lic review." In addition, the reform plan effectively drops many provisions in the current NIHRAC guidelines covering gene-therapy reviews—or apparently gives authority over those provisions to the FDA.

Objections to the plan to reform gene-therapy reviews were raised in several quarters. The FET, for one, urged NIHRAC officials not to relinquish full public review of gene-transfer protocols. Jeremy Rifkin, head of the FET, who calls the reform plan "arbitrary and capricious," argues that, if implemented, it will "substantially restrict public participation." Hence, he threatens a lawsuit against the NIH if the plan is not withdrawn.

At its autumn meeting, members of the NIHRAC convinced NIH and FDA officials to retreat—or at least slow down—on the implementation of their gene-therapy reform plan. However, the NIHRAC's deliberations at times verged on the surreal, as NIHRAC members struggled with several peculiarities. First, the NIHRAC, which ultimately answers to NIH's Varmus, is, in effect, trying to overturn one of Varmus' decisions. Further complicating this already strained relationship is the fact that Varmus has informed the NIHRAC that he has ordered an outside review body to determine the committee's worthwhileness. And, second, FDA and NIH officials presented to NIHRAC members an outline of their reform plan to streamline gene-therapy reviews, rather than a fully drafted plan, making it impossible for NIHRAC members to fully judge the plan.

"This is a very puzzling situation," says committee member Alexander Capron from the Law Center of the University of Southern California (Los Angeles, CA). "AIDS activists want streamlining of gene-therapy protocols. But others say we're going too fast."

—Jeffrey L. Fox

Gene therapy off to slow start

WASHINGTON, D.C.—A belief that human gene therapy is still in a very early and unproved phase was echoed often during a recent hearing convened by the House of Representatives' Committee on Science, Space, and Technology, even by some of the technology's most enthusiastic backers. Kenneth Culver, director of the Human Gene Therapy Research Institute (HGTRI, Des Moines, IA), pointed out that gene therapy has a "bright future" but that it is "very much in its infancy." And Nelson Wivel, director of the National Institutes of Health's (NIH, Bethesda, MD) Office of Recombinant DNA Activities, adds that "while the rapid developments in the field are encouraging, many scientific and technical problems still require solution."

Indeed, the NIH Recombinant DNA Advisory Committee has over a four-year period approved some 90 protocols involving gene therapy in humans. Although a wide variety of diseases is being studied, so far the number of patients enrolled in these trials is modest—altogether about 220—and available data on safety and efficacy are scanty.

Representative George Brown (D-CA), who chairs the House committee, heartily welcomed the star of the hearing, Ashanthi De Silva, an eight year old with a rare, inherited disorder—a deficiency of the enzyme, adenosine deaminase (ADA)—which leads to severe combined immunodeficiency and which is characterized by chronic illnesses and, frequently, early death. In an effort to overcome these medical problems, some of Ashanthi's T lymphocytes were removed from her bloodstream in 1990, engineered with a working ADA gene, and then reinfused into her. Before and since this gene therapy, Ashanthi has been regularly treated with a polymer-bound version of the enzyme, known as polyethylene glycol-ADA (PEG-ADA), which is marketed by Enzon (S. Plainfield, NJ) as Adagen.

According to HGTRI's Culver, the PEG-ADA treatments administered before gene therapy enabled Ashanthi to show a "modest decrease" in infections and "an improved quality of life." But her health improved significantly following several treatments with the ADA-engineered T lymphocytes. Indeed, Ashanthi now "leads a life that is essentially no different from her classmates," says Culver.

—Jeffrey L. Fox