to communicate with the community. Dr. Ruiz Bravo said a "post-mortem" takes place after each round and agreed open communication has made electronic submission work. She stressed, however, there is more to be done, such as with complex mechanisms and training grants. Dr. Torok-Storb said a big lesson is that NIH, as the funder, has power to impose its requirements over applicant organizations.

In response to a question from Dr. Ramm about how much of the system-to-system transmission of data was conducted by service providers, Ms. Columbus said an analysis had not been done, but many were from these providers rather than directly from institutions.

A New Model for Predicting the Number of NIH Grant Applications

Dr. Kitt introduced Mr. Chris White, a consultant who has been developing a new model for CSR that looks at a variety of factors that influences the submission of grant applications.

As an overview, Mr. White said improving the ability to forecast the numbers of applications would help NIH improve planning related to staffing and paylines. Results from common statistical models are sometimes unsatisfactory. Instead, Mr. White has developed a forecasting model using a simulation approach called system dynamics (SD) invented at MIT. People both internal and external to NIH were interviewed, and the model was based on these interviews.

Traditional Forecasting versus Structural Modeling
Mr. White first exhibited a traditional forecasting model that, depending on whether a linear or polynomial trend was used, made different predictions in the long term. The previous CSR model had forecast a decline, when in fact applications increased. The model is highly dependent on good data from a series of activities, but it treats the activities themselves as a black box. In a stable situation, this is fine, but not when the future situation will present very different conditions than the present. In contrast, the structural model peels open the black box. If activities can be modeled, then there is a higher confidence in forecasts as the activities change.

He presented a causal loop diagram that depicts activities involved in submitting grants for review and in reviewing and funding decisions. It can show the cause-and-effect relationships in the system at a very high level. For example, the number of applications influences how many are reviewed, while the NIH budget influences how many are funded. When applications are unfunded, this affects whether they are resubmitted. The success rate can also influence how much an institution wants to invest or be dependent on NIH and the institution's staff size.

Mr. White presented a diagram that illustrates what Dr. Zerhouni has referred to as a "perfect storm," in which demand for grants increases as the supply of funds decreases.

For the simulation, some of the elements were de-scoped, such as constraints on NIH's capacity to conduct reviews. A proof of concept showed the simulation model had reasonable results compared to events. He noted that the structural model, although incomplete, showed an increase, born out by the numbers, while the previous statistical model had not predicted the rise. The structural model can be a decision support tool to understand the system and what levers may be changed to influence behavior. Because the model is incomplete, he warned against looking at long-term findings.

Next Steps
Next steps include training NIH staff in the use of the simulation tool, finalizing reporting requirements, and enhancing the model to include more internal and external processes as well as integrating it with a PI simulation model.

Mr. White closed by explaining the system dynamics methodology with some hypothetical examples.

Discussion
Future projections: Dr. Mochly-Rosen said the key component in the simulation is to know how many scientists will be funded. Many institutions have projected how many scientists they will have in the next 20 to 30 years. The most important element is knowing the gross number of scientists and how many of them will apply for funding. Another key component is the size of future labs, which some institutions have studied. This kind of census will improve predictions. Many deans of research, in part because of the wake-up call from NIH, are planning for the future in such areas as the number of students that they will train and the size of labs. One possibility is that the number of faculty will grow but lab space will be smaller, thus the number of grants needed will be smaller. She suggested NIH try to get this information from institutions.

Dr. Torok-Storb asked for clarification about what is meant by NIH review capacity in the model. Mr. White said review capacity was ultimately removed because it was not viewed as a limiting factor, under the assumption that every application submitted will be reviewed. Taking out this information allowed for seeing the dynamics of the system and how things play out.

Accuracy: Dr. Murray said behavior models depend partly on their topology, but much more strongly on the coefficients of different coupling constants, which can change over time. He questioned the model's accuracy. Mr. White said sensitivity testing helps. Some of the connections in the feedback loop can have an enormous impact on metrics, while others will not result in much change. Thus, resources can be focused on relationships with the greatest impact.

Dr. Martinez observed the output data in the model do not match known data. Mr. White said the model is not a fully closed system, and some limiting factors were removed. The first model was a proof of concept to see if it is worth pursuing further. The statistical approach may present an answer closer to reality at this point because of system momentum. The structural model looks at the dynamics in more detail. The model is not yet ready to make decisions, but it can

give insight into how decisions and policies at NIH influence what institutions are doing and how that then comes back to influence NIH.

