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Information for Contributors appears on pages 600-602 of the 31 July 1992 issue. Editorial correspondence, including requests for permission to reprint and reprint orders, should be sent to 1333 H Street, NW, Washington, DC 20005. **Science Telephone:** 202-326-6500, TDD 202-408-7770. London office: 071-435-4291. **Subscription/Member Benefits Questions:** 202-326-6417. **Other AAAS Programs:** 202-326-6400.

The Readers' NIH

In answer to Bernadine Healy's request (Policy Forum, 17 July, p. 312), I suggest a mechanism that would generate research on important, unsolved, and understudied problems through the National Institutes of Health's (NIH's) extramural grant system. It would be funded by money currently awarded by Requests for Application (RFAs), a mechanism inappropriately used for funding basic research. The extramural grant administrators would hold meetings just as they do now on unexplored, underfunded, but critical, problems that they perceive are in need of resolution. The audience for these meetings would consist of experts on the subject, but also of an equal number of invited excellent scientists from other disciplines who know little or nothing about the problem. All NIH grantees would agree to attend one such meeting outside their field each year. At the meeting the experts would explore every facet of the problem. The outsiders would ask questions and become educated. The hope is that once in a while a scientist outside the field would be lured into it by thinking of a novel set of experiments that his or her expertise brings to mind. An unsolved problem is always a lure for a bright scientist, but there is also bait. The bait consists of some agreed-upon small set-aside of the research project grant (RPG) budget, perhaps 2 to 5%. The existence of this fund and the rules for tapping it would be widely publicized. A scientist could ask for a small amount of seed money to enter the new field, maybe the cost of a postdoctoral fellow or a piece of equipment. There should be a simple application procedure to encourage the transition, and the extramural branch chiefs could meet periodically to review the proposals selecting the most meritorious requests for funding. No new study section would be needed.

An alternative to these meetings that are generated by the extramural administration would be through traditional scientific meetings that NIH is asked to fund. In order to receive NIH funding, the meeting organizers would agree to have one or more session(s) on an intractable, understudied problem with invited experts to present the state of research on the topic. Presumably, the selected problem would be as closely relevant as possible to the topic of the meeting. This method differs from the current RFA mechanism and has the following advantages:

1) It would lure but never force the best (already funded) scientists into a field doing the experiments they consider important.

2) If the problem is not yet ready for study, it would remain ignored, as it should, to be brought up periodically.

3) The seed money would be small but sufficient to entice a first-class scientist to buy in. It is hoped that it would lead to an RO1 grant application and a convert to the problem.

4) The request for funds would be handled competitively but expeditiously.

This plan has an important role for the extramural administration who would choose the general topics for meetings, invite and schedule the participants, and review the proposals, but the specific scientific choice would be left in the hands of bench scientists. In contrast with a traditional RFA that often attracts those who cannot be funded otherwise, this plan would try to attract the best scientists already in the system.

Donald D. Brown

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On the basis of my understanding of the proposed NIH strategic plan, as described by Healy, I strongly urge that additional consideration be given to two factors.

The first is medical costs. In other portions of the government, there is a belief that advanced technologies are increasing the costs of providing medical care, and there seems little doubt that the reduction of these costs will be one of the primary political issues of the next decade. This suggests that NIH's choice of technologies to support should, in part, reflect estimates of the costs likely to be incurred to implement those technologies. In particular, for example, it would encourage support of approaches that are likely to lead to vaccines or to prevention as distinguished from those likely to lead to expensive new surgical procedures.

The second factor is the increasing internationalization of science and, at least potentially, of medicine. The international scientific community is much stronger than when NIH was created. And the needs for medical care in the developing world are overwhelming. We now need a global NIH. The developing world needs are not purely

an altruistic issue for the United States—science for developing nations is likely to overlap with that needed for some of our own poorer communities and, with AIDS, we are already learning of the possibility of new forms of global epidemic.

