NCI begins overhaul of late-stage cancer trials

After nine months of discussion, the National Cancer Institute's (NCI) Clinical Trials Implementation Committee (IC) has produced an action plan based on the recommendations of an earlier incarnation, the Armitage Committee, to overhaul the NCI clinical trials process. The Armitage Committee had described the complexity of the trials process as having "bred inefficiencies and eroded the ability of the system to generate new ideas to reduce the cancer burden." Thus, it was the aim of the IC's plan, presented in late September to the Institute's Board of Scientific Advisors, to make the clinical trials process more open, less bureaucratic and faster.

This is the first time in almost two decades that any substantial changes have been made to the clinical trials structure.

At present, protocols are reviewed internally, with no mandated approval time. The length of review depends on how many changes are made to the protocol and how long it takes to go through a multi-layer Investigational Review Board (IRB) process, says Ellen Feigal, deputy director of NCI's Division of Cancer Treatment and Diagnosis. The greatest change is that the entire process will be opened up to those outside of the traditional NCI channels.

For now, the overhaul focuses on phase III studies, which are conducted primarily by the NCI's Cooperative Trials Group Program, comprising 12 groups and 20,000 patients at 1,500 institutions across the country. Among other things, the plan recommends that two pilot tests comparing different systems for approving protocols be run, and if either or both is suitable they will be adopted.

For the first pilot study, to be carried out on protocols for gastrointestinal cancers and leukemias, ideas will continue to come from within NCI groups, and will still be reviewed by internal panels. The difference is that the Cooperative Groups will be able to have access to new Clinical Trial Support Units (CTSUs), which will consolidate redundant administrative tasks, link physicians and patients to the best trials and direct trial funding.

The second pilot, centered on urologic and lung tumors, will test a "state of the science" meeting, which will "identify new research opportunities in specific cancers or gaps in research portfolios." These meetings will be open to all-comers such that any investigator—not just those in the Cooperative Groups—can submit a protocol idea to yet another new group called the Disease-Specific Concept Review Committee. This

gathering will select studies for funding with a goal of approving protocols within 60 days. Trials will again be coordinated and overseen by CTSUs.

But not everyone supports the idea of disease committees, which would be made up of clinical investigators, patients and advocates, and statisticians. "I think it's a major departure from what we're doing now, and we have no experience with it...it's a hypothesis," says Board of Scientific Advisors member Sharon Murphy of Northwestern University.

The IC also proposed creating a single national IRB to speed protocols into the clinic; currently, they are reviewed by a multitude of local and regional IRBs. However, Marc Lippman, director of the Lombardi Cancer Center at Georgetown University Hospital, told *Nature Medicine* that a national IRB might meet with resistance: "many Co-op Groups are worried about their survival, so they're particularly alarmed that something would be set in motion that would cost them their independence."

The IC's work seems to be a counterpoint to criticism that NCI has been too bogged down in basic research (*Nature Med.*, 4; 992, 1998). In fact, IC co-chair John Glick of the University of Pennsylvania Cancer Center, says since Richard Klausner came to the agency in 1995, it has been looking more closely at how to get drugs out to patients.

Joe Harford, NCI Associate Director for Special Projects, says that the budget for clinical trials has increased in roughly the same proportion to the increase in the NCI budget as a whole during the Klausner years. "It would be a gross oversimplification to use these numbers as some sort of barometer of how much or little anyone at the NCI cares about clinical trials," says Harford, adding "we want to fund more both research in the laboratory and more research that is patient-oriented."

Allen Lichter, president of the American Society of Clinical Oncology, who has become an increasingly vocal critic of the NCI's policy on clinical research, supports the new process, but warns the effort won't amount to much without increased NCI funding. The IC estimated that testing the new pilot schemes will cost \$9.5 million, \$6.8 million of which will have to come from previously unrequested funds. "If we don't add more funds, we can pilot things until the cows come home and we're not going to optimize the system," says Lichter.

ALICIA AULT, WASHINGTON D.C.