Dr. Pugh said it would be interesting to use the model to go back before the doubling and ask whether it was good policy. It could also be helpful in hiring policies to see many years out it takes for changes to play out in the system. Mr. White said the focus has been on relative scale and, thus, on relative changes. The model can help understand how interconnections play out.

Dr. Brenner said institutions are heterogeneous and sometimes unpredictable in how they respond to stress. The model will have difficulty because of the variability of human beings and the institutions in which they work. One source for information about how different institutions behave is the Association of American Medical Colleges. Mr. White agreed on the unpredictability but said the structural model can show what will play out if institutions react in various ways, at least in terms of the direction of change.

Dr. Murray noted many research institutions plan without regard for NIH budget realities. Dr. Torok-Storb said salaries at her institution are NIH-based and NIH funding is looked at closely.

Dr. Kitt thanked Mr. White. CSR will continue to see how the model plays out and the influence of different variables.

Shortening the R01 Application

Dr. Robert Finkelstein, Director of the Division of Extramural Research in the National Institute of Neurological Disorders and Stroke (NINDS), and Dr. Don Schneider, Director of the Division of Molecular and Cellular Mechanisms in the Center for Scientific Review, are co-chairs of the NIH Grant Application Committee. The committee, created by the External Activities Working Group (EAWG), is charged with considering changes to the length and format of the R01 research plan.

Activities to Date
As background, Dr. Finkelstein said many applicants and reviewers believe the R01 application focuses too much on detail and too little on significance and impact. It is comparatively long and time-consuming to prepare and review, which may affect the difficulty in recruiting sufficient numbers of high-quality reviewers. The preliminary finding in conversations with extramural scientists was that the majority preferred shortening the application. A Request for Information (RFI) sent to the extramural community had an overwhelming response of more than 5,000. A similar RFI went to NIH staff. CSR analyzed a subset of the responses, while the committee analyzed 500 randomly selected responses in detail.

Based on PRAC feedback, the RFI went out with four different models of applications, ranging from 5 to 25 pages. Because of the no-survey rule, the RFI could not include many straightforward, multiple-choice questions but rather broader essay questions.

Results of the RFI
Dr. Schneider showed a table that broke down the 5,078 responses by page preference preferred by all respondents, as well as subgroups of new PIs, clinicians, and NIH staff. Most people prefer a shorter application, with 15 pages the most frequently selected. New PIs favor a shorter application, which was contrary to expectations. Clinicians were less enthusiastic, although a majority still favored a shorter form. NIH staff members were the least favorable.

Dr. Schneider summarized responses to a series of questions:

Would a shorter application affect the ability to present scientific ideas? There was a division of opinion, with about half thinking one's ability would remain the same, 30 percent less, and 19 percent greater.

Would a shorter application take less time to prepare? About 27 percent thought it would take the same amount of time, 50 percent less, and 22 percent more time.

Would a shorter application affect the ability to judge scientific merit? About 32 percent said it would be worse, 33 percent said the same, 24 percent said better, and 12 percent did not answer.

Would an equivalent number of shorter applications affect the willingness to review? The question was phrased as willingness to review the same number of applications (not more), and 49 percent said they would be more willing, while 10 percent said their willingness would decrease, 31 percent said it would stay the same, and 11 percent had no answer.

If the application were shorter, should the review criteria be changed to emphasize ideas/impact? With 65 percent saying yes (29 percent, no), Dr. Schneider said clearly the community thinks that if the application were shortened, something should be done about the review criteria and possibly restructuring the application.

If the application were shortened, would any groups be disadvantaged? The results did not show any particular group felt they would be disadvantaged. Although 27 percent thought new PIs would be disadvantaged, the new PIs, as shown earlier in the presentation, favor a shorter form. Other groups registered 5 percent or fewer.

Do clinical research plans require more space? Fifty percent of self-identified clinicians said they did not require more space, and 39 percent did not know or did not answer. Dr. Schneider stressed clinical protocols would go elsewhere and not be subject to a smaller page limit.