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At present, in addition to NIH and several other agencies within the Department of Health and Human Services, relevant research on vaccine development in the United States is funded by the Department of Defense (DOD), the Agency for International Development, the Agricultural Research Service, and possibly the Department of Energy and the Veterans Administration. This is not an efficient arrangement. Much of the DOD research is carried out under the Army's Biological Defense Research Program (BDRP). The BDRP is unclassified. It is not designed or intended to provide protection to the civilian population, although work on bona fide biowarfare threat agents as well as on other disease agents has civilian relevance. In order to reap all possible benefits, both military and civilian, from the BDRP's biomedical activities, they could better be carried out under civilian control. Centralization under NIH would optimize the quality of the research, eliminate overlap and inefficiency, and ensure maximum return on the public investment. It would also guarantee the openness that would underline U.S. compliance with the Biological Weapons Convention, which prohibits the development of biological agents or toxins as weapons.

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I suggest that NIH restore training programs for graduate students by awarding predoctoral fellowships to graduate students. Graduate students can then choose the appropriate graduate program for his or her interest.

I also suggest the establishment of satellite research centers based on the density of biomedical researchers and on a regional basis. A model for such centers could be those of the French INCERM (Institut National de la Santé et de la Recherche Médicale). Such centers would be under NIH control and would provide a centralized location for an animal care facility, electronics shop, machine shop, tissue culture media, and large, costly items of research. A permanent house staff would be employed to

oversee the centers. Individual investigators who receive RO1 grants would then apply for research space and would be granted leave from their home institution for the percentage of their time that is required to perform their research. The university would retain the services of the faculty member for a proportion of time in accordance with the institution's percentage of the faculty member's salary. The research universities would retain their academic responsibilities for education and pure science without having to build and maintain costly research facilities that are often built on costly city real estate and that reduce the city's tax base.

C. Paul Bianchi
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Healy states, "The alternatives to peer review are barely imaginable, but they could only be more bureaucratic and certainly more political." This is not necessarily so. There are certainly ways of improving peer review that are imaginable and would be less bureaucratic and less political than the present system.

One improvement could come from delegating some (or even much) of the peer review to the colleagues of the investigators. Colleagues on the scene can know the originality, competence, and productivity of the scientists with whom they work better than a panel of experts who have never met the applicants. I suggest that a part of the budget for extramural grants be assigned directly to the dean of a school of medicine or other director of a research institution. The deans could assign 20% of what they receive, as they think best, but they would be required to pass 80% to the chairmen of departments. The chairmen, in turn, could assign 20% of their share, as they think best, but would be required to divide the remaining 80% of their share among existing investigators. The discretionary funds held by the deans and chairmen could be used by them to give starting funds to beginners who do not yet have an investigation under way.

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Regional research-funding consortia should be set up across several institutions that would be asked to peer review the "smaller" grant applications arising from member institutions (R29 or RO1 grants with a total direct cost of \$350,000 or less). Memberships on these local study sections could be drawn from local qualified investigators (from the consortia) complemented by a few

nationally recognized experts. This approach would take away some of the bias that only applicants from "famous" research institutions have the proper environment in which to carry out their proposed research. Furthermore, the participating institutions could use part of their overhead reimbursements to pay for this local peer-review system. This is a variation on the Agricultural Experimental Station concept used by the U.S. Department of Agriculture.

Policy should be developed in the review process to make it difficult (if not impossible) for any one principal investigator to receive more than \$1 million of total direct cost in research support from NIH. The reduced work load on the individual reviewer under this regional-national review system might make the peer-review process less biased and more thorough.

A similar peer-review process should be developed for intramural research projects, and details such as the name of the intramural investigator, the title of the project, and the amount of funds released should be widely publicized annually. This approach would rectify the public perception that NIH intramural investigators and their projects are above public scrutiny.

