POLICY FORUM: SCIENCE POLICY

Proposed Changes for NIH's Center for Scientific Review

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The National Institutes of Health (NIH) is a major funder of publicly supported research in the United States, at a cost of $15.6 billion for fiscal year 1999. The peer-review system at NIH is designed to ensure that the resources are allocated as the result of a fair and rigorous competition among scientists. The long-range purpose of this research is to develop knowledge that will add, both directly and indirectly, to the improvement of human health. At the same time, the research supported by NIH plays a critical role in training the next generation of biomedical scientists.

The NIH's peer-review system is recognized as the cornerstone of the NIH extramural program, because it is the principal mechanism by which the institutes and centers identify high-quality research that is worthy of funding. Established over 50 years ago, this review system may be the most important single reason for the remarkable success of our federally funded biomedical research enterprise.

Approximately 40,000 applications are subjected to the peer-review process at NIH each year. Of these, approximately three-fourths are evaluated by the Center for Scientific Review (CSR). These are primarily individual investigator-initiated (R01s), but also fellowship (F32s), and Small Business Innovation Research Program (R43, R44) applications (*1*). Currently, 20 integrated review groups (IRGs), each consisting of a cluster of scientifically related study sections, serve as the functional units of review. For example, seven study sections review applications related to various aspects of molecular, cellular, and developmental neuroscience; all are organized into one IRG, much as multiple courses on related subjects are organized into a single academic department's curriculum.

Since its establishment, the CSR peer-review system has evolved continuously. However, rapid progress in biomedicine and its accelerating rate of change now challenge the CSR review system to keep pace. Through self-assessment and extensive outreach to the extramural research community, CSR's director has identified concerns regarding study section organization and composition (*2*). Although they are based on subjective impressions that are hard to document, they are worthy issues and sufficiently common to suggest consideration of new ways to organize the review process. For example, researchers perceive that there are no appropriate study sections for many newly emerging fields. Applications describing some of the most productive, highest-impact work may be assigned to too few study sections, causing much of the "best science" to compete with itself. The scope of some study sections is restricted to research with relatively low impact, resulting in undeserved "entitlements." The breadth of knowledge needed to assess the importance and potential impact of research proposals is sacrificed when review committees are too narrowly focused. In addition, certain segments of the research community, including clinical researchers, behavioral scientists, bioengineers, and developers of technology and instrumentation, believe that they are inadequately served by the existing system.

Many researchers fear that conservatism in the system and an undue requirement for preliminary data discourage innovation. They also note the need to define best practices and institute procedures that can be applied consistently throughout the review and administration process. External advisory groups are being established for each IRG, to provide input for continual improvement of the IRG review processes. However, there has been no overall assessment as to whether current IRGs and study sections are properly configured to respond to existing and future research opportunities, so as to best promote the public's long-range health goals.

For this reason, our Panel on Scientific Boundaries for Review was established in April 1998, as an ad hoc working group of the CSR Advisory Committee to undertake a comprehensive examination of the organization and function of the CSR review process. Our examination is being carried out in two phases. In both phases, we are relying heavily on extensive input from the scientific community.

Phase 1 recommendations can be found in our draft report, whose full text is available on the World Wide Web (*3*). It proposes a set of 21 IRGs [see the table on the left and note (*4*)]. In designing them, we have been guided by three principles. (i) There should be a home for the review of all science that is relevant to contemporary biomedical research. (ii) The research topics encompassed by each IRG should be sufficiently cohesive to allow the external advisory group for that IRG to provide advice regarding its entire scientific scope. (iii) The research related to a given system or disease, including fundamental studies, should be clustered for review within a single IRG or a related set of IRGs.

