US animal biotech regulations "may not be adequate"

Although available evidence suggests that genetically engineered animals, including cattle, pigs, and fish, are probably safe to eat, it would be wise to prevent them from escaping captivity, reproducing, and possibly spreading their genes into wild relatives or other species, according to a report, prepared for officials of the US Food and Drug Administration (FDA; Washington, DC), by a scientific panel assembled by the National Research Council (NRC) of the National Academy of Sciences (NAS; Washington, DC). NAS released the NRC report, *Animal Biotechnology: Science-Based Concerns*, late in August. Aside from safety concerns, the NRC committee acknowledged that the regulatory framework "may not be adequate" to deal with animal biotechnology issues.

"As is the case with any new technology, it is almost impossible to state that there is no concern, and in certain areas of animal biotechnology we did identify some legitimate ones," says zoologist John G. Vandenbergh of North Carolina State University (Raleigh, NC), who chaired the NRC committee. "By identifying these concerns, we hope we can help this technology be applied as safely as possible without denying the public its potential benefits." Some concerns include health risks to genetically modified animals themselves and also risks that meat or milk from animals engineered to produce specific drugs might enter the food supply and cause harm to consumers.

Additional important concerns revolve around effects such animals could have in the environment, according to committee member Eric M. Hallerman, an associate professor in the Department of Fisheries and Wildlife Sciences at Virginia Polytechnic Institute and State University (Blacksburg, VA). Laboratory experiments and other controlled efforts intended to simulate environmental conditions and behaviors of such organisms may never be fully sufficient to predict their fate, he says. "At some point, there will be a decision to go ahead, and we will need a regime [that includes] monitoring and adaptive management."

The "greatest concern," according to the NRC report, relates to the ability of certain genetically engineered organisms to escape and reproduce in the natural environment. Genetically engineered insects, shellfish, fish, and other animals that can easily escape, that are highly mobile, and that easily become feral are of particular concern, especially if they are more successful at reproducing than their natural counterparts. For example, transgenic salmon with genes engineered to accelerate growth might, if released, outcompete wild salmon for food and mates (*Nat. Biotechnol.* **18**, 143, 2000).

Although engineered animals such as fish are probably safe to eat, steps should be taken to prevent them from escaping captivity, reproducing, and possibly spreading their genes into wild animals, according to the NRC.

Laboratory experiments and other controlled efforts intended to stimulate environmental conditions and behaviors of such organisms may never be fully adequate to predict their fate.

However, the assignment of authority under the longstanding federal regulatory regime makes it awkward, if not impossible, for the FDA to address such issues, according to the NRC report, which contains no policy recommendations. Vandenbergh says that committee members were particularly concerned about the agency's "legal and technical capacity" to identify environmental hazards associated with animal biotechnology. Most of the regulatory concerns identified by the committee "have to do with the scope of the regulatory authority of FDA under animal drug provisions," which is how the agency derives authority for regulating genetically modified animals, adds committee member Michael Taylor, who is a senior fellow at the environmental think tank Resources for the Future (Washington, DC) and a former top official at the FDA.

Evaluating such issues could prove problematic for FDA officials, according to Taylor. He also suggests that "a forum other than FDA should be found" for dealing with the range of social and ethical issues—several of which are mentioned in the NRC report—associated with the development, care, and use of transgenic animals.

Well before the NRC report was complete, public interest groups and activists were objecting to how the agency regulates animal biotechnology. For instance, the Campaign for Responsible Transplantation (CRT; New York City, NY)—pointing to the risk that exotic infectious diseases could be transferred from the organs and tissues of animals into humans through xenotransplantation—brought a lawsuit against the FDA nearly two years ago, seeking detailed information on more than a dozen clinical trials involving xenotransplantation (*Nat. Biotechnol.* **19**, 6, 2001).

In March 2001, six biotechnology companies (Diacrin, Genzyme, Diacrin/Genzyme, Circe Biomedical, Nextran, and Novartis) joined the FDA in its defense against that lawsuit, seeking to limit or prevent disclosure of FDA-held documents to the CRT. Early this September, however, Judge Ricardo M. Urbina of the US District Court for the District of Columbia (Washington, DC) ruled in favor of the CRT, giving agency officials until November to provide a fuller explanation of why some 27,000 records describing xenotransplantation procedures should continue to be withheld from the CRT and the public.

Against this fractious backdrop, PPL Therapeutics Plc (PPL; Edinburgh, UK) announced late in August its production of the first "double gene knockout piglets." These pigs are missing both copies of the α1,3-galactosyltransferase gene, which encodes an enzyme that adds specific sugars to the surfaces of pig cells, making them recognizable as "foreign" by the human immune system. Without those surface sugars, pig tissues and organs are considerably less likely to trigger the acute immune response that leads to hyperacute rejection of xenotransplant tissue—making such pig-derived materials potentially more attractive to clinical investigators.

The NRC committee considered the role of the public in reviewing safety issues in the context of animal biotechnology, according to committee member Taylor. "There is a heightened need to consider how the public can participate and how to resolve issues of uncertainty," he says. "But we made no policy recommendations."

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