Thomas C. K. Chan
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I suggest that a fraction of the grant applicants be selected for funding by a random process, regardless of the ratings they received in peer review. Another fraction of applicants would be chosen for which the selection process would be modified from the current procedure (for example, by blinding, requiring the referees to sign, or other experimental treatments suggested in the literature). In short, a scientific approach to resource allocation methods is suggested. True experiments are needed, not just retrospective studies. In succeeding years other modifications would be tested. After about 5 to 10 years, evaluation of performance in the three experimental groups could be performed. The random group would provide a standard against which the other selection processes could be judged.

Alan Peter Rudell
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With respect to extramural NIH-funded research, too many mid-rate institutions are pushing their faculty, trying to become first-rate institutions. The result is a system clogged with grant applications from people who would rather be teaching. NIH extramural research dollars should be focused on fewer institutions. Allow the caliber of the institution to weigh more heavily in the

priority score. This will increase the competition among the best scientists trying to obtain positions at those institutions, but, once they are there, they would be able to spend less time writing grant applications because funding would be easier to obtain.

With respect to intramural NIH research, to my knowledge, no one has tried to compare the efficiency of a dollar spent on extramural versus intramural research. Even the simplest comparisons, of researchers supported or of papers published, are impossible to come by. However, many researchers (admittedly mostly extramural researchers) feel that our extramural dollars are more productive. If this is true, then the intramural program should be scaled back in favor of extramural research.

Charles A. Gardner

Subcommittee on Human Resources and Intergovernmental Relations, Committee on Government Operations, B372 Rayburn House Office Building, Washington, DC 20515

The 6-month delay between submission of an NIH proposal and receipt of the review and priority score exacts a heavy toll on scientists' lives and careers, and could be reduced to just 6 weeks, like that for AIDS proposals.

Reviewers' tenure should be reduced from 4 to 2 or 3 years to spread the burden and the privilege. Most reviewers experience a dismaying drop in their scientific productivity, which is only partially compensated for by the opportunities to help determine the future of their field. We all take this responsibility very seriously and are often torn by competing principles in trying to arrive at the right assessment, but, truly, it is hard to know whether we were right or wrong: unfunded research leaves no trace.

Denis Pelli

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Concerning Healy's question, "How can NIH reinvigorate the nation's declining scientific brain trust and reverse its seemingly relentless 'graying'?", develop a cooperative arrangement with research universities, asking them to restructure their departments to achieve the following goals.

1) Reduction of the pressure on professors to garner research grants (for the purpose of bringing in overhead money) and to publish large numbers of papers. Allowing only one grant and perhaps two to four papers to "count" toward career advancement is one way to do this. Professorships would thereby become more attractive to younger people.

2) Establishment of career cycles at the departmental level so that "graying" researchers can honorably make lateral moves

into teaching (especially undergraduates), thereby withdrawing from the "survival" mode and providing more replacement slots for younger researchers who are in their "expressive" modes. More slots would increase the choices of university and location, thus appealing to younger scientists.

3) Development of research partnerships whereby two (or more) principal investigators could combine their efforts to win a single grant (much as attorneys and physicians form partnerships and joint practices). Researchers could thereby achieve significant gains in the battle against workaholicism and make professorships more attractive to younger investigators. Younger scientists (especially women) are interested in having more time and opportunities for personal growth and family participation, as well as career advancement.

In return, NIH could reward departments that achieve these goals with graduate student fellowship funds, equipment grants, and faculty development funds (similar to career development awards).

George M. Malacinski

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One way to admit cross-disciplinary innovation to the NIH system might be to create a new category of individual investigator grants. A study section would rate applications for these grants separately from the usual ROI's. Their ratings would be highly leveraged by innovative ideas and would be funded by the NIH Council from a pool independent of that of the usual ROI's. Such a scheme could help study sections sponsor young or cross-disciplinary investigators because they would not be in direct competition with the ROI's. A reasonable goal might be to fund these grants at a rate of, say, 5% of ROI funding.

