

EDITORIALS



Grants, Politics, and the NIH

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Investigator-initiated grants are the engine driving our biomedical research machine. This process is exemplified by the National Institutes of Health (NIH) and its grant-review system for extramural research — arguably the most productive and widely emulated of its type in the world. The selection of research for funding is based solely on merit; politics has no place in this system. Thus, it is of immense concern that over the past year the NIH has had to deal with about one request per week from members of Congress concerning the details of specific grants. Some of these requests, such as one in the form of an amendment to a bill that came within a few votes of being passed by the House of Representatives this past summer, imply that funded grants, if not politically acceptable, should be rescinded (see <http://www.cossa.org/toomey.htm>).

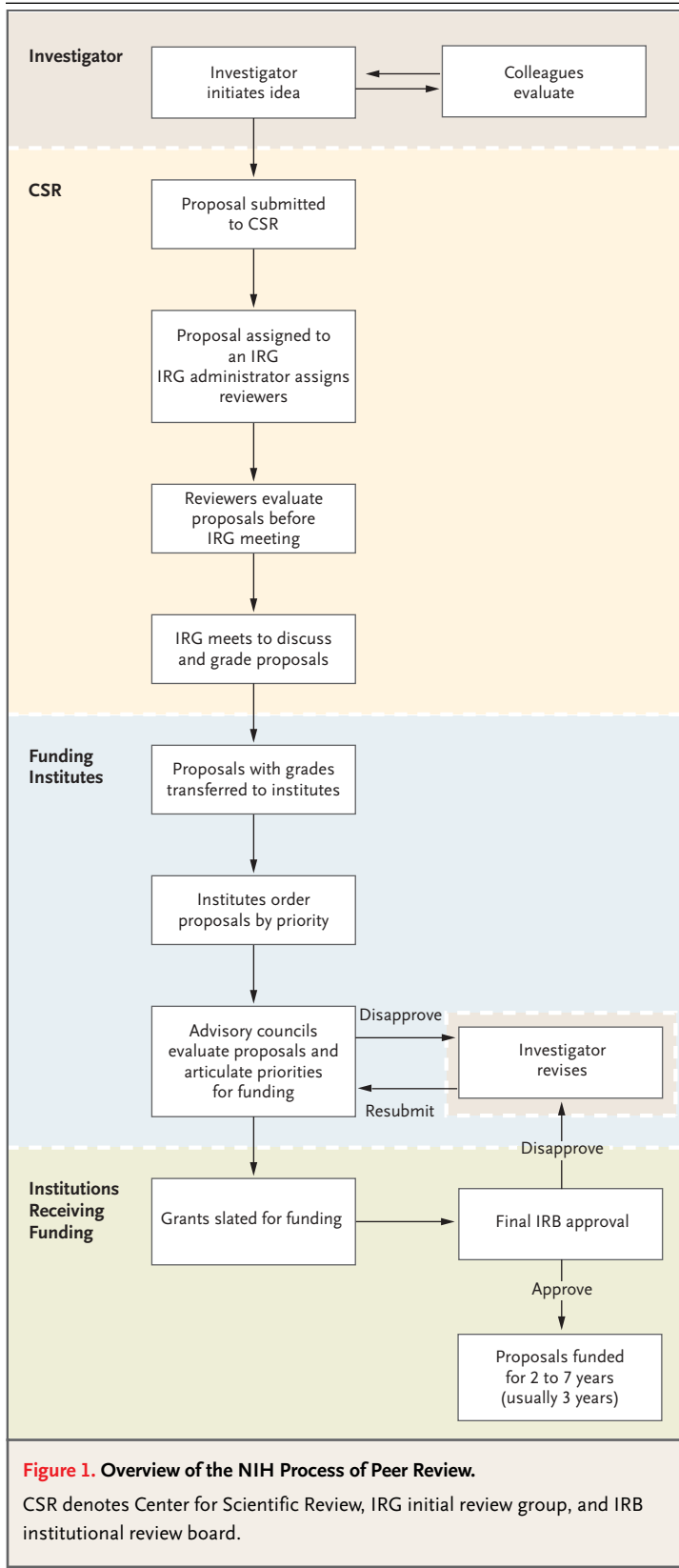
One of the most recent of these requests asked staff at the NIH to justify the present funding for about 200 grants on a list compiled by a political action group, the Traditional Values Coalition, which questions the funding of projects that address behavior in so-called at-risk groups. This political action group has described some of the research it targets as “smarmy projects,” alleging that investigators are wasting federal funds by studying ways to assess and affect the behavior of people considered to be at high risk for spreading sexually transmitted diseases or by studying family structure and its impact on children. We disagree. Grants for work concerned with social issues are crucial to the mission of the NIH. Without the knowledge derived from this work, we do not know how to reach high-risk groups, and our ability to bring laboratory discoveries to the people who need them can be “lost in translation,” in Lenfant’s phrase.¹

