quarter of the applications were directed, the actual success rate for Type 1 grants averaged only 9.2% (Table 1). The National Institute of Child Health and Human Development, the National Institute of Mental Health, and the National Institute for Nursing Research had the lowest rates (mean = 7.9%). The National Eye Institute, the National Center for Research Resources, and the Human Genome project had slightly higher success rates, but these represented a total of only 4% of the submitted R01 applications.

For R29 awards, the success rates for *unamended* competing proposals for fiscal years 1993 and 1994 were 23.1% and 19.0%, respectively. In general, the distribution patterns for R29 and R01 applications were similar, but the success rate for R29 grants was a little higher. The total pool of these relatively low-cost R29 applications was much smaller, however.

There has been a progressive deterioration over the past 10 years (Fig. 1) in the funding of unsolicited, competing, unamended R01 applications for new (Type 1) and renewal (Type 2) applications. The data on renewal applications indicate that two out of three established investigators cannot continue their ongoing research programs. They are also deterred from proposing highly imaginative but speculative ideas that might lead to major scientific breakthroughs (*2*).

Debates for the budget for fiscal year 1996 have begun, and further cuts in the NIH budget have been proposed. The NIH has shown itself to be an excellent financial investment, as measured by improved health care for our citizens as well as the progress of our biotechnology industry (*3*). Our political leaders must have the understanding and courage to protect government expenditures that have proved to be invaluable for this country and for mankind.

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References and Notes

1. Data provided by Statistics Analysis and Evaluation Section, Information Systems Branch, Division of Research Grants of NIH.
2. Whereas the number of Type 1 applications reviewed did not change appreciably over the past 10 years, there was a small decrease in Type 2 requests (Fig. 1).
3. S. C. Silverstein, H. Garrison, S. Heinig, *FASEB J.* **9**, 833 (1995).

Regulation of Human Gene Therapy

We, the undersigned members of the National Institutes of Health Recombinant DNA Advisory Committee (RAC), wish to reply to the recent letter by Gerard J. McGarrity and W. French Anderson (2 June, p. 1261). They suggest that the RAC reduce its role in the supervision of human gene therapy and specifically suggest that the RAC end protocol-by-protocol review and review of Phase I follow-up studies. We believe that separate issues are involved in these two suggestions that require further public discussion.

With regard to protocol-by-protocol review, it should first be pointed out that an accelerated review process not requiring a wait for a quarterly meeting of RAC already speeds the approval of replicative protocols. For instance, at its recent June meeting, the RAC reviewed nine new protocols while it heard about the approval of three accelerated reviews and four minor modifications. The relative number of accelerated approvals compared to full RAC review could certainly be increased. Second, we believe that substantial safety issues, particularly regarding long-term potential effects of gene therapy experiments, remain sufficiently important to merit discussion in a public setting. It has not yet been 5 years since the approval of the first human

gene therapy experiment. Some of the viral vectors being used for gene therapy have long-term potential for causing cancer, and the public RAC review of such consequences still seems relevant.

With regard to Phase I (toxicity) follow-up studies, the RAC public review is also relevant to the determination of the potential harmful consequences of human gene therapy. Since most of the protocols approved have been Phase I/II studies, information about efficacy (or lack thereof) is also elicited. Perhaps it is the latter aspect that might be controversial.

In summary, while we recognize the need for streamlining the regulatory processes in this area to conform with both commercial interests and the needs of severely ill patients, the removal of large portions of the review process from public scrutiny and loss of advice from experienced professionals representing diverse points of view would frustrate the concerns of many U.S. citizens about this new form of medical experimentation. Painful lessons have been learned in both the nuclear energy and biomedical research fields about the danger of too much secrecy when scientific methods with long-term risks and benefits to humanity are under development. Out nation must continue to profit from these lessons rather than repeat the mistakes of the recent past.

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Ph.D. Education

Floyd E. Bloom, in his editorial "Degrees of uncertainty" (12 May, p. 783), clearly disapproves of what he sees as a recommendation by the National Academy of Sciences' Committee on Science, Engineering, and Public Policy (COSEPUP) to create "graduate programs that sound like graduate technical colleges and [to recruit] students who have formulated more realistic career expectations." Like those before us, we are attracted to science because we are curious. How wonderful it would be to enter graduate school and not worry about getting a job afterward! Unfortunately, most of us need jobs to survive. Responsible educators must enhance their students' and postdocs' abilities to be employed and to use their scientific training. That could mean doing as COSEPUP suggests: make Ph.D. programs shorter and more flexible, and provide timely, accurate career counseling.

An alternative would be to reexamine the entire employment structure for Ph.D.'s, including developing desirable post-postdoctoral research and teaching opportunities in academia. Industry currently employs and promotes Ph.D.'s along two "tracks," research and management. Ph.D.'s receive equivalent compensation, respect, and on-