

# Growing Pains for NIH Grant Review

The grant review system at the National Institutes of Health (NIH), the main mechanism by which NIH identifies research worthy of support, has been through a major overhaul. Scientists who spearheaded the change say it is time to assess how the new system is working.

There is no doubt that the grants system of the National Institutes of Health (NIH) is under strain. After a doubling of its budget to \$27 billion from 1998 to 2003, NIH funding in the past three years has not kept up with inflation (see Figure 1). Researchers at all stages of their careers are frustrated by difficulties in having their grant applications approved, and some have even started pinning the blame on the NIH administration itself. In a recent editorial, which spurred a flurry of passionate responses from the research community, *Journal of Clinical Investigation* editor Andrew Marks charged NIH director Elias Zerhouni with irresponsibly funneling precious funds away from investigator-initiated research supported by traditional R01 grants.

But as that debate continues to fester, a number of scientists and professional societies are focusing their attention on improving the system of peer review for NIH grants. The NIH study sections, the functional units of grant review, have been reorganized in a process that began over six years ago and was completed last year. Now the new structure needs to be evaluated for potential hitches. "Personally I think this is one of the most important issues at this time, when many people are not getting funded," says Bruce Alberts, former president of the National Academy of Sciences and currently at the University of California, San Francisco. Alberts chaired the Panel on Scientific Boundaries for Review, an independent advisory group that recommended the new organization for NIH study sections. "The heart of our proposal was to create a structure that would be amenable to continuous oversight by scientists," he adds.

## Grant Review at a Glance

The Center for Scientific Review (CSR) at the NIH manages the review of most investigator-initiated applications, including R01s, fellowships, and small business applications. Individual NIH institutes and centers manage the review of applications in response to specific program initiatives, such as Requests for Applications (RFAs), multicenter clinical trials, and so on.

Grant applications to be reviewed within CSR—comprising about 70% of all applications submitted to NIH—are assigned to one of 23 so-called integrated review groups (IRGs), each consisting of a cluster of scientifically related study sections. CSR then assigns applications to the appropriate study section within the IRG. Study sections meet independently three times a year near the NIH campus in Bethesda, Maryland to discuss and score applications.

After CSR completes its review of the application it sends a summary statement containing a score and, in some cases, a percentile ranking to the responsible institute or center.

Advisory councils then make funding recommendations based on the CSR evaluation, taking into consideration the institute's or center's scientific goals.

In 2000, NIH reviewed 44,000 grant applications of which 32,000 were handled by CSR. But by 2005, the total number had grown to 73,000 with 52,000 of these being handled by CSR. As more investigators submit R01 grants (R01 applications from new investigators jumped from 9,595 in 2001 to 18,047 in 2004) and each investigator submits, on average, more grant applications, the number of R01s awarded by NIH has gone down slightly. These factors combined have sent success rates for grant applications plummeting (see Figure 2).

## Reorganizing the Study Sections

In 2000, the Panel on Scientific Boundaries for Review recommended a new organizational structure for IRGs, which would more accurately reflect the types of research applications that NIH receives. "The first study sections were established in

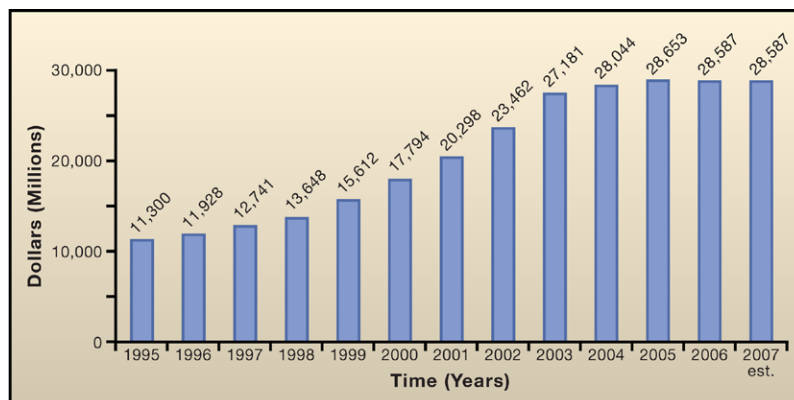
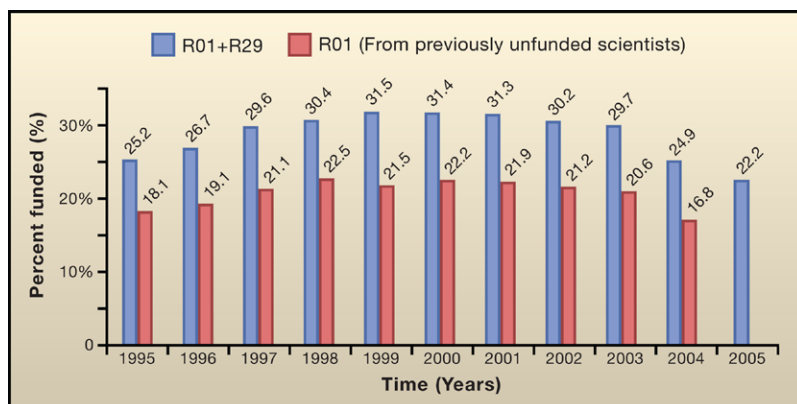


