Industry sceptical of new gene therapy review

The Recombinant DNA Advisory Committee (RAC) of the US National Institutes of Health (NIH) last month agreed formally to a simplified review of routine gene therapy protocols.

The biotechnology industry had campaigned for such changes, and ostensibly should have been pleased by the decision. Nevertheless, many within the biotechnology industry remain sceptical. How well the new process of 'consolidated review' works "remains to be seen", said Alan Goldhammer, director of technical affairs at the Biotechnology Industry Organization, which represents the industry.

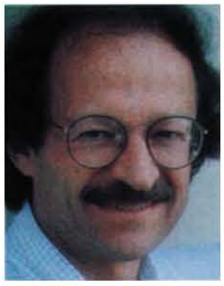
In the past, both the RAC and the US Food and Drug Administration (FDA) have reviewed gene therapy protocols. Now, protocols will go to the FDA and the Office of Recombinant DNA Activities (ORDA) at NIH. ORDA, in consultation with a small group of reviewers, will weed out those proposals that do not contain controversial new areas of science, or raise new safety and ethical issues, and thus do not need review by the full RAC committee.

The need for such changes was raised last year by the National Task Force on AIDS Drug Development. This group is supposed to identify and remove barriers to AIDS drug development. The dual review process of routine protocols by both the RAC and the FDA was identified as such a barrier in the case of gene therapy for AIDS.

Biotechnology company officials were fretting about how long it takes the RAC — compared with the FDA — to review protocols (in some cases, months more). Also, as the first wave of gene therapy products moves from toxicity testing (phase I) to efficacy (phase II) trials, and thus closer to becoming therapies, companies are concerned about confidentiality, says Richard Daifuku, head of clinical trials at Targeted Genetics, Seattle, Washington. Goldhammer points out that criminal sanctions that apply to the FDA if it violates confidentiality do not apply to the RAC.

Last month, Viagene, San Diego, California, became the first company to receive approval by the RAC to move from toxicity to efficacy trials for an AIDS treatment. The company did not initially seek approval for this latest trial on the basis that it had already received approval for the earlier toxicity trial. However, those institutions with funding from NIH said that approval by the RAC would be necessary.

Consequently, Viagene went ahead with the recruitment of patients at institutions that received no support from NIH (with full approval from the FDA and local institutional review boards) and applied for expedited review on the grounds that the trial was under way at some sites. This the RAC granted, but voted down a general proposal put forward by Sheryl Osborne, director of regulatory affairs for the company, that approval should not be necessary for a move from toxicity to efficacy trials.



Varmus: voiced concerns about RAC.

The RAC also voted against Osborne's proposal that the director of NIH (who has to sign off on any decisions made by the RAC) should be constrained to take action within 15 days of its final approval. Both votes seem to have contributed to scepticism within the biotechnology industry about how consolidated review will work.

This scepticism is deep-rooted, and is fed by concern that scientists associated with rival companies serve on the RAC, and that the nearer one gets to commercialization, the more issues of confidentiality and conflict of interest will arise.

At the same time, Harold Varmus, director of NIH, has voiced concern about the quality of the RAC's scientific review. His agenda, obviously, is to get the best possible science during a financial squeeze. Yet the RAC is not intended to be a body that carries out peer review.

The question of the extent to which the RAC is responsible for a review of the quality of the science as well as ethical issues will be examined by an *ad hoc* group set up at Varmus' instigation. This group is expected to report its findings in about a year. And the RAC, not for the first time in its twenty-year history, faces redefinition.

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Male contraceptive with DMSO in trials

Worried about the declining numbers of men opting for vasectomy, family planning and government officials in overpopulated India are aggressively pursuing a new experimental alternative — chemical sterilization. This new approach, which the researchers claim can be reversed, is said to interfere with a sperm's ability to fertilize an egg. It is hoped that the promise of reversibility, and the fact that the procedure leaves the vas deferens intact, will make chemical sterilization a more acceptable alternative to vasectomy.

To date, the main focus of India's national family welfare programme has been on male and female sterilization. Vasectomy was a well-accepted procedure in the 1950s and 1960s. In 1970, it accounted for 74% of all sterilizations performed. However, since then, there has been a steady decline in the number of vasectomies. In 1991–1992 (the last year for which data are available), vasectomies were a mere 4.2% of all sterilizations, despite the lure of monetary and other incentives offered by the Ministry of Health and Family Welfare.

A team led by Sujoy K. Guha, head of the Centre for Biomedical Engineering at the Indian Institute of Technology in New Delhi developed the new procedure after more than a decade of research. Instead of cutting the vas deferens, the new technique involves injecting into the vas a non-toxic polymer, styrene maleic anhydride. (More solvent is then used to flush out the polymer to reverse its effect.)

Animal studies in rats and monkeys, carried out at the Central Drug Research Institute in Lucknow, as well as early safety trials in humans undertaken at the Lok Nayak Jaya Prakash Hospital in New Delhi, have produced some encouraging results. The project did suffer a setback, however, when Guha was asked by the health ministry in 1986 to repeat animal toxicity studies after scientists from the US National Institutes of Health, as part of a delegation sent to New Delhi by the World Health Organization, were concerned that the solvent dimethyl sulphoxide (DMSO) — used in the formulation to dissolve the polymer — could be carcinogenic. Guha says that studies later showed these fears to be unfounded.

Now, with backing from the health min-