Fauci said such a contract is now being drafted between NIAID and the two companies involved in the only human tests whose results were presented at the meeting. The trial combines two separate vaccines in hopes of delivering a one-two punch against the AIDS virus. This strategy "primes" the immune system with a vaccine made by Pasteur Mérieux-Connaught that contains one or more HIV genes stitched into a canarypox virus that is harmless to humans. When injected into a human, the canarypox enters cells and manufactures the given HIV protein or proteins. When displayed on the infected cells, these "endogenously" made HIV proteins should activate cytotoxic T lymphocytes (CTLs), immune cells that can specifically obliterate HIV-infected cells. A "boost" with the Biocine vaccine, which contains gp120, is then supposed to stimulate production of antibodies that can neutralize HIV floating freely in the bloodstream.

As Fauci explained, NIAID is now funding "phase one" trials of this prime-boost strategy that involve a total of about 100 people. Preliminary results presented at the meeting show that the vaccines easily stimulate production of antibodies and trigger CTLs in anywhere from 12% to 44% of the people vaccinated. Before these vaccines can move on to the next phase, the companies and NIAID have agreed that at least 90% of the people who receive both vaccines must produce neutralizing antibodies and at least 30% must produce CTLs. If the vaccines meet those milestones and are shown to work in a nonhuman primate study, they could move into efficacy trials by the middle of 1998.

Already, some leading researchers are questioning how NIAID officials arrived at such specific criteria, as well as how they'll be used. "It concerns a number of people that we don't know what's going on," says the University of Minnesota's Ashley Haase, who headed NIAID's AIDS vaccine working group until it disbanded in 1994. "They're essentially setting up numbers arbitrarily."

Fauci concedes that these criteria are "semiarbitrary" and were based on the results already seen. But however they are set, some criteria are necessary, Fauci maintains. He says one of the main criticisms of the earlier gp120 trials is that they hardly elicited any CTLs, and NIAID came up with these criteria after the working group Haase headed said it was "impossible" for them to do so. Fauci also stresses that these are "minimal criteria" and are subject to change if new scientific information surfaces. "I made the leadership decision we want to deal in good faith," says Fauci. "Either we're going to have a vaccine program or not."

Fauci will not explicitly say that if these minimal criteria are met, NIAID will definitely move the vaccines forward. Both Haase and Duke's Bolognesi have strong reservations about NIAID making any such commitment. Then again, Bolognesi thinks it makes sense to set minimal criteria, so that "a floor" is set and companies don't feel jilted if NIAID decides to stop testing their vaccines. "It's a good thing to do right now with the industrial partners that are left in the world," says Bolognesi. That's a sober response to NIAID's earnest new development plans—and it speaks volumes about the state of the AIDS vaccine search in 1996.

–Jon Cohen

REGULATORY AGENCIES

FDA Reform Starts Down the Track

Congressional efforts to reform the Food and Drug Administration moved into the spotlight last week as a Senate panel devoted 2 days to a Republican proposal that would prod FDA into processing new drug applications more quickly. The bill has won support from academics and drug company officials, who see timely reviews as an important factor in getting products to market. Although the bill's prospects in the Senate appear good, its ultimate fate may rest with House colleagues, some of whom want to remove FDA's authority to conduct in-house reviews of new drugs and devices.

Last week's hearing before the Senate Labor and Human Resources Committee focused on a bill introduced by its chair, Senator Nancy Kassebaum (R–KS). The bill would press FDA to meet its current requirement to review new drug applications within 6 months—a standard that it now falls far short of. It would also force FDA to approve within 120 days drugs to treat life-threatening illnesses or those for which no other treatment exists. If the FDA failed to meet these goals by mid-1998, it would be required to contract out new applications. In addition, products that had passed review in the United Kingdom or the European Union would be allowed on the market unless FDA could show the product was unsafe or ineffective.

Testifying at the hearing, FDA Commissioner David Kessler said a 1992 user fee program has helped the agency meet, 3 years ahead of schedule, a goal to process most drug applications within 12 months. But he's troubled by the strict timetables. "If you rush too much," he said, "you're either going to do something potentially dangerous or turn down applications and take longer in the end." An overemphasis on speed, he added, would also force FDA to divert scarce resources from helping companies prepare for clinical trials. Kessler is also concerned about the agency's ability to protect confidentiality and avoid conflict of interest if reviews are contracted out, although he said the agency is testing the idea on a small scale.

"If you rush too much, you're either going to do something potentially dangerous or turn down applications and take longer in the end."
—David Kessler

Louis Lasagna, dean of the Sackler School of Graduate Biomedical Sciences at Tufts University and an FDA critic, sympathizes with Kessler on one point: FDA could be "tempted to cut corners" to meet tight deadlines on reviews, he told *Science*. But he said Kessler's fears about outside reviews are unwarranted, noting that a contractor used several years ago in a pilot project "did a good job quickly and inexpensively."

Drug companies see the bill as a good start toward needed reforms. The Pharmaceutical Research and Manufacturers of America have praised the bill, noting that the deadline and contracting provisions could speed reviews. However, the group would like to add a provision to eliminate FDA requirements for raw patient data and make other changes.

Although Kassebaum hopes to mark up her bill this month, it may face tough going when measured against proposals, some more radical than hers, being drafted in the House. In particular, Kassebaum's counterpart, Representative Thomas Bliley (R–VA), chair of the House Commerce Committee, is said to favor a bill that would turn over the entire review process to outside review groups and mandate other fundamental changes in how the FDA operates (*Science*, 25 August 1995, p. 1038).

The ongoing budget morass and a limited legislative calendar during an election year could also derail plans for significant reform. As a result, some observers doubt that anything more than a bill affecting exports or medical devices is likely to pass this year. "I am skeptical [that a major reform bill will pass]," says Washington attorney William Vodra, a former FDA associate chief counsel for drugs. But Kassebaum has a major incentive to wrap up a reform bill this year: She is retiring from the Senate this fall after 18 years, and reforming FDA is a priority item on her political to-do list.

–Jocelyn Kaiser