The responses, he stressed, were extracted from essays. Embedded in the essays were profound thoughts and valuable suggestions. Among the 500 responses analyzed, 93 independently suggested shorter applications could emphasize critical points, 57 people said the change would decrease the burden for applicants and reviewers, 12 said shorter applications would lead to more of them submitted, and 11 said shorter applications would favor well-known applicants. He considered these last two as potential complications that would have to be further explored.

Committee Recommendations
Dr. Finkelstein presented the committee's three recommendations. First, the application should be shortened, with a focus more on critical issues and less on methodological detail. Most members of the Application Committee favor 15 pages, while a minority prefers 10 pages or fewer, to lessen the burden on applicants and reviewers. Generally, those in the 15-page group feel the application process is not broken and that a more drastic change in application length is not warranted; the minority thinks a paradigm shift is necessary. Second, instructions to applicants and reviews should be modified to emphasize impact over methodological detail, even if the review criteria are not changed. Third, sections of the application should be modified to align more closely with review criteria.

Most of the committee members do not believe a shorter application will solve the problem of reviewer recruitment. Most of the committee, as well as many RFI respondents, oppose assigning an increased number of shorter applications to each reviewer. In various presentations made to other NIH groups, there was overwhelming agreement on this point. Most importantly, the committee believes changes in the application or any aspect of peer review must be coordinated. It would be disturbing and unsettling if NIH made changes in a piecemeal way.

Discussion
Dr. Ramm noted the NIH Review Policy Committee (RPC) and Extramural Program Management Committee (EPMC) agreed with shortening the application to 15 pages.
Dr. Finkelstein pointed out these groups also concurred that shorter applications would not result in high-quality reviewers taking on more applications to review.

Proceeding with caution: Dr. Pugh shared several slides that he had prepared for the discussion. He said that changing the application size represents perhaps the largest change of all because it is a cultural, rather than administrative, change. Currently, stakeholders perceive the review process embodies fairness, integrity, and competence. In a period of low funding, dissatisfaction increases, which cannot be solved by a change in peer review or application size. Supporters have suggested a shortened application could solve several problems, but each must be thoroughly investigated. He urged a period of careful preparation, to clarify the rationales for the change, predict the effects, and consider unintended consequences. If not done right, a change this large would destabilize the system in unforeseen ways. He recommended development of an evaluation instrument up front with outside expertise. He proposed an experiment that would not be irreversible, such as a one-year trial of a 15-page application, rather than a pilot study.

Dr. Scarpa said, on average, reviewers spend 7 hours on an application. We do not know if they would review eight or nine shorter applications, rather than the six they review now, but we will not know unless it is tried. He agreed it is a huge cultural change that must be looked at properly. Although it is unknown whether people would submit more applications, based on experience in other countries, it takes the same amount of time to prepare a 15-page application as one that is 25 pages.

Dr. Ramm agreed it was necessary to proceed slowly. She pointed out Dr. Berg and Dr. Tabak are on committees that are looking at many aspects of peer review and any changes should occur in a coordinated fashion. She said the RPC and EPMC agreed. Rather than a pilot, they also prefer coordinating a switch with all the evaluative pieces in place and then trying it for perhaps one year. Dr. Finkelstein said some ICs have shorter applications, which could be seen as pilot-like experiments. However, the committee felt no meaningful pilot that would compare X to Y could be developed. They agreed with the type of experiment proposed by Dr. Pugh.

Dr. Martinez said his initial reaction to a shorter application was enthusiasm. In thinking further, however, he said more thought needs to go into any change to the 25-page application, which is the basis for the best science in the world. He compared reviewing these applications to the much shorter applications for the Pioneer Award. He questioned whether the science can always come through in a narrative if the application is too short, which makes judging scientific merit difficult. Dr. Kitt said this concern shows the need for ensuring that review criteria in the summary statement design are consistent with what the application asks for. Tremendous education and communication with all stakeholders would be necessary.

Coordinating changes: Dr. Mochly-Rosen agreed changes need to be made in a coordinated fashion, but warned against resistance to change. She has reviewed shorter applications in other countries and they are easy to evaluate. Dr. Ruiz Bravo agreed changes need to be made thoughtfully as they would affect investigators greatly. We cannot lose track of the fact that the system operates as a whole.

