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Regulating Clinical Xenotransplantation in the United States

Eda T. Bloom

The shortage of human organs available for transplantation coupled with recent advances in technology and pharmacology that have been important for achieving success in allotransplantation have led some to propose xenotransplantation, initially attempted almost 90 years ago,\(^1\) as a potential solution to the human allograft shortage.\(^2\) In addition, the use of nonhuman animal cells has been proposed for restoring physiological or functional deficiencies and treating chronic debilitating disorders.\(^3\) Although clinical xenotransplantation may provide substantial benefits, there are biological and ethical issues that must be addressed.

Perhaps the single most serious public health concern for the clinical use of xenotransplantation is the potential for the transmission of infectious disease from nonhuman animals to human xenotransplantation recipients and then to others in the human population. Because of this potential risk to the public health, four agencies of the United States Public Health Service (PHS), together with the Office of the Assistant Secretary for Planning and Evaluation (OASPE) of the Department of Health and Human Services (DHHS), have worked to develop a xenotransplantation policy that is based on scientific evidence and public input, and is intended to minimize the infectious disease risks. The four PHS agencies include the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resource Services Administration (HRSA) and National Institutes of Health (NIH).

In 1996, the PHS published a “Draft Guideline on Infectious Disease Issues” in Xenotransplantation (Federal Register 61:49920, 49932, 1996) for public comment. The Draft Guideline identified general principles for the prevention and control of infectious diseases that may be associated with xenotransplantation and that may pose a public health hazard. These principles addressed such issues as source animal selection, isolation of patients, pre- and post-transplant monitoring of patients, and informed consent and education. In response to written public input, public commentary gained at several public meetings, including a public workshop held in Bethesda, Maryland, January 21-22, 1998, entitled Developing U.S. Public Health Policy in Xenotransplantation, and advances in relevant science, the guideline has been revised. (Internet access through http://www.fda.gov/cber/xap/xap.htm).

The PHS defines xenotransplantation as “any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (A) live cells, tissues, or organs from a nonhuman animal source or (B) human body fluids, cells, tissues or organs that have had ex vivo contact with live nonhuman animal cells, tissues, or organs.” Xenotransplantation products are defined as “live cells, tissues or organs used in xenotransplantation.” A crucial part of both of these definitions is that the nonhuman cells, tissues, or organs used in xenotransplantation and in the manufacture of xenotransplantation products must be alive. Part B of the xenotransplantation definition is intended to include xenotransplantation products in which human cells, tissues or organs, having had ex vivo exposure to live animal materials, are administered to humans. Ex vivo contact is thought to pose risks for transmission of xenogeneic infectious diseases qualitatively similar to those posed by implantation of xenogeneic cells, tissues or organs. This concept was discussed by FDA advisors at two meetings of the Xenotransplantation Subcommittee of the Biological Response Modifiers Advisory Committee.
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The regulation of xenotransplantation continues to evolve as information accumulates. Thus, whether regulatory policies become more liberal or more restrictive will depend upon future scientific and clinical data as well as public input. FDA will continue to update and revise its advice appropriately. In addition, the U.S. is working with appropriate officials from other countries toward international cooperation.
collaboration and coordination of this important health policy area.

**REFERENCES**