NIH proceeds with overhaul of grant system

A report released at the beginning of September by the National Institutes of Health (NIH) describing a major restructuring of its grant review process has generated highly publicized criticism from some researchers, but other scientists support the changes and contend that the protests are misguided.

The controversy centers on recommendations made in a draft report by the Center for Scientific Review (CSR), the NIH body that reviews 70% of the grant applications sent to the agency. The CSR, spurred by researchers' concerns that the current grant review system is unfairly biased against new interdisciplinary projects and innovative approaches, began overhauling the system in 1997 (*Nature* **387**, 642; 1997), but the draft report is the first official description of the changes being considered.

Elvera Ehrenfeld

The CSR reviewed around $9.4 billion worth of extramural grants in 1999. Under the current system, these grants are sent to study sections composed of volunteer peer reviewers from particular areas of research. In turn, these study sections are grouped into 20 Integrated Review Groups (IRGs) that encompass specific disease categories or research techniques. For example, the "AIDS and AIDS-related research" IRG category includes seven study sections covering one disease.

In Phase 1 of its overhaul of the 50-year-old system, CSR has proposed a new list of IRGs, grouping study sections by general scientific discipline rather than by specific disease. So under the new scheme, the AIDS study sections for example, would be distributed between groups such as 'immunology' and 'infectious diseases and microbiology'.

The changes, although seemingly logical, have encountered vocal opposition from AIDS researchers in particular. Mario Stevenson, an HIV virologist at the University of Massachusetts, says, "the [current review] system works well, but isn't perfect," and adds, "from what I've seen of the proposed changes, they're not a step for improvement but potential harm." Because AIDS research often relies on techniques from several different fields, separating virology from immunology study sections would be a mistake, say many AIDS researchers.

Elvera Ehrenfeld, director of the CSR, insists that grants will still be reviewed by qualified study sections, and that the current report only describes the reorganization of the IRGs: "Some of the criticism comes from scientists who are expressing concern regarding the absence of details about specific study sections that have been deliberately deferred to Phase 2. These concerns will be addressed at that time, as was stated in the Phase 1 draft report."

The CSR will release a final report establishing the new grant review process early next year. Phase 2 of the overhaul will then begin with an evaluation of the study sections, a process expected to take at least two years.

"Although we're being told that the review groups won't be disassembled, my concern is that once we get to Phase 2 ... what we'll start to see is AIDS grants being reviewed by general virologists," Stevenson warns. "Sometimes I get the feeling that the motives behind the CFR are to defuse the concept that AIDS is a special case," he adds. Other AIDS researchers concur, speculating that NIH may be trying to dissolve the AIDS-specific category as a way of dodging criticism from activists lobbying to establish special categories for other diseases.

Outside the AIDS field, though, the changes have been warmly, if cautiously, received. Vincent Racaniello, a professor of microbiology at Columbia University and editor of the *Journal of Virology*, believes that the new criteria defined in the draft report will encourage study sections to favor more innovative research. He dismisses the idea that AIDS studies will be harmed. "Apparently the HIV people think they are going to lose their seven study sections," says Racaniello, "but that clearly won't happen, since they exist by political, not scientific mandate." Congress determines the funding levels of the different NIH institutes, which then set the funding priorities that determine the number of study sections for a particular field.

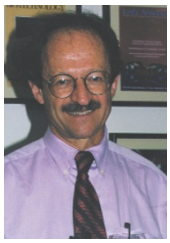
According to Ehrenfeld, Racaniello's response is more typical of the researchers who have offered feedback on the report: "There has been criticism from a few research communities...but the great majority of respondents endorse the activity."

Some respondents have offered more constructive criticism on specific aspects of the report. Sebastian Doniach, former director of the Stanford Synchrotron Radiation Laboratory at the Stanford Linear Accelerator Center, advocates broadening study sections by soliciting mail-in reviews from a larger number of researchers. "This will help alleviate the problems which arise when a given section does not have sufficiently objective expertise to adequately assess a proposal, or where the 'resident experts' tend to represent a built-in cartel," says Doniach.

ALAN DOVE, NEW YORK

Varmus bows out

The director of the National Institutes of Health (NIH) Harold Varmus, has confirmed that he will leave his post at the end of the year and become President and Chief Executive Officer of Memorial Sloan-Kettering Cancer Center in New York City. The post of NIH director is a political appointment and in a letter to President Clinton, Varmus urged him to hire another medical research scientist to head the agency before Clinton finishes his second term at the end of 2000.



Harold Varmus

The consensus in the biomedical community is that Varmus set an exceptionally high standard as director and will be a hard act to follow. He is credited with almost single-handedly persuading Congress to invest so heavily in biomedical research. Under Varmus' leadership, the NIH budget grew to $15 billion in FY99 from less than $11 billion. The budget could rise by a further $2 billion in FY00 depending on the outcome of current Labor–HHS appropriations discussions between the House and the Senate in the US Congress. (see http://medicine.nature.com/breaking_news)

KAREN BIRMINGHAM, LONDON

SAAVI awards first AIDS vaccine grants

The South African AIDS Vaccine Initiative (SAAVI), a public–private initiative to produce a national HIV/AIDS vaccine (*Nature Med.* **5**, 252; 1999), has announced its first award recipients. Four research proposals were selected from a total of ten, and each will receive substantially more funding than that meted out by the country's other grant-giving bodies, which typically dispense R300,000–500,000 (US$50,000–83,000) per project.

