Overhauling AIDS Research: Views From the Community

A massive review of the National Institutes of Health's (NIH's) entire $1.4 billion AIDS research portfolio, now entering the final stretch, is expected to call for some fundamental, far-reaching changes in the way funds are managed and spent. Begun last May in response to Congress's overhaul of NIH's Office of AIDS Research (OAR), the review has brought together more than 100 leading scientists from academia and industry, and a sprinkling of AIDS activists, to take a hard look at where this money has gone and where it should be going. The much-anticipated report is expected to be released in March, but *Science* has obtained drafts of reports written by three subpanels that are expected to form the foundation for at least half the final report.

Judging from these documents and interviews with key players in the review, the "NIH AIDS Research Program Evaluation," as the assessment is formally known, will argue for the following: more critical evaluation of whether expensive clinical trials of new drugs and vaccines should be launched; a better balance between investigator-initiated and targeted research; efforts to attract higher quality scientists to the field; elimination of research from the AIDS budget that is not clearly related to AIDS; more sharing of data and resources; and more stringent review of research done within NIH's intramural program. "No one's ever grappled with taking on a program this large," says William Paul, head of OAR. "I've been very impressed with the enormous amount of work that's gone into this with many of the participants. It's much more than you usually see." Like others close to this review process, Paul is reluctant to discuss details, however. "It's far from clear what the final report will look like," he says.

The review group consists of six "area review panels" that have been feeding their reports to an executive "working group," co-chaired by Arnold Levine of Princeton University and Harold Ginsberg of Columbia University. The working group, which will meet twice this month to comb through those hundreds of pages of documents, is writing its own overview. Ultimately, it will decide what makes it into the final report.

Working group member and immunologist Barry Bloom of the Albert Einstein College of Medicine cautions that people should not expect too much from the final document. "It isn't going to shake up the universe," says Bloom. "But I'd like to think it's going to affect things more than at the margins."

Below are specific recommendations culled from draft reports written last fall by the three area review panels whose reports have been obtained by *Science*:

Etiology and pathogenesis. This panel, which looked at studies that focus on the cause of AIDS and how HIV destroys the immune system, gives NIH "high marks overall" but notes that there is "ample room for improvement."

The panel's draft report notes that it "is the consistent impression of all of the panel members that about a third of the portfolios of the lead [NIH] institutes in the area of pathogenesis, to nearly the entire portfolio in some instances, represents research which the panel considers to be of dubious quality and relevance." Singled out for criticism are a rabbit model for HIV pathogenesis that the National Institute of Allergy and Infectious Diseases (NIAID) funds to the tune of $3.5 million a year, "generic work" on opiate receptors supported by the National Institute of Mental Health, National Cancer Institute (NCI) studies of "endogenous retroviruses with no linkage to AIDS research," and studies of the effects of alcohol on the immune system funded by the National Institute on Alcohol Abuse and Alcoholism.

The panel also faults some pathogenesis researchers themselves. In particular, it flags "many examples of a closed-shop mentality in the use of some of the resources" that researchers should make widely available to their colleagues, such as monkeys, transgenic mice, and samples of tissues and blood from patients. Recommended fixes range from establishing new NIH guidelines for sharing clinical samples to making more monkeys available by redirecting some of the $10 million that the National Center for Research Resources (NCRR) now spends on chimpanzees—which, according to the panel, are an inferior animal model for AIDS pathogenesis. (There is only scant evidence that chimps get sick from HIV; Asian macaques infected with SIV, HIV's simian cousin, develop AIDS.)

Finally, a "recurring theme" in panel discussions was "why so few exceptionally distinguished scientists were actively involved in AIDS pathogenesis research." To attract better researchers—especially more immunologists—the panel recommends doubling support for investigator-initiated AIDS research through what are known as R01 grants. "There was a resounding consensus that the R01 pool of funds currently is simply insufficient," the panel writes.

Vaccine research and development. As this panel explains in a draft "executive summary" of its report, it has serious worries that without "a strong stimulus" from NIH, "the waning private-sector interest in an HIV vaccine may vanish altogether." The panel—which is divided into basic research, targeted research, and clinical trial subpanels—has amassed a truckload of recommendations to make NIH-sponsored AIDS vaccine research "more vigorous and effective."

A draft report from the basic science subpanel notes that although NIH says it spends $125 million on AIDS vaccine research, the "true expenditure on core topics of vaccine development was likely to be very significantly less." The reason: Much of the money has funded programs that bear "only a marginal relevance to the subject"—such

NIH AIDS RESEARCH PROGRAM EVALUATION

Panel	Chair	Recommendations
Etiology and Pathogenesis	Ashley Haase, University of Minnesota	Double R01 budget, cut intramural program, encourage better sharing of animals and clinical samples, shift money from chimps to monkeys
Vaccine Research and Development	Dani Bolognesi, Duke University	Cut NCI's intramural program, centrally coordinate primate research, boost targeted budget and R01s
Clinical Trials	Richard Whitley, University of Alabama, Birmingham	Fold clinical trial networks into AIDS Clinical Trials Group, establish oversight committee, cut NINDS
Natural History, Epidemiology, and Prevention Research	King Holmes, University of Washington	Cut several big-ticket NIH intramural programs
Drug Discovery	Emilio Emini, Merck Research Laboratories	Cut NCI's $53 million per year AIDS drug screening program
Behavioral, Social Science, and Prevention Research	Thomas Coates, University of California, San Francisco	Replace generic drug abuse and alcohol research with AIDS-related research

Six views. Recommendations from the first three panels are from draft reports obtained by *Science*; recommendations from the other three were described by participants in the review process.

as work on cancer vaccines and basic molecular virology of a distant HIV relative, HTLV-1. More alarming still to this group, only $11 million goes to R01s for preclinical vaccine research. "The 'discovery engine' for AIDS vaccines is presently a 50-cc two-stroke model, which is attempting to power a Cadillac," admonishes the draft report.

