OKAYING GERM-LINE THERAPY?

U.S. WATCHDOGS STUDY GENE THERAPY

WASHINGTON, D.C.—The U.S. federal regulatory bodies overseeing biotechnology are taking a close look at human gene therapy. The Food and Drug Administration (FDA, Bethesda, MD) is in the final stages of releasing a Points to Consider document outlining agency policies towards products to be used in gene-therapy procedures. Meanwhile, this month, the National Institutes of Health Recombinant DNA Advisory Committee (NIHRAC, Bethesda, MD) will reconsider streamlining its current two-tier approach to evaluating gene-therapy protocols—a review that overlaps with FDA's. On yet another front, NIHRAC's Human Gene Therapy Subcommittee (HGTS) has edged towards contemplating germ-line manipulations of human genes—a realm that previously was deemed strictly off limits.

In the new FDA Points to Consider document, agency officials seek to clarify current policies on gene therapy and make them more explicit for investigators in both the public and private sectors. What FDA expects of would-be gene therapists "shouldn't be confusing," explains an agency official. "This is not a mysterious process." Thus, for example, the new document emphasizes the importance of describing the "nuts and bolts" of how particular biological products are manufactured before they are approved for use in a gene-therapy clinical trial.

FDA is "legally mandated to review biological products," the official notes. That mandate defines broad responsibilities for FDA, covering most, if not all, gene-therapy protocols. It also accounts for the overlap—critics call it frank duplication—with NIHRAC. Technically, at least, NIHRAC insists on reviewing only those investigators who receive NIH funds, and even then reviews are, strictly speaking, voluntary. Private-sector investigators who come before NIHRAC and HGTS risk having flaws in their protocols exposed to public view, but can benefit if they receive the NIH imprimatur, observers point out.

Officials at both federal agencies acknowledge the duplication inherent in these two processes, but they argue that important differences help to make the processes complementary rather than redundant. Perhaps the key difference between the two is that FDA review can and usually is conducted under a blanket of confidentiality, whereas NIHRAC meetings are open to the public.

Other differences are more subtle. Instead of emphasizing a biological product's "nuts and bolts," NIHRAC focuses principally on the recombinant-DNA-based steps of proposed clinical procedures. However, committee members frequently raise broader safety and efficacy questions when considering a proposal. Moreover, legal and ethical concerns frequently are aired. Because discussions have been free wheeling and wide ranging, NIHRAC proponents argue, much of the initial resistance to considering—much less conducting—gene-therapy clinical trials has subsided.

Additional concerns over duplicative review are again being raised within the context of the NIHRAC full and subcommittee structures. Earlier in the year, this issue was seemingly laid to rest when NIH investigator W. French Anderson offered, but then quickly withdrew, a proposal to collapse the HGTS back into the full committee (*Bio/Technology* **9**:602, July '91). After mulling over that idea, however, several subcommittee members now want it reconsidered at the full committee meeting this month. If the subcommittee is dissolved, NIHRAC would likely move to a quarterly meeting schedule instead of the current regimen of three full and three subcommittee meetings per year. That change conceivably could slow rather than expedite the overall review process, insiders note.

Besides putting its future on the line, the NIHRAC subcommittee also forwarded several new clinical proposals involving manipulations of somatic cells to the full committee. Perhaps more importantly, it has broached the heretofore forbidden topic of germ-line therapy. Thus, in July, the subcommittee approached the task of drafting a points to consider document on this topic—a process that would take several years at a minimum. The undertaking is "not imminent," says NIHRAC executive secretary Nelson Wivel. However, mere mention of the possibility is renewing latent controversy over the issue, promising to raise temperatures when the full committee meets in October.

—Jeffrey L. Fox