Our proposed organization includes some IRGs designed to review research applications that must be evaluated in a fundamental context, without regard to a specific organ, biological system, or disease. However, whenever reasonable, the basic research that underlies clinical or applied studies on specific diseases, organs,

PROPOSED INTEGRATED REVIEW GROUPS

- Chemical Biology and Biophysics
- Molecular Approaches to Gene Function
- Molecular Approaches to Cell Functions and Interactions
- Fundamental Genetics and Population Biology
- Fundamental Bioengineering and Technology Development
- Health of the Population
- Risk, Prevention, and Health Behavior
- Behavioral and Biobehavioral Processes
- Immunology
- Infectious Diseases and Microbiology
- Oncological Sciences
- Hematology
- Cardiovascular Sciences
- Endocrinology, Metabolism, and Reproductive Sciences
- Bone, Muscle, Connective Tissue, and Skin
- Digestive Sciences
- Pulmonary Sciences
- Molecular, Cellular, and Developmental Neuroscience
- Integrative, Functional, and Cognitive Neuroscience
- Brain Disorders and Clinical Neuroscience
- Surgery, Applied Imaging, and Applied Bioengineering

The authors are members of the Panel on Scientific Boundaries for Review, an ad hoc working group of the Center for Scientific Review Advisory Committee, National Institutes of Health. Their affiliations are available at http://www.csr.nih.gov/bioopp/select.htm. Comments should be addressed to this Web site and not to individual authors.

physiological systems, or general health problems should be reviewed within the broader biological and medical context to which it will ultimately be applied. Thus, we have attempted to place review of as much fundamental research as possible in the IRG to which that research is most relevant, such that all types of research related to a given system or disease will be clustered in the appropriate IRG. For example, the IRG for cardiovascular sciences would include basic studies of heart and vessel development and physiology, studies of pathophysiology of the heart and vasculature, and clinical studies pertaining to specific cardiovascular diseases and their treatment.

This organizational scheme differs from the current structure in ways that we believe will better serve the overarching mission of NIH. It should facilitate the translation of progress in the basic science laboratory into progress at the bedside, as well as the translation of progress from the bedside to the laboratory bench; promote identification of more ambitious and interdisciplinary research proposals; and ameliorate the current situation in which many investigators who are using a particularly powerful methodology tend to compete against one another based on that methodology. For example, an application proposing an investigation of the detailed mechanisms that cause specific genes to respond to hormonal ligands would likely be reviewed in the Cell Development and Function IRG in the present system. In our system, the application would likely be reviewed in a study section in the Endocrinology, Metabolism, and Reproductive Sciences IRG, albeit one with a molecular focus.

In addition to designing a set of IRGs in our phase 1 report, we have outlined some cultural norms that we believe should govern the CSR review process, as well as the principles to be followed in creating study sections. We believe that an appropriate peer reviewer is an active researcher who is fully aware of (or can easily learn about) the research goals and the research means being proposed. Peer reviewers thus need not be "competitors" of the applicant, or even be studying the same disease or organ system. However, they should be experienced researchers who are reasonably diverse in seniority, outlook, geographical location, gender, and ethnicity. The peer reviewers' only role is to judge the research proposed. Advocacy or gate-keeping for a field, discipline, or style of research is not the function of a peer reviewer (nor of the peer-review system). Although it may be appropriate for peer reviewers to provide some helpful general advice on ways to improve the application, they should not be in the business of educating the applicants or designing the next experiment or grant application. Rather, reviewers should judge grant applications on their fundamental merits and convey the rationale for the score in the summary statement.

We are also concerned that in practice the present system tends to discourage risk-taking and undervalue new ideas. The traditional emphasis on "hypothesis-driven" research has been narrowly interpreted as a formal exercise in the proposal and proof of a well-circumscribed idea. Under these conditions, exploratory research in which new technology is used or developed suffers, and the ability of NIH to accomplish its mandate may be impeded. Furthermore, although preliminary data can reassure reviewers that the applicant has the means and the understanding needed to carry out the proposed studies, we caution that an obsession with preliminary data discriminates against bold new ideas, young scientists, and risk-taking.

