deputy who will oversee a half-dozen staffers and work cooperatively with science program managers. NSF hopes to fill the top slot by this winter, at a salary of about $130,000.

Marx, a professor at the State University of New York, Stony Brook, now working full-time as an RSVP project manager, is eager to work with the new office as an NSF-funded project. In the meantime, he'd welcome more "transparency" in how selections are made. "I think it's wonderful that NSF has more good ideas than money to build them," he says. "It just would be nice to know what's going on." –JEFFREY MERVIS

AIDS RESEARCH

Debate Begins Over New Vaccine Trials

PHILADELPHIA, PENNSYLVANIA—Government health officials are wrestling with a tough decision: Should they approve the most ambitious clinical trials to date of an AIDS vaccine, even if the two candidates have clear shortcomings? At a meeting* here last week, the U.S. military and the U.S. National Institutes of Health (NIH) unveiled detailed plans to launch phase III "efficacy trials" next year of nearly identical vaccines. The separate trials would cost a total of at least $95 million and involve nearly 27,000 participants from the United States, Thailand, and several countries in the Caribbean and South America (see table). But, as a vigorous debate here indicated, some researchers have deep reservations about whether these tests should go ahead.

David Baltimore, the Nobel laureate who heads NIH's AIDS Vaccine Research Committee (AVRC) and runs the California Institute of Technology in Pasadena, summed up the dilemma: "We have no other materials that are worth considering for phase III trials. It will take at least four more years for that. And four more years will be demoralizing for the entire vaccine enterprise." But then again, Baltimore and other researchers acknowledged that these two candidate vaccines have serious weaknesses, because in smaller human tests they have not triggered powerful immune responses against HIV.

The proposed trials would test vaccines used in a one-two punch called a "prime-boost." The first vaccine, the "prime," consists of HIV genes stitched into canarypox, a bird virus that does not harm humans. Made by the Franco-German pharmaceutical company Aventis Pasteur, the vaccine aims to teach the immune system to produce "killer cells" that would home in on and destroy HIV-infected cells. The "boost" would come from a genetically engineered version of HIV's surface protein gp120. This second shot, made by VaxGen of Brisbane, California, stimulates production of antibodies that, theoretically, can prevent HIV from infecting cells in the first place.

The debate surrounding these efficacy trials echoes a dispute that rocked the field in 1994 over plans to test gp120 vaccines singly (*Science*, 24 June 1994, p. 1839). At the time, NIH decided not to fund efficacy trials of gp120 vaccines made by two California biotechs, Genentech and Chiron, because phase II data suggested that antibodies triggered by the vaccines could only stop wimpy strains of HIV.

Researchers from both the U.S. military and NIH's HIV Vaccine Trials Network (HVTN)—a collection of academics who design and conduct the tests—said that they will stage efficacy trials of prime-boost vaccines only if phase II studies now being completed show that at least 30% of vaccinated people developed killer cell responses at some point during the trial. Larry Corey, who heads the HVTN's Core Operations Center at the Fred Hutchinson Cancer Research Center in Seattle, Washington, says the 30% benchmark will provide enough statistical information to determine whether levels of killer cells in vaccinated people correlate with protection from HIV infection. But data from phase II trials of these vaccines suggest that meeting this 30% goal is far from a given, as Mark de Souza of the Armed Forces Research Institute of the Medical Sciences in Bangkok, Thailand, described. Early results from a U.S. military study of canarypox in that country indicate that only about 22% of vaccinated people developed killer cells, de Souza reported. "It's going to be close," acknowledges the lead AIDS vaccine researcher for the U.S. military, John McNeil of the Walter Reed Army Institute of Research in Rockville, Maryland. "But I think [the vaccine is] good enough to go forward."

Other investigators are skeptical about the 30% target. "That's not good enough for me," says Douglas Richman, a virologist at the University of California, San Diego. Richman, who sits on the AVRC, worries that if only 30% of people develop killer cells, the vaccine might fail too often to be of practical use. Mark Feinberg of Emory University in Atlanta further questions whether such a low response would truly allow researchers to determine whether the killer-cell responses correlate with immunity. "We have a hard time figuring out correlates of immunity in AIDS vaccine monkey experiments where we study the animals much more intensively," he notes.

Both Feinberg and Richman, like many of their colleagues, reserved judgment about whether the efficacy trials should proceed, saying they first want to review the phase II data. But Brigitte Autran, an immunologist at Hôpital Pitié-Salpêtrière in Paris who has evaluated killer-cell responses in recipients of the canarypox vaccine, says that "there's no good scientific basis for these trials." She is especially dubious about conducting two similar trials. Susan Buchbinder of the San Francisco, California, Department of Public Health, who described the HVTN trial at the meeting, counters that the two trials complement each other and may pool data.

The military hopes to review its phase II trial data over the next few weeks and make a decision before the end of the year. HVTN will not complete its phase II study until December and will probably need at least a month to collate the data—just in time for January's meeting of NIH's AVRC. NIH may also sponsor another public meeting to weigh the risks and benefits of proceeding with this costly, complex trial.

–JON COHEN

PROPOSED AIDS VACCINE EFFICACY TRIALS

Sponsors	Vaccines (HIV subtypes)	Participants	Projected costs (millions)	Locations	Earliest start
U.S. military, Royal Thai govt., Mahidol U., Aventis Pasteur, VaxGen	VaxGen Canarypox w/HIV gag, protease, and env + gp120	15,800	$35–$40	Thailand	Summer 2002
NIH HVTN, Aventis Pasteur, VaxGen	Canarypox w/HIV env, gag, protease, pol, and nef + gp120	11,080	$60–$80	U.S., Brazil, Haiti, Peru, Trinidad (Possible: Argentina, Dominican Republic, Honduras)	December 2002

* AIDS Vaccine 2001, sponsored by the Foundation for AIDS Vaccine Research and Development, 5–8 September.

CORRECTION

A news story in the 31 August issue misreported a charge in a lawsuit involving a study of lead paint cleanup and children's blood levels. A correction appears on page 1997.