US FDA to issue new rules on xenotransplantation

The US Food and Drug Administration (FDA) has announced that it will publish new guidelines on xenotransplantation this fall in the Federal Register. They will advocate long-term monitoring of organ recipients and may prohibit the use of non-human primates as organ donors. The FDA will also establish a registry to archive patient and donor samples, which will be funded both by the FDA and the National Institutes of Health.

The new guidelines are based on suggestions gathered at workshops involving scientists and the public, plus the latest scientific data. They go beyond the September 1996 regulations (*Nature Med*, 2; 18, 1996) in calling for long-term monitoring. According to Andrew Dayton of the FDA's Blood Advisory Committee, "the guidelines will call for counselling of recipients, informing them that they should not donate blood or organs." They will also require the informed consent and education of recipient's partners regarding their increased potential of being infected with an unknown pathogen. "We are also considering long-term monitoring of patients' partners—although this is kind of a gray area right now," adds Dayton.

Some scientists are skeptical as to how effective the monitoring procedures will be in preventing any kind of outbreak. Jonathon Allan, virologist at Southwest Foundation for Biomedical Research, says that by the time the tracking system detects a viral infection among transplant recipients, it may have already been spread among the population. "The guidelines can outline a tracking program, but they can't limit the behavior of transplant recipients and their close contacts."

Dayton insists that precautionary measures will be adequate: "There is no need for a public scare, we will monitor recipients closely. If any infectious agent arises, we will find out soon."

Irrespective of the updated regulations, Fritz Bach, professor of immunology at Harvard Medical School and an outspoken proponent of a moratorium on xenotransplantation (*Nature Med.*, 4; 141, 1998) still feels that the technique should be approached with greater caution because the risks involved cannot yet be estimated. "Everybody agrees that xenotransplantation is a risk—even the head of the FDA. We don't know whether the first or any other patient receiving a transplant could start an epidemic," says Bach. He would rather the decision on whether to proceed with xenotransplantation be made by an ethics committee made up of the mainstream population, rather than by the FDA. "At this point we're putting the cart before the horse. Suddenly, the public is confronted with something that the government has already done."

One important omission in the guidelines is the definition of which animal species are permitted as donors. There is fear that although non-human primates are not considered safe for xenotransplantation in the US and most of Europe, the absence of a strong statement against their use in the guidelines may cause researchers in the rest of the world to think that primate donors are acceptable as long as they are screened for known viruses.

"If this is not included in the guidelines, we are not sending a statement to the rest of the world that primates should not be used for xenotranspantation," says Allan.

Last spring, as discussion of the guideline revisions began, Allan and 40 other prominent virologists sent a letter to the Public Health Service recommending a ban on primates as xenotransplant donors. "For some reason the US does not want to take a leadership role on [the primate] subject. This leaves a loophole and a risk—not just to transplant patients, but to everyone else."

The Centers for Disease Control and Prevention in particular does not feel that species-specific regulations should be included in the guidelines. There is speculation, however, that the FDA will take a stronger stand on the primate subject by issuing an independent statement against their use in xenotransplantation.

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Spain releases xenotransplantation guidelines

Already a world leader in terms of the number of organ donations per year (over 30 donors per million people), Spain is now tackling the issue of xenotransplantation. It claims to be the first country to draw up official guidelines for the procedure. These were released in a report by the Spanish Commission on Xenotransplantation on June 17th.

Far from asking for a moratorium on full-scale xenotransplantation trials as some have done in the US (*Nature Med.*, 4; 131 & 141 1998), the general feeling among European specialists attending a June 22nd meeting held in Madrid to discuss the Spanish report was that a Europe-wide agreement may be soon reached to begin trials, according to the meeting's organizer, Jose Maria Mato. The most optimistic forecasts suggested that trials transplanting pig hearts into humans may be only three years away.

The Spanish guidelines require that before human trials can begin, preclinical studies must demonstrate a minimum six-month survival and function period of cells, tissues and organs to be transplanted. There must be a similar record of absence of infectious pathogen transmission.

Moreover, informed consent documents are required not only from the organ recipient but also from their family and close friends, with whom intimate contact is not advised. The duration of this isolation will be determined at a session of the Spanish Health Ministry which will meet to discuss the guidelines. Relatives and friends must also be checked for xenoviruses in addition to the recipient. In conclusion, the report recommends that the first human recipients of xenotransplanted organs be subjected to life-long monitoring.

Rafael Matesanz

The committee comprises 15 experts in organ transplantation, bioethics, laws, infectious diseases, immunology, public health and virology. It is chaired by Rafael Matesanz who also heads the Transplantation Commission of the European Council, which has approved the creation of national committees for the evaluation, authorization and follow-up of current and future research in all from European Union countries. These groups are expected to begin work this October.

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