Government ddI Trials on Trial

As clinical trials to test the efficacy of a new AIDS antiviral drug get under way, federal health officials face a troubling question: Will the decision to permit wide-scale distribution of the drug outside of the research program make it impossible to find adequate numbers of patients willing to participate in the trials? A second, potentially more troublesome question is, if it becomes difficult to recruit volunteers, will that spell the end for the parallel track, an as yet untested plan to get drugs to the patient community faster?

These questions have been weighing heavily on the minds of federal researchers, but they felt that the jury was still out on the answers. So when a front page article in the *New York Times* of 21 November proclaimed the wide-scale distribution program was already interfering with ddI trials, their reaction was one of shock and outrage.

Last summer, National Institute of Allergy and Infectious Diseases Director Anthony S. Fauci described the parallel track as a way to meet the demands of patients anxious for new therapies and researchers who need data on a drug's efficacy (*Science*, 28 July, p. 345). But details of the plan are still being worked out, and ddI was ready for phase two efficacy trials. So on 28 September the Food and Drug Administration invoked existing mechanisms—the treatment IND (investigational new drug) and compassionate use programs—to permit ddI's manufacturer Bristol-Myers to make the drug available to patients with advanced ARC (AIDS related complex) or AIDS who either cannot tolerate or did not benefit from the only approved anti-viral therapy, AZT.

At the same time the NIAID AIDS Clinical Trials Group (ACTG) started three different clinical trials, two comparing ddI with AZT and one comparing different doses of ddI. The three trials are intended to enroll approximately 2600 patients.

Daniel F. Hoth, director of the division of AIDS at NIAID, says it's too early to tell whether the alternative access to ddI is cutting into recruitment of patients. Individual ACTG centers are just receiving approvals from their institutional review boards, and Bristol-Myers has just begun to deliver the drug. So far, 2717 have received ddI through one of the alternative tracks, whereas 157 are getting the drug in controlled trials.

Fred Valentine, principal investigator for the ddI trial at New York University, is optimistic about the trials, but admits there are legitimate reasons for concern about recruitment. He says private physicians like being able to prescribe new drugs for their patients, and there are far more private physicians than clinical centers conducting trials. So why should a patient bother going to a clinic when his own physician can supply the drug?

But Valentine says it is unfair to assume that the trials will be a failure at this point because they have really just gotten off the ground. He is surprised so many people assume ddI will be a better drug than AZT, which has already been shown to improve the health of AIDS patients.

"There are patients and doctors, too, who have already made up their minds" about ddI, says Valentine. "They must have better predictive capabilities than I do."

AIDS activists also bristle at the suggestion that fewer patients will now enroll in clinical trials. Just the opposite is happening, according to Rebecca Smith of the Community Research Initiative. She says AIDS patients have been more willing to trust the medical research establishment now that access to drugs is being streamlined.

But there are still many clinic directors who remain unconvinced. One senior investigator with ACTG, who spoke on condition of anonymity, says it's virtually certain that patients won't bother with the strict requirements of a clinical trial if they can get a drug they are interested in far more easily through their own doctor.

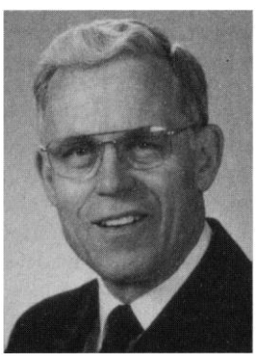
If the current experience with ddI is negative, it will most likely have serious consequences for the parallel track. Under parallel track, drugs that have completed phase one trials to determine tolerable doses may be made more widely available at the same time they begin efficacy trials. Parallel track is supposed to make drugs available even earlier than the treatment IND, but that distinction is being blurred by the ddI experience.

Fauci says federal officials are aware of the risk that alternative access may interfere with recruitment for clinical trials, and they are considering strategies for parallel track to avoid that.

Details of the parallel track scheme should appear shortly in the *Federal Register* for comment. ■ **JOSEPH PALCA**

Panel to Redesign NIH Director's Job

On 4 December, Assistant Secretary of Health James O. Mason convened the first of several planned meetings with an elite group of advisers whose goal is to refashion the NIH director's job so that someone of stature will take it. The group met in camera, a spokesman for Mason said, lest public presence inhibit "free and frank" discussion of the job.



James O. Mason

NIH has been in search of a director since summer when James B. Wyngaarden was asked to resign so that the White House could name its own person to the job. Although no one said so at the time, it now seems apparent that abortion was a key issue. The Administration wanted to find an NIH director who shared its opposition to abortion.

But none of the candidates recommended by the search committee could pass the abortion litmus test. Once its existence was reported by *Science* (6 October, p. 27), the Administration publicly dropped it. But even the apparent demise of the abortion litmus is not sufficient to attract top candidates to a post of limited authority and independence. At an informal gathering a few weeks ago, many of the same people who are now on Mason's advisory panel told Health and Human Services Secretary Louis Sullivan that the NIH job ought to be changed (*Science*, 17 November, p. 880). The problems they cited include a low salary coupled with a prohibition of outside income, no money for distribution at the director's discretion, and limited authority over the NIH's 11 institutes.

Now, Mason's committee will tackle them one by one.

Members of the Mason panel on NIH are **Theodore Cooper**, Upjohn; **Eugene Cota-Robles**, Berkeley; **James F. Dickson**, Boston University; former NIH director **Donald S. Fredrickson**; **James R. Gavin**, University of Oklahoma; **Paul Gray**, MIT; **Paul A. Marks**, Memorial Sloan-Kettering Cancer Center; **Edmund D. Pelligrino**, Georgetown University; former congressman **Paul G. Rogers**; **David Satcher**, Meharry Medical College; **Benno C. Schmidt**, former chairman of the President's Cancer Panel; **Maxine F. Singer**, Carnegie Institution of Washington; **Samuel O. Thier**, Institute of Medicine; **P. Roy Vagelos**, Merck; and **Linda S. Wilson**, Radcliffe. ■ **BARBARA J. CULLITON**