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Healy clearly and emphatically articulates the need for a "sophisticated and highly trained talent pool" in critical technologies such as molecular and cell biology and molecular genetics that undergird NIH's broader scientific enterprise. While Healy may be referring to doctoral-level and post-doctoral-level scientists, the need is just as critical for well-educated, technically sophisticated, experienced, baccalaureate-level research assistants and associates to

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support these senior scientists.

Baccalaureate programs in the United States that provide this type of education are few in number. There are no significant federal-level efforts, and virtually no state-level efforts, to establish an organized approach to ensure that the number of such suitably educated and experienced entry-level scientists is sufficient to meet the current and projected future needs.

Tom Frederick

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Many lab heads are reluctant to let productive protégés apply for independent funding. NIH should allow grant applications to be submitted without institutional endorsements and give successful applicants a 2-year grace period to arrange institutional approval before beginning funding. Successful applicants could then find a supportive institution, thus liberating this un- and underfunded young talent.

Kevin Jon Williams

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Concerning communication with Congress and the public, articulate loudly and clearly that funding of research makes jobs. It makes jobs for technicians and for the manufacturers of supplies. When equipment is funded, it

makes jobs for those who manufacture and sell equipment. The same is true of defense spending. However, our product helps the public and increases knowledge.

For communication with the public, have a regular weekly program on public radio or television, or both. Consider an annual awards ceremony on television. Develop an NIH logo that goes on the face sheet of every scientific publication supported by NIH.

Concerning peer review, have individuals appointed to study sections serve one probationary year. Occasionally, there are suboptimal appointments. Limit the number of grants that any study section reviews. Randomize the order of grants, so that old grants are not reviewed first. Consider developing a way for evaluating the quality of grant reviews. Outstanding individuals should be invited to serve on advisory council or ad hoc study sections. Be certain that political considerations do not influence appointments to the advisory councils.

Concerning RO1 policy, consider a time limitation (say 30 years) on any one grant. Consider a limit, say, 40 years, for any one individual to get the majority of his salary from NIH grants. That would help bring young people into the system.

Penalize those who abuse the system. I have heard of awards given to young phy-

sicians who were then forced to do extensive clinical work. When individuals do not renew their grants, there is no penalty for a failure to make even an effort to perform the research that was funded.

Concerning intramural research, develop criteria for what should be done on the Bethesda, Maryland, campus and what should not be.

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A fallacy has been perpetuated that the current NIH funding level is appropriate because the NIH budget in recent years has kept pace with inflation in real dollars. Funding for biomedical research should be measured, not against inflation, but against the dollars spent on health care by the entire nation (as a part of the gross national product) or by the government (as part of the federal budget). When measured against these yardsticks, the funding of NIH has actually plummeted over the last two decades. Those negotiating with Congress should constantly reemphasize this message and not accept the notion that the only problems are the management and the distribution of seemingly adequate funds. The public should be convinced that past NIH-supported research has actually paid off in ways that completely justify the investment. This must be done in terms that everyone can understand, by painting "what if?" scenarios. For example, simple computer modeling should show that if the basic research of the 1970s in cancer biology, immunology, molecular biology, and virology had not subsequently allowed rapid identification of the human immunodeficiency virus and the cleanup of the blood supply, the AIDS epidemic of the 1980s would have killed many more Americans. Federal health care costs for AIDS would have been much higher than they are today, and the difference would be greater than the original dollar investment in research. Likewise, one could calculate how many more Americans would now be incapacitated by mental illnesses (and hence be expensive wards of the state) if fundamental research in neurobiology, neurochemistry, and psychiatry had not yielded new approaches to the management of the major psychoses. Using such scenarios, we must convince the public and Congress that investment in fundamental biomedical research will repay itself many times over in the future, in actual savings to the taxpayer.

Ajit Varki

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