Figure 1. NIH Budget for Fiscal Years 1995 to 2007

Source: FASEB Office of Public Affairs (<http://opa.faseb.org/pdf/NIHFundingTrends.pps>).



**Figure 2. Success Rates for All Competing NIH Grants for Fiscal Years 1995 to 2005**  
Source: FASEB Office of Public Affairs (<http://opa.faseb.org/pdf/NIHFundingTrends.pps>).

1946 and had not been revised since, despite the fact that science has changed dramatically. Reorganization was one option to address this issue," says Anthony Scarpa, who became CSR director in July 2005. Another issue the panel grappled with was that some of the most cutting edge research was assigned to too few study sections causing the best science to compete with itself, whereas relatively low impact work had little or no competition. The goal of the new IRG structure was to even out the playing field.

The panel recommended a new set of IRGs and invited public comment and suggestions from the scientific community. Then groups of scientists with expertise in different areas decided what types of study sections should populate each IRG. Under the new structure, basic science research that applies to physiological problems was assigned to study sections with a broader focus than in the past, enabling review of grants containing both basic and disease-oriented research. "It was an important but difficult undertaking," says Keith R. Yamamoto, vice dean for research at the School of Medicine, University of California, San Francisco, who chaired the CSR advisory committee. "It was like turning a huge ship."

### Is the New System Working?

The final study sections were put in place last year, prompting former

panel members to urge NIH to evaluate the changes. "Part of the reason for the reorganization was that we envisioned that a relatively small group of experts could keep the system working effectively," says Alberts. The plan, says Alberts, was that a group of about 8 to 10 scientists could oversee each IRG, by sitting in on study section meetings as ad hoc reviewers, to determine if adjustments to the new structure were needed. "It is more important to have this kind of oversight in place at the early stages [of the reorganization]," he says.

In particular, the panel suggested that the scientific expertise in each study section be monitored to ensure that it matches the scientific areas covered by the grant applications. "We finalized the structure about 2 to 3 years ago. But fields are changing in a big hurry. We need to make sure that each IRG covers its respective field and that the number and focus of the study sections is appropriate," says Peter H. von Hippel, a chemist and molecular biologist at the University of Oregon and former member of the panel. Says Yamamoto, "No matter how refined a process is, even with thoughtful input from thousands of people, the chances of doing it perfectly the first time are next to zero. CSR needs to be alert to problems and quickly react to them."

Another concern is that "in some cases, basic science expertise is not

well-represented, so basic science grants are not getting expert review," says Heidi Hamm, a pharmacologist at Vanderbilt University Medical Center who is president-elect of the American Society of Biochemistry and Molecular Biology (ASBMB). "With the reorganization something like 5 to 6 basic biochemistry study sections are gone, and thus grants in a wide range of expertise are being funneled to just a few, much larger, study sections." Others echo the concern. "One of the big concerns before the reorganization was that translational science was not getting a fair review. Now we may have gone to the other extreme. The emphasis may have now swung to translational research to the detriment of outstanding basic science," says Judith Bond of Penn State University, ASBMB's current president.

### Calling All Reviewers

Each year, thousands of reviewers are asked by CSR to serve on study sections for 1 to 3 months a year. Currently, one third of reviewers are permanent members who serve a four-year term on a particular study section; the rest are ad hoc or temporary members. The recent increase in grant applications and lower success rates have contributed to what Scarpa refers to as "reviewers fatigue." According to Scarpa, there is a reluctance not only to participate on study sections but also to take on the usual load of a dozen or so grants per review cycle. "The review system is under significant stress. When you need 18,000 reviewers a year, you sometimes have limited choice as to who to ask," he says. "The real crisis is not being able to always have the best reviewers."