Each proposal was evaluated by two non-South African referees. Two basic science projects (both targeting clade C which is the predominant HIV subtype in South Africa), one "Education and Advocacy" program and one "Ethical Issues in HIV/AIDS Vaccine Development" project were selected for funding. A fifth program of "Immunological Support" is to be subjected to further review before a funding decision is taken.

The projects have been allocated a combined total of R7 million from the R20 million SAAVI budget. William Malegapuru Makgoba, president of the South African Medical Research Council, which oversees SAAVI, told *Nature Medicine* that the remainder of the money will be held in reserve because SAAVI is hoping to support Phase I clinical trials in South Africa of the North Carolina company AlphaVax's Venezuelan equine encephalitis virus vaccine—a project that received $4.6 million funding from the International AIDS Vaccine Initiative last year (*Nature Med.* **5**, 5; 1999).

Both SAAVI basic research projects are lead by female scientists, a sign of changing times in South African research. Anna-Lise Williamson from the Health Sciences Faculty at the Observatory Cape Town, principal investigator and co-ordinator of one of the selected projects, told *Nature Medicine* that her team will receive R3 million for the first year, and is using *env* and *gag–pol* genes from a local HIV clade C isolate to construct vaccines based on recombinant BCG- and plant-derived virus-like particles.

"If these approaches are successful the technology already exists in South Africa to produce candidate vaccines, and they will be relatively inexpensive," says Williamson. The vaccines will be compared to modified vaccinia Ankara (MVA) and DNA vaccines expressing the same HIV subtype C genes. Combinations of different vaccines will then be assessed, using one to prime, and the other to boost, the immune response.

The second basic research project centers on a more unconventional approach and is lead by Estrelita Janse van Rensburg, head of the department of Medical Virology at the University of Stellenbosch. Her group receives R2 million and will focus on the development and production of HIV proteins by recombinant strains of filamentous fungi, *Aspergillus* sp. and *Pichia stipitis*. "The idea is to use the recombinant fungus vaccine in a prime-boost strategy, in combination with a subtype C DNA vaccine," says van Rensburg.

Rensburg's team also plans to clone *env* and *gag* genes of clade C isolates and, through collaboration with the US Department of Microbiology in the Faculty of Science, will establish fungal eukaryotic expression systems for the production of HIV proteins. In parallel, they will genotype the HLA of the lymphocytes used to determine the best, 'common' HIV-derived CTL epitopes. The predominant HLA types in South Africa are presently unknown and their elucidation will help not only South African vaccine R&D but also worldwide efforts.

Each project must re-apply for funding annually, and Makgoba has to submit a progress report to the Ministry of Health and the president every four months.

KAREN BIRMINGHAM, LONDON

PACHA adopts more lenient stance to government efforts

The President's Advisory Council on HIV/AIDS (PACHA), an advisory panel on AIDS research and policy, has a history of criticizing the government agencies charged with developing an AIDS vaccine and implementing policy for those infected with the virus (*Nature Med.* **4**, 477; 1998). However, there was a more conciliatory tone at this year's annual meeting held in Washington, D.C. on 4–5 October, and the 35-member panel went so far as to voice some support for current government initiatives in HIV/AIDS research and prevention.

One of PACHA's recurrent complaints in recent years has been the foot-dragging in staffing AIDS research leadership positions at the National Institutes of Health (NIH), including the absence of a director for the NIH's new Vaccine Research Center (VRC). However, Gary Nabel, who was appointed to the post in March (*Nature Med.* **5**, 362; 1999) addressed the group on the first morning of the meeting. He discussed VRC's structural organization, HIV vaccine development strategies, and noted that the hiring of several staff members with backgrounds in the pharmaceutical and biotechnology industries, a move PACHA had strongly urged previously, is imminent.

Although one speaker challenged that, at present, the VRC is just Nabel, a secretary, and some good will, Nabel assured *Nature Medicine* that, in the absence of a functional building on the NIH campus, his laboratory at the University of Michigan has become an off-site NIH laboratory. "We're in a position now where we can implement some [research] ideas," he says. For example, his laboratory could develop constructs for HIV vaccine research. The new building will be operational next year with around 120 laboratory scientists and support personnel.

The VRC's FY99 budget was $18.5 million and its FY00 budget is projected at $22 million. Nabel expects that when the VRC is fully operational, the annual budget will be around $30 million; but comments from PACHA members that this is a small amount of money if the center is to be involved in clinical trials, he agreed that PACHA was "right to be concerned that our costs can be higher."

Although PACHA has long requested that White House Office of National AIDS Policy increase its control over AIDS vaccine development initiatives, that has not happened. And with NIH making its leadership role in the development of an AIDS vaccine even clearer, as evidenced by Nabel's presence at the PACHA meeting, most do not believe PACHA's request, which once filled many basic scientists with angst, will reach fruition.

Deborah Birx, director of the U.S. Military HIV Research Program—a cooperative agreement between the