Part of the problem, the subpanel argues, is that R01 grants for vaccines often are not considered to be "cutting-edge science" by the NIH "study sections" that review them. To help correct this, the subpanel recommends that NIH form a study section devoted to vaccine research, rather than sending these proposals to sections that focus on, say, immunology. Another fix suggested by the subpanel is to gut NCI's $14.8 million intramural AIDS vaccine program. Estimating that "up to half" of that money has not been spent on AIDS vaccine research, the subpanel "strongly" recommends a "major reduction in funding for NCI" and feels "most strongly that an expert peer review of the entire vaccine research program administered by NCI was essential."

The subpanel that focuses on so-called "targeted" research, for its part, suggests that research at the primate centers, which receive about one third of the $40 million spent on targeted work, should be centrally coordinated. Currently, there is "immense confusion" about the meaning of animal studies with vaccines, because they have been done under different conditions and cannot be compared. And, for reasons this draft report doesn't clarify, the subpanel recommends that NIH find $25 million to $50 million each year in new money for what is described vaguely as "an expanded" targeted AIDS vaccine effort. The full panel report says this might include vaccine production by the government, rather than industry.

The third arm of the vaccine group is analyzing the $42 million that NIH claims to spend annually on AIDS vaccine clinical trials—an amount the panel says is probably "seriously overstated" because of "inaccurate reporting and coding." This subpanel comes down hard on HIVNET, a $16-million-a-year network of researchers set up mainly to lay the groundwork for HIV vaccine efficacy trials at domestic and international sites—none of which are currently on the drawing boards at NIH. "A serious danger is that, in the absence of a vaccine efficacy trial, HIVNET will undertake trials of other interventions [such as counseling and vaginal microbicides] without adequate review of the need for such studies," says the draft report from this group, which suggests cutting HIVNET in scope or even folding it into another program.

Clinical trials. *Science* obtained only the executive summary from this panel, so the reasoning behind its recommendations remains sketchy. One big recommended change is to fold all four clinical trials networks now being sponsored by NIAID into what the panel considers the best of the lot, the AIDS Clinical Trials Group (ACTG), which tests new treatments at 30 academic medical centers spread across the country. In addition, the panel pointed out that several other NIH institutes besides NIAID also test experimental treatments and preventive strategies in humans, and it said it was "distressed that there is no overall coordination." To resolve this shortcoming, the panel "strongly recommends" that NIH set up a clinical trials oversight committee.

This draft executive summary is especially critical of AIDS clinical trials funded by the National Institute of Neurological Disorders and Stroke, which the panel charges is not "committed" to evaluating neurological manifestations in AIDS and also does not "express a responsibility" to do neurologic evaluations of people in ACTG trials.

Insiders say the working group will not water down these draft reports. In fact, "we're pushing them to be tougher," says working group member Bloom. "I'd be astonished if the final report was weaker than the drafts." The working group is also urging the panels to be more realistic about money matters. "Everyone wants more resources, but no one wants to put anything on the chopping block," says one person close to the process who asked not to be identified by name.

The panels have had a hard time finding candidates for the ax, however, in part because they have found it difficult to unravel how NIH's intramural program spends AIDS money. "You can only hit what you can see, and the intramural program is good at hiding things," complains one panel member, who also requested anonymity. Another catch is that some programs the panels have recommended cutting from the AIDS budget are going to have to find NIH money elsewhere. Take the call to move some of the $10 million spent on chimps into monkey studies. "There's no logistical way of doing it and making sure the chimps are maintained," says Judith Vaitukaitis, head of NCRR. "We just can't abrogate our responsibilities."

Once the final report is written, it must be approved by the OAR's advisory council. NIH institute directors will then work with OAR to help it write an "implementation plan." If they can turn that around quickly, OAR's Paul believes they may be able to influence the 1997 budget request, which still is in limbo because of the battle between Congress and the White House over the 1996 budget (see p. 589).

Although some panel members say they are far from convinced that NIH has the backbone to follow through on their recommendations, Paul dismisses those worries. "There's no good having a report if we don't do anything about it," he says. The clock will start ticking soon.

–Jon Cohen

OCEANOGRAPHY

Hearing Highlights Hopes, Realities

In a rare departure from the partisan rancor of the past year, members of three congressional committees last week declared their commitment to oceanographic research in tight fiscal times. Speaking at a 4-hour session that was part pep rally and part reunion, legislators from both parties agreed that ocean sciences deserve more attention—even if they can't have more money.

RICK KOZAK

In the swim. Leading scientists and federal officials urged Congress to support oceanography.

The hearing was convened by subpanels of the House science, resources, and national security committees, each with jurisdiction over ocean programs. The goal was to find common ground among legislators, federal officials, and researchers at a time when the overall budgets of many of the agencies that fund ocean sciences—in particular the Navy and the National Oceanic and Atmospheric Administration (NOAA)—are taking a dive.

Representative Curt Weldon (R–PA), who chaired the hearing as head of the military research subcommittee that oversees some $35 billion in defense R&D, emphasized the need for dual-use technology that would benefit both civilian and defense sectors. The heads of the several research agencies who testified—from the National Science Foundation as well as the Navy and NOAA—let legislators know about the importance of ongoing programs. And former Energy Secretary James Watkins, a retired admiral who is now president of the university-based Consortium for Oceanographic Research and Education, took the opportunity to promote his idea for a leader-