A number of professional societies are helping CSR to address this issue. The American Society for Cell Biology is reaching out to its members at society meetings to encourage them to serve on study sections. "It is one of the major problems we are focusing on," says spokesman Kevin Wilson. The ASBMB took a more proactive approach by conducting a formal survey of its membership. They found

that 70% of associate and full professors are willing to participate in study sections. "In the past there was an unspoken rule that if you have served a four-year term on a study section as part of your professional requirement then you had done your job. We are trying to change that," says Hamm. ASBMB has provided a list of 700 individuals that NIH can tap as potential reviewers, provided that they meet all the necessary requirements. "[Our members] are very engaged in wanting the system to get better," she adds.

Some are concerned about the increase in the number of junior faculty on study sections. In May 1998, about 1% of the permanent reviewers were assistant professors. By May 2005, that number has grown to about 7.5% percent. "[Assistant professors] are inexperienced and may tend to address technical issues rather than the real important problems. Also it's not fair to them to sit on study sections as it is an onerous task," says Hamm. Suzanne Pfeffer, chair of the department of biochemistry at Stanford University School of Medicine, agrees. "I do advise my junior faculty not to serve on a formal study section mostly because of the amount of time required. It is a very big responsibility," she says. "I agree it can be a useful learning experience, but I advise them to focus on their own work until they have tenure."

Although scientific societies are doing their part to urge their constituents to participate, CSR is implementing some practical changes to make the review system more accessible to busy senior investigators. For example, the center is experimenting with asynchronous Internet-assisted discussion in secure chat rooms, to allow reviewers to meet and comment on grant applications without having to fly to

the NIH campus for formal meetings. CSR is also considering making R01 grant applications shorter than the current 25 dense pages with unlimited appendices. "We have talked to various groups about this and some are in favor of the idea. Each reviewer would be able to read more grants and we would need fewer people," says Scarpa.

### Young Investigators

If the funding situation is frustrating for established scientists, junior faculty are feeling the pinch. Grants from new investigators consistently fare worse than those from experienced investigators—for example, in 2004, 14.6% of R01 applications from new investigators scored in the top 20<sup>th</sup> percentile compared to 17.7% from experienced investigators. In addition, more new investigator applications (47.8% compared to 40.6% for established investigators) were "streamlined," a process in which the bottom 50% of applications to a study section are not discussed at the review meeting and are not scored.

"There has always been great concern about facilitating careers of young scientists. These times when funding is tighter, there should be even more concern," says Yamamoto. In January of this year, NIH announced its Pathway to Independence Award Program. Starting in the fall of 2006, NIH will issue between 150 and 200 awards to provide support during the transition between a postdoctoral fellowship and independent investigator position. "What NIH has done sends a positive message," says Yamamoto.

R01 applications contain a box to be filled out by new investigators, which alerts reviewers to be more lenient. "Reviewers are instructed to put more emphasis on training,

environment and innovation when assessing applications from new investigators and CSR monitors these reviews," says Scarpa. But others say that more could be done. "CSR should make two lists of initial priority scores, listing young investigators separately from established ones," says von Hippel. Study sections would have to discuss and prioritize the top applications from new investigators, regardless of how they are initially ranked in comparison to those of established investigators, thereby reducing the number of new investigator applications that are streamlined.

Scarpa has adopted other measures to speed up the review of grants submitted by young investigators. In a pilot study of 6,000 new investigators, CSR scheduled study section meetings earlier than usual, provided applicants with their scores, critiques, and panel discussion summaries within a week of the study section meeting, and extended resubmission deadlines by 3 weeks. "Normally if you submit a grant in February, by the time you get comments back and make revisions, you have to wait until November to resubmit the application. Our goal was to allow resubmission of the grant at the next cycle," says Scarpa. Once the new system is evaluated, CSR plans to extend these changes to all investigators.

The funding situation is unlikely to improve anytime soon but optimizing the NIH grant review system might relieve some of the strain researchers are feeling. "The peer review system looks like it is in crisis because of the funding situation. If money were plentiful, it would mask any problems with it," says Yamamoto. "A solution can be achieved by providing more money, but when this is not possible you need to fix other problems."

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