Dr. Torok-Storb praised Dr. Pugh's comments. She favors a shorter application that makes the applicant responsible for communicating the science in a succinct and lucid manner.
Dr. McClain said he also favors a shorter application while agreeing with Dr. Pugh's concerns. He noted the Veterans Administration uses a shorter application successfully, along with external reviewers. Dr. Collins, while favoring a shorter application, said she often goes through 90 pages of supporting material before getting to the meat of the application and asked when the 25-page limit was instituted. Dr. Anita Sostek, Director of the CSR Division of Clinical and Population-Based Studies, responded the page limit was 20 pages in the 1980s and changed to 25 pages around 1989 or 1990.

Dr. Collins said the scientific community has gone through other changes and this would go smoothly if everything were coordinated. She supported the suggestion that an application change be coordinated with review criteria. Dr. Kitt said SRAs remind reviewers to look for significance and discuss it at study sections.

Dr. Story Landis, Director of the National Institute on Neurological Disorders and Stroke, said the ability to pull up any published paper is a transformative event of the last 10 years. A lot of detail is no longer required, and it will probably be harder to write a compelling 15-page application without it.

Dr. Murray agreed with Dr. Pugh that changing the application represents one of the biggest changes an investigator could face. However, the peer review system tends to be conservative, and long grant applications encourage that conservatism. He said he worries that people will try

to cram 25 pages of information into 15 pages, thus making it harder for reviewers. He argued for a complete transformation—10 pages, focused on why the proposal matters. He said he would be willing to review 50 percent more of such 10-page applications.

Dr. Landis said this discussion would be shared with other committees looking at review and to the EAWG. She also noted a ripple effect on other mechanisms if the R01 form is shortened.

Dr. Murray suggested obtaining data from funding organizations that require a shorter application to see what people think about fairness of the process. Dr. Scarpa said reviewers who have reviewed for NIH and others that require shorter applications were asked. Dr. Murray suggested looking at scores for proposals submit to organizations that have a shorter form. If scores are highly correlated, it gives some assurance that the length of the application is not the major determinant in how the applicants rank.

Dr. Collins stressed an evaluation should look at whether reviewers would review more applications if they were shorter. A shorter application may in fact take more time to review.

Dr. Kitt summed up that PRAC supported a shorter application, with caveats as the committee proceeds to determine what the application design and review criteria would look like. They would need to be done in concordance, along with an evaluation piece. She acknowledged staff working on the effort, including Terri Kowalczyk, a consultant who read all the responses to the RFIs and provided statistical analysis, and CSR staff members Don Luckett and Kristeena Sigler. Dr. Finkelstein also acknowledged OER staff, particularly Denise Russo and Tom Turley.

NIH Director's New Innovator Award Program and the Proposed NIGMS EUREKA Award Program

Dr. Berg presented information on these two new initiatives. As context, President Bush signed into law the NIH Reform Act for 2006, a blanket reauthorization that included three big pieces: strong endorsement of NIH, institutionalization of the Common Fund so that the Roadmap process is now written into law with no formula for growth, and authorization (but not appropriations) for substantial budget increases in FY 2007–2009. In addition, in the FY 2007 Joint Resolution to fund NIH and other agencies, Congress appropriated about $600 million more than had been anticipated. Some of this new money supports the Common Fund, which frees up funds that the ICs had been providing for the fund. Another large part of the money is for vulnerable established investigators and for new investigators.

Vulnerable investigators—those whose applications scored within 10 percent of the nominal pay line of the Institutes—are now eligible for a one-year Bridge award, the first round of which are expected to go out shortly. Dr. Berg expressed hope these awards will relieve some anxiety and keep the scientific enterprise flowing.

Director's New Innovator Award
The NIH Director's New Innovator Award Program was created with some of these funds. It is for highly innovative researchers who have independent positions at U.S. institutions and are within 10 years of their terminal degree or residency. The 10-page application is due to

Grants.gov between April 25 and May 22. At least 14 awards will be made by September 30. The full five years of the program are funded with this FY 2007 money.

The application and review are modeled after the Pioneer program. The application focuses on a project description, innovativeness, and investigator qualifications. Review will take place electronically, with each reviewer responsible for about 20 applications. They will rank their top four candidates, and then an advisory committee will conduct a second level of review. The NIH Director will make final decisions. Because of the unexpectedness of the funding, the program came together quickly. The RFA was published within one month of the initial discussion. If the program continues, it will be adjusted as needed.

