FDA rules for somatic-cell and gene therapy

The new FDA policy will help to demarcate areas of agency oversight, particularly for somatic-cell therapy.

WASHINGTON, D.C.—The Food and Drug Administration (FDA, Bethesda, MD) recently issued a statement clarifying how it plans to regulate somatic-cell-therapy and gene-therapy products. The FDA also convened an advisory committee to consider safety-testing procedures at gene-therapy production facilities because of concerns over the use of certain viral-based vectors in gene-therapy clinical protocols.

The FDA policy statement, published simultaneously in the *Federal Register* and the *New England Journal of Medicine*, will help to demarcate areas of agency oversight. Particularly for somatic-cell clinical procedures, it has not been entirely clear what falls within the FDA's jurisdiction.

For instance, widely used bone-marrow-transplant procedures are to remain outside FDA regulatory review. However, significant embellishments of those procedures, including *ex vivo* selection and expansion of bone-marrow cells, will "be regulated as products for somatic-cell therapy," according to the FDA policy statement. Other steps—such as inserting genetic material, inducing differentiation, or causing secretion of active factors—that "alter the biologic characteristics of the cells" also will bring such clinical procedures under the FDA's regulatory umbrella, says the statement. Moreover, chemical or biological agents used to purge bone-marrow cells are subject to FDA approval, though the purged cells themselves are not.

Some of the regulatory "logistics" for somatic-cell-therapy procedures are expected to differ from those involving gene therapy. For example, biotechnology firms developing products for gene-therapy procedures—such as gene-carrying viral vectors—will continue to follow familiar FDA product and production-facility licensing procedures. However, because somatic-cell therapies—such as expanding a patient's bone-marrow cells—usually will involve procedures that need to be done at local facilities like hospitals, FDA licensing "will probably be more complicated," and "every such facility will need to be licensed," says the statement.

The FDA policy statement does not propose departing from current practices when it comes to assigning primary review responsibilities for gene-therapy and somatic-cell-therapy products within the agency. For instance, although chemically synthesized products for gene therapy—such as oligonucleotides—will be regulated as drugs by the agency's Center for Drug Evaluation and Research, most products—such as gene-carrying viral vectors—will continue to be regulated as biologics by the agency's Center for Biologics Evaluation and Research.

For its part, the FDA advisory committee focused on the risks involved when virus-based vectors are used to shuttle genes in gene-therapy protocols. Specifically, the committee members reviewed information describing two recent instances when "replication-competent" viruses were detected among vector production lines of viruses that had been engineered not to replicate. One of the cases occurred at Genetic Therapy (Gaithersburg, MD) and the other at Viagene (San Diego, CA).

Both cases were detected before causing harm. But the appearance of these replication-competent viruses, which arose presumably through multiple recombinant events, remains surprising. To help assure that such viruses are detected as early as possible, FDA officials now are recommending that manufacturers check both supernatant fluids and pellets of their vector preparations at every step. Meanwhile, FDA scientists say they are contemplating a new round of risk-assessment studies to see whether spontaneously derived replication-competent viruses cause diseases in animals. Agency researchers are still deliberating over what kinds of animals—whether primates or rodents or both—are appropriate for such tests.

—Jeffrey L. Fox

Dutch okay streamlined rules for GMOs

OXFORD, U.K.—Dutch biotechnology researchers now have an effective one-stop shop for getting permits to conduct experiments with genetically modified organisms (GMOs), as officials at the Dutch Ministry of the Environment (MoE, The Hague) recently introduced a streamlined and harmonized permit-authorization process. "We now have one regulation implementing the European Community's (EC, Brussels) contained-use directive and deliberate-release directive," explains Piet van der Meer, the MoE's biotechnology legislation coordinator.

The new process takes much of the burden away from the local authorities. Previously, Dutch municipalities—of which there are about 700—were responsible for authorizing permits under a law that was about 90 percent harmonized with the EC's GMO regulations. "Although the municipalities could get advice from the national advisory board, there was the potential for a diversity of interpretations. Furthermore, the authorization procedure needed people with high levels of expertise, which the local authorities struggled to achieve," says van der Meer.

He believes that the new process will be welcomed from all quarters. "The local authorities still have much of their original power, but are not burdened with the technical problems associated with authorization. Industry now has a harmonized and consistent interpretation of the rules. And environmentalists will get easier access to information by getting it from one source rather than 700 different ones," van der Meer says.

The new regulations will not be too burdensome for industry, according to Rob van der Meer of the Netherlands bioindustry association (The Hague). "These are workable procedures, and we are not necessarily against them, although we will be working to make sure they are improved," he says.

—Mike Ward