The Traditional Values Coalition suggests that little thought goes into funding grants that focus

on social issues. Andrea Lafferty, executive director of that group, states, “Nameless, faceless bureaucrats are doling out money like a federal ATM.”² In fact, however, the review of grant applications involves intense scrutiny by many respected and accomplished scientists and contains myriad steps in which both the science and the ethics of every application are evaluated. NIH grants cover a remarkably wide range of research, from basic-science investigations that have identified the molecular basis of various types of cancer, heart disease, and infectious disease to public-health studies that provide invaluable information about how to understand and curtail epidemics such as smoking, obesity, and infectious diseases that affect millions.

The United States and the world are faced with a particularly virulent scourge — AIDS, caused by the human immunodeficiency virus, which is spread by human activities, including sexual contact and intravenous exposure. Millions of people around the globe will succumb to this single disease, and understanding how to curb the epidemic is crucial. Knowledge of human behavior and how to modify it is essential if AIDS is to be stopped. It is just such research that the Traditional Values Coalition would end.

The coalition questions the way grants are awarded, suggesting that “there needs to be some adult supervision at the NIH.”² Such pejorative statements could not be less accurate. To understand this point, it is important to appreciate the process by which investigator-initiated extramural research grants at the NIH are reviewed (Fig. 1). As the first step in this sequence, an investigator conceives of an idea for a research study that lies within the broad mission of the NIH. Successful investigators often discuss their ideas with colleagues to refine and focus their thinking. They then prepare an application, typical-



ly about 12,000 words (the length of four or five research articles in the *Journal*), in which they detail the rationale for the project, how it would be executed, and how the results would advance knowledge in their specific scientific field.

Grants are submitted to the Center for Scientific Review at the NIH, a body that is independent of the standing institutes and that has within its purview a large number of initial review groups (IRGs), often called study sections, each of which is composed of approximately 20 eminent scientists from a variety of areas germane to the area covered by the particular IRG. Each application is reviewed by three or four scientists with relevant expertise; the reviewers are chosen with meticulous attention to ensure that they have no personal or professional conflicts of interest with respect to the applications. A reviewer will typically spend between 12 and 24 hours considering each grant, poring over the science and writing a detailed review before the meeting of the IRG. The reviewer assesses each proposal's merit on the basis of its importance to the field of interest, the planned approach, the qualifications of the investigators as reflected in their published work, the environment in which the work will take place, the appropriateness of the budget, and the ethics of the research. Considering all of these criteria, the reviewer assigns a priority score from 100 (indicating "best") to 500 ("worst").

Each IRG meets three times a year. At each meeting, applications judged to be in the top 50 percent are discussed in detail. One reviewer outlines the proposed work, and the others give their opinions and describe the scientific basis for these opinions. A vigorous discussion ensues among the assigned reviewers and all the other members of the IRG, who have also received the grant applications for inspection. Discussions about submitted grant proposals are incisive and critical but always centered on the scientific issues; neither the politics of the investigator nor the political implications of the work constitute review criteria.