EUREKA Awards
The National Institute of General Medical Sciences (NIGMS) is developing a new program called the EUREKA (Exceptional, Unconventional Research Enabling Knowledge Acceleration) Awards to replace the R21 mechanism. The R21 did not seem to fund the high-risk research for which it was intended. The EUREKA will use an R01 mechanism to fund up to four years.

The Request for Application (RFA) is not yet out, but it is contemplated as an eight-page application that addresses the importance of the problem, novelty of the hypothesis or methodology, magnitude of the potential impact, and size of the community affected. It will include a limited biographical sketch, with, as suggested by Dr. Keith Yamamoto at the August 2006 PRAC meeting, a publications list limited to the five most relevant, five most significant, and five most recent publications. Preliminary data are not required, but are allowed. The program is not intended for new investigators.

Discussion
In response to a question from Dr. Pugh, Dr. Berg said a detailed evaluation plan for both programs is being developed. One aspect will be whether truly innovative ideas are submitted. Reviewers will also be contacted for feedback. Both programs will be highly competitive, and the review process for both programs is tailored to get the top applications.

Dr. Ramm said the EUREKA program seems like a good alternative to the R21, which has morphed into a "mini-R01." Reviewers have to be taught that the R21 requires no preliminary data and is to fund unique ideas and the willingness to take big chances. Dr. Mochly-Rosen said it is important to learn what happened with the R21 so EUREKA meets its goals. She also suggested it serve as a learning opportunity about how the experience can be made more stimulating so people will want to serve as reviewers. She asked whether NIGMS had considered ways to make reviewing the program exclusive and not just business as usual. Dr. Berg said this should occur as the success rate will be low, and thus, by that criterion, the program will be exclusive and prestigious. Dr. Mochly-Rosen said knowing the Pioneer Award is an exceptional program led reviewers to look at truly out-of-the-box ideas. Some kind of barrier may be needed so that people do not apply unless their idea is truly innovative. Otherwise, there will be too many to review and it will become burdensome.

New investigators: Dr. Martinez asked whether thought had been given to funding the first year of the New Innovator program and then having ICs pick up future years, so that more new

investigators could get support. Dr. Berg said this might happen in the future. Another piece of the puzzle, in terms of supporting new investigators, is Dr. Zerhouni's commitment to Congress to fund 1,500 new investigators this year. Dr. Zerhouni challenged the ICs to fund a targeted number of new investigators or risk having funding reallocated to others that can.

Dr. Martinez also asked about continuation of the New Innovator program, noting that the R29s for new investigators ceased when recipients' Type 2 applications failed. Dr. Berg said an analysis of the R29 pointed to cultural and monetary problems. In terms of cultural, they were not regarded as a real endorsement of someone's work. The Director's New Innovator Award should carry more prestige. Also, the money in an R29 was not very high and people over time were underfunded. They suffered when they had to compete for an R01. Dr. Berg believes the New Innovator recipients will be savvy, although they will still need mentoring.

Reviewer issues: Dr. Murray said it would be important to review EUREKA Awards apart from R01s, which hurt the intent of the R21s. Dr. Berg said the intent is to review them separately. Although there is some concern to ensure the scientific expertise is present to review them properly, this method has worked with the Pioneer Award. Dr. Brenner requested Dr. Berg report back to PRAC to share what is learned about application length and other experiments. Dr. Berg noted the programs are an experiment with multiple variables, which makes them hard to evaluate.

Dr. Torok-Storb asked whether a pre-proposal or letter of intent was considered to keep the number of applicants to a manageable level. Dr. Berg said the idea was discussed but not pursued, although some triaging will take place so the process does not overburden reviewers. Dr. McClain expressed concern about the number of applications that may come in. The vast majority of new investigators will be rejected in their first NIH grant with bad critiques. Dr. Berg said they are working hard on the feedback aspect to make clear the program is very competitive, and a lack of success should not be interpreted as negative. Dr. Torok-Storb suggested characterizing them as "non-responsive" without a critique. Dr. Berg said they are working on ways to streamline the process. Dr. Mochly-Rosen suggested a "non-responsive" could be gleaned from abstracts.

Dr. Pugh asked if separating the financial from the scientific aspects of an application had been considered to reduce the effort and help in writing better applications. Dr. Berg said supporting information is collected just-in-time, so, for example, animal protocols are not collected until they are needed. Modular budgets are permitted.

