



ANIMAL
PROTECTION
INSTITUTE

February 24, 2000

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Dockets Management Branch (HFA-305)
Food and Drug Administration (FDA)
5630 Fishers Lane - Room 1061
Rockville, MD 20852

Re: **FDA Docket No. 99D-5347**
Precautionary Measures to Reduce the Possible Risk of Transmission of Zoonoses by Blood and Blood Products from Xenotransplantation Product Recipients and Their Close Contacts.

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Dear FDA:

The Animal Protection Institute (API) is a nonprofit organization established in 1968 with 80,000 members nationally. Our members are very concerned about xenotransplantation. Since 1994 API has researched the topic extensively, attending conferences and soliciting opinions from a variety of experts regarding organ transplantation, animal care, infectious disease, health care policy, and organ procurement. I have written articles, made presentations at meetings, and served on panels at conferences (including the 1/21-22/98 FDA workshop "Developing U.S. Public Health Service Policy in Xenotransplantation").

II. Background:

It seems to be accepted in this document that animal transplants into humans will be both beneficial and inevitable. There does not seem to be sufficient evidence to justify this statement. To date there have been no major serious to increase the supply of human organs, no serious evaluation of alternatives, and no cost/benefit analysis of xenotransplantation. The published research assessing infectious disease risk to humans from pigs to date has been limited and inconclusive.

In addition many statements in this section present a rather frightening view of the potential infectious disease transmission risk posed by xenotransplantation:

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"Because transplantation necessitates disruption of the recipient's usual protective physical and immunological barriers, xenotransplantation may facilitate transmission of known or as yet unrecognized agents to humans. These can include unknown retroviruses, which may remain latent for a period of time before causing clinically recognized disease. Because they are integrated into the species genome, endogenous retroviruses may not be eliminated from source animals by herd surveillance and screening programs. In the natural host, these endogenous retroviruses may not be expressed, but may be able to productively infect cells of another species (xenotropic). The clinical consequence of the introduction of endogenous retroviruses into immunocompromised human hosts remains, in most cases, undefined.

Xenotransplantation provides a unique environment for adaptation and cross-species transmission of infectious agents because: (a) the recipient is typically immune-suppressed; (b) in many instances, the xenotransplantation product is in direct contact with recipient's cells; and © if the xenotransplantation product is long-lived in the recipient, the chronic exposure of the recipient to virus may provide an environment primed for the adaptation of a virus to a human host."

Nothing in these statements make one comfortable regarding the safety of xenotransplantation. According to the Institute of Medicine (IOM) in 1996, the risk of transmission of an infectious disease through xenotransplantation is "greater than zero"; hardly a scientific estimation. There appears to be enough concern and risk to stop xenotransplantation now so that these guidelines are not even necessary.

III. Recommendations:

A. Donor Deferral - All recipients, contacts of the recipient, and health care workers should be permanently banned from blood donations. "Indefinitely deferred" is not enough to protect the public. There should be no exemptions for anyone who answered affirmative to the "three questions" and no exceptions for "certain ex vivo exposures".

This basic proposed donor deferral system seems totally inadequate when considering the enormous risk of exposure

of xenotransplantation. A detailed national donor base registry would need to be developed and seriously maintained. Is this even possible given privacy issues and the cost to set up and manage a registry of this size and complexity? And what of the possibility of human error?

According to well-documented reports by both the IOM and the General Accounting Office (GAO) in the 1990's, there have been serious problems with the FDA's oversight of the nation's blood supply. Stricter procedures and better oversight management by the FDA are essential. Given the FDA's history of monitoring blood donations and the immense risks of xenotransplantation, it does not appear to be possible to protect public health.

B. Blood Product Quarantines and Withdrawals - Blood and blood products named in this section should be destroyed. No exceptions should be made in this section. None of these "quarantined" products should be distributed.

Conclusion - Animal Protection Institute:

- These guidelines ignore the basic conclusion that xenotransplantation is a serious public health risk. These proposed guidelines certainly acknowledge this risk. Known infectious diseases transmitted from pigs to humans are well documented - let alone the possibility of unknown ones. These guidelines are "after-the-fact" and deal with containment rather than stopping the experimental practice, xenotransplantation, at the front end. Surveillance would not be necessary if we didn't put the public at risk in the first place.
- General health care policy including insurability, accessibility, and allocation of services needs to be significantly explored before xenotransplantation is "accepted". The costs of this highly controversial experimental procedure will most certainly outweigh its benefits when taken in the greater context of public health.
- Alternatives need to be **seriously** explored:
 - Intensified efforts to increase human organ donations; a presumed consent law, state mandated choice legislation, and/or other related legislation needs to be enacted.

- Consideration of gene therapy, tissue engineering, artificial and bioengineered organs and advanced surgical procedures.
- Humane research into the causes, diagnosis, prevention, and treatment of major diseases which create the need for organ transplantation