In phase 2 of our effort, which will begin in 2000 and probably extend through the next 2 years, groups of expert extramural scientists and NIH staff will create the scientifically related study sections that will populate each IRG on the basis of principles outlined in the report. Recommendations will be implemented over the following years, with extensive involvement of the extramural research community.

In designing the overlapping study sections that will populate each IRG, we recommend that the phase 2 subpanels be guided by principles that include the following. The range of science considered for each study section should be broad yet coherent. The review of applied subjects should be informed by the perspective of basic scientists and vice versa. Study section membership should be balanced with respect to breadth and depth. Depending on the field, the study sections within an IRG may be designed to cluster similar types of research applications to different extents; for example, for many IRGs, some study sections are likely to review only molecular approaches, whereas others are likely to be confined to patient-oriented studies. When different approaches to a problem are reviewed in the same study section (for example, patient-oriented studies and laboratory studies; or the development of new technologies and hypothesis-driven research), no single type of application should represent less than 30 percent of the applications assigned to that study section for review.

Many details and adjustments remain to be made in phase 2, and we recognize that judgment will be required to balance an obvious tension between worthy goals. However, the effectiveness of phase 2 will depend on development of a valid framework on which to flesh out the details. We intend to complete the phase 1 framework in November 1999, after considering your comments and suggestions. We request that these be submitted by 15 October 1999, via the electronic mechanism that is supplied on the Web site containing the full report (*3*).

Ours is a very challenging task. While recognizing that perfection is unattainable, our goal is to optimize the CSR review system to provide a review process that encourages risk-taking and innovation, while being flexible and responsive enough to keep up with the many new opportunities developed by the striking advances in biomedical science. We hope that the final result will be a dynamic system in which new ideas and all research styles are better appreciated—a system that facilitates acceleration of the progress in biomedical research through an improved, merit-based competitive review of all applications.

References and Notes

1. Approximately one-fourth of the applications are evaluated in scientific review groups managed by the Institute to which the applications are assigned. In general, review of these applications requires greater programmatic context [for example, Center (P50) and Institutional Training (T32) grant applications].
2. E. Ehrenfeld, personal communication.
3. The full 27-page phase 1 draft report, including 14 pages of appendices, is available on the Web at http://www.csr.nih.gov/bioopp/select.htm.
4. In the proposed organization (see the table on page 666), the six IRGs created to integrate the review of neuroscience research and behavioral and social sciences research from the former Alcohol, Drug Abuse, and Mental Health Administration Institutes [Molecular, Cellular, and Developmental Neuroscience; Integrative, Functional, and Cognitive Neuroscience; Brain Disorders and Clinical Neuroscience; Social Sciences, Nursing, Epidemiology and Methods (titled Health of the Population in the new structure); Risk, Prevention, and Health Behavior; and Behavioral and Biobehavioral Processes] have been retained essentially intact in proposed IRGs. Three current IRGs (Biochemical Sciences, AIDS and Related Research, and Nutritional and Metabolic Sciences) are eliminated and their research applications widely dispersed. Another 7 of the 20 current IRGs (Biophysical and Chemical Sciences; Genetic Sciences; Immunological Sciences, Infectious Diseases, and Microbiology; Oncological Sciences; Endocrinology and Reproductive Sciences; Musculoskeletal and Dental Sciences), while altered in their scope, clearly relate to proposed IRGs. In general, the current Cell Development and Function IRG would be divided into the Molecular Approaches to Gene Function and Molecular Approaches to Cell Functions and Interactions IRGs; the current Surgery, Radiology, and Bioengineering IRG into the Fundamental Bioengineering and Technology Development and the Surgery, Applied Imaging, and Applied Bioengineering IRGs; the current Pathophysiological Sciences IRG into the Digestive Sciences and the Pulmonary Sciences IRGs; and the current Cardiovascular Sciences IRG into the Cardiovascular Sciences and the Hematology IRGs.

5. We are grateful for the skillful assistance of L. Engel, the executive secretary for this panel.