Dr. Kitt thanked Dr. Berg and said other experiments from Institutes that have used short applications will be shared at future PRAC meetings.

Study Section Realignment Update

Dr. Don Schneider presented recommendations from two working groups on potential study section changes related to neuroscience and to nanotechnology in the CSR Division of Molecular and Cellular Mechanisms.

Neurotechnology
At the last meeting, Dr. Schneider brought recommendations to PRAC from a neuroscience working group to form two recurring SEPs in neuroengineering and neuroinformatics/imaging. PRAC members requested more information before making a decision.

A crosscutting working group of external advisors and NIH staff was formed. They worked under the premise that existing study sections would not be sources of applications, but rather how best to handle applications that now go to several relatively small, inefficient SEPs. They considered a range of options: continuing the SEPs as needed, posting their guidelines and thus formalizing them; closing them; and establishing regular study sections.

They concluded that the neuroscience context is important and would be diluted or even lost if the applications were reviewed outside of that context. Sending technology-based applications to more hypothesis-driven regular study sections would also be a disservice. They recommended forming two regular study sections in Molecular Neurogenetics and Neurotechnology, with a third in Neuroinformatics/Imaging and Neuroengineering when the workload merits it.
Dr. Schneider reviewed the topics that the two proposed study sections would cover, their shared interests with other existing study sections, and how decisions could be made as to which study section to refer an application.

Nanotechnology
Nanotechnology and nanomedicine were launched at NIH as a Roadmap activity. In 2005 and 2006, eight trans-NIH centers were formed. In response to nanotechnology-related announcements asking for R01 and R21 applications, the numbers have grown from 67 applications in 2003 to 335 in 2007. Within other study sections, about 75 other applications per year relate to nanotechnology. The Nano Roadmap group requested CSR to look at how to deal with the growing number of applications in this area.

Dr. Scarpa agreed to form a working group, which met in March. The group felt strongly that nanotechnology is a discipline or area of research that has come into being and needs to be reviewed in its own study section rather than shunted into other areas. They were given the same range of options as the neuroscience working group.

They said nanotechnology research in its initial stages should be considered in a separate study section. Once the research moves beyond the initial stage, however, the working group felt the applications should be considered in other, more hypothesis-driven study sections. Dr. Schneider reviewed some of the areas that would be covered in a new study section and the shared interests with existing study sections.

In conclusion, Dr. Schneider noted both working groups were concerned about context and the cluster of expertise in making their recommendations. He asked PRAC to consider the two new neurotechnology study sections and the one new nanotechnology study section.

Discussion
Dr. Martinez said the recommendations make sense, and it was good to see CSR on the frontier of knowledge in these areas. Dr. McClain asked how neuroscience investigators would know

about the new groups. He suggested making slides available so they can see how best to direct their applications. He also said nanotechnology covers a great diversity of topics and questioned how to get appropriate reviewers. Dr. Schneider said the guidelines would be posted on the Web, with Dr. Scarpa's approval.

Dr. Pugh said the guidelines would benefit investigators, SRAs, and reviewers. The neuroscience field might grow as a result of having study sections, rather than SEPs, in place to review applications. He also said nanotechnology provides a good example of how innovation enters the NIH system and gradually gets incorporated and grows, as evidenced by the rise in applications. The Roadmap efforts helped launch the field.

Dr. Torok-Storb agreed Dr. Schneider did an outstanding job in defining and thus justifying the three study sections. Dr. Mochly-Rosen agreed with the need for a nanotechnology study section, noting this is a period in which the technology needs to be shared. But she is concerned about developing too many study sections in neuroscience. Dr. Schneider said the challenge is applications that do not seem to fit existing review groups, and the intent was to find homes for them. Dr. Murray said various groups of specialists would argue for study sections to better cover their specialty. Dr. Kitt responded not many recommendations for study sections are received. At the CSR Open House held in March, for example, no new study sections were recommended. The question is also asked on the CSR Web site.

Dr. Kitt asked for a motion to approve the two neuroscience study sections, which passed unanimously. She then asked for a motion to approve the nanotechnology study section, which also passed unanimously. Dr. Kitt said the flow of applications into the study sections will be monitored closely.

Automated Referral Workflow System Update

Dr. Thomas Tatham, CSR Associate Director for Knowledge Management, presented information on a new system to make referral of applications to IRGs more efficient. He explained the existing process, in which as many as five people and steps are involved. Electronic submission of applications provides the opportunity to automate many steps and reduce the process from several weeks to a few days or even hours for a high percentage of the applications.