After the meeting, the scientific review administrator for each IRG compiles a list of the reviewed grants in the order of priority assigned to them and transfers them to the funding institutes, which review the results of the various IRG meetings and decide which grants will be presented to their advisory councils for possible funding. Each advisory council, in turn, reviews the IRG recommendations to be sure that the proposals fall within the mission of the institute and that the review by the

IRG was fair and appropriate. The advisory council then makes a funding recommendation to the institute. Decisions about funding are made by institute staff largely on the basis of the priorities assigned by the IRG and the advisory council, as well as the funds available for the specific type of research under consideration. Over the past 30 years the rate of approval of grant applications, depending on the institute, has varied from a low of 1 out of 10 or 12 applications to a high of 1 out of 3 or 4.

The system works remarkably well. Proposed projects must be innovative and rigorous in order to receive a score high enough to lead to funding. Applications that do not clearly lead the field are usually not approved. Grants are awarded for finite time periods. Once their research project has been funded, investigators know that the clock is ticking and that they must produce real results if their grants are to be renewed. The goal is to get the work done and the results published, so that the field is advanced and progress can continue. Wisely, the NIH requires remarkably little information, only a brief annual progress report, from investigators during the period covered by an award; the rationale for this approach is that progress will speak for itself. On the other hand, the institution receiving the funds must supply detailed records to the NIH during the funding period, ensuring that the monies are being expended to achieve the research goals.

Some grants are extremely productive, generating effective new therapies for difficult-to-treat illnesses, innovative ways to solve problems in health care delivery, and strategies to stem the spread of disease. Others are less so. However, most grants lead to discovery and to useful information. Investigators who are not productive are not re-funded. The unique success of the widely appreciated and emulated NIH peer-review process is that it rewards excellence and research productivity.

The NIH system for vetting investigator-initiated research is rigorous and comprehensive, identifying and funding the most meritorious work. Once grants are awarded, investigators should be left to focus on their work and should not be diverted by wasting time responding to the whims of interest groups. Only through a broadly based research program can we advance the health of all citizens. The NIH has a record of doing this well. The gem of worldwide biomedical research should not be rubbed in political dirt.

Drs. Drazen and Ingelfinger report having received grants from the National Institutes of Health. Dr. Drazen serves on the Advisory Council of the National Heart, Lung, and Blood Institute.

1. Lenfant C. Shattuck Lecture: clinical research to clinical practice — lost in translation? *N Engl J Med* 2003;349:868-74.
 2. Weiss R. NIH faces criticism on grants: coalition assails "smarmy projects." *Washington Post*. October 30, 2003:A21.
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Screening Virtual Colonoscopy — Ready for Prime Time?

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Many professional societies in the United States recommend screening for colorectal cancer in asymptomatic, average-risk adults, beginning at 50 years of age. Screening achieves two goals: the detection of early-stage nonmetastatic cancers that are surgically curable and the identification and removal of benign adenomatous polyps, the precursor lesions of nearly all adenocarcinomas. Several approaches to screening are available, ranging from the least expensive and least invasive, fecal occult-blood testing, to the more costly and invasive procedures — flexible sigmoidoscopy, barium enema, and colonoscopy. Each of these tests has inherent strengths and weaknesses related to cost, risk, sensitivity, specificity, and availability.¹

Fiberoptic colonoscopy, the current gold standard for screening against which other tests are

usually compared, provides very high sensitivity (>90 percent), with a false-negative rate of approximately 6 percent for adenomas of 1 cm or more in diameter.² Flexible sigmoidoscopy is unacceptable to some physicians and their patients because it screens only the left side of the colon. Barium enema may be recommended as an adjunct to flexible sigmoidoscopy for the evaluation of the proximal portion of the colon that lies beyond the reach of the sigmoidoscope. Colonoscopy has substantial drawbacks as a screening test, including the need to insert an intravenous catheter for the administration of sedatives, a recovery time of 30 to 60 minutes, and the requirement for a driver to accompany the patient home. The total time for admission, the performance of the procedure, and monitoring afterward is approximately two hours. Colonoscopy is