At the December 2007 meeting, he presented historical data in which almost half (47 percent) of the applications came in with a PI request for a study section; in most cases, these requests were honored. For those that came in without a request, automated content analysis worked on about 40 percent of total incoming applications. At least 80 percent of the time, the machine decision was concurrent with the actual referral to an IRG that had been made by CSR staff experts.

February Deployment
In February 2007, the technology was deployed in which an application was received at NIH electronically and the Automated Referral Workflow System (ARWS) immediately started to mine it for referral. The ARWS did what he called a "fuzzy match" in which the system looked for full study section names or acronyms in a cover letter. The system can separate applications

into high confidence, reduced confidence, and no request categories for referral, depending on what the cover letter contains.

In an analysis of applications received in February 2007, 60 percent of PI letters contained study section requests (up from the 47 percent two years ago). The key metric in a retrospective analysis is how well the AWRS would have predicted the referral to the correct IRG chief. In 92 percent of high-confidence cases, the IRG predicted by the AWRS, in fact, was the same IRG to which the CSR Division of Receipt and Referral had referred the application. The remaining 8 percent were largely not error, but rather cases in which an IRG chief received a request but talked with the PI about the application being more suitable elsewhere.

Increasing High-Confidence Levels
A goal is to increase the number of applications in the high-confidence category through better algorithms. Another way might be through structured cover letters. He presented a proposed format for a structured cover letter in which a PI could request ICs and/or Scientific Review Groups where they would or would not like their application to be reviewed. The proposal for the structured format, which would be included in instructions for grant applicants, is being considered in various NIH committees.

A question that frequently arises is why not require all investigators to request a study section. The likelihood of a request being made seems to be related to an investigator's experience with the NIH system. Fewer R21 applications come in with requests, as do only 14 percent of SBIR applications. It would require too much of a cultural change to require requests, so the system still must have the capability to make predictions when an application comes in without a request. Various algorithms are being developed to look at different sections of the application and make a match based on where the 15 most similar applications were referred.

He is encouraged that his data are now based on the most recent round, rather than relying on older information. A user interface has been developed with a tool called Exit Ramp. He presented a screen shot of it. In the next round, they will use the tool in receipt and referral.

Next Steps
Interface with IMPAC II is critical for more widespread use of the AWRS. The structured cover letter would allow for greater efficiencies, if it is adopted, and more technical improvements will be developed over time. The benefits could include a reduced referral staff and time savings that can translate either into earlier meeting dates or later receipt dates.

He closed by acknowledging support from the Office of the Director and the EAWG, as well as efforts of the ARWS Project Team.

Discussion
Dr. Pugh suggested a dropdown menu or some other way to provide suggestions for selecting a review group as part of electronic submission. He asked whether IRG exclusion raises any concerns about conflicts of interest. Dr. Tatham clarified an IRG chief would still have responsibility for referrals and would see any conflict-of-interest information, as would SRAs.

Dr. Martinez had suggested a checklist at the previous meeting, but he said a structured letter, or a dropdown list as suggested by Dr. Pugh, moves in that direction. Dr. Tatham said, even if approval were granted, a dropdown menu on the SF424 (Research and Related) form would not gain much in terms of efficiency. Dr. Martinez also disagreed with the assumption that requiring study section assignment requests would lead to an increase in assignment requests that are discrepant with SRG and IRG referral guidelines.

Conclusion

Dr. Kitt asked for other questions or comments. Dr. Torok-Storb requested PRAC consider encouraging CSR to issue a well-crafted statement that disabuses people of the idea that a nonscored application is the same thing as a NRFC (Not Recommended for Further Consideration], which can have a negative impact on a person's career. Dr. Ruiz Bravo suggested perhaps a communications campaign is needed to better disseminate the information, as it is available.

Dr. Kitt then asked for a motion to adjourn the meeting. PRAC adjourned at 2:34 p.m.

We do hereby certify that, to the best of our knowledge, the foregoing minutes of the April 2007 meeting of PRAC are accurate and complete. The minutes will be considered at the August 2007 meeting of the Advisory Committee, and any corrections or comments will be made at that meeting.

Cheryl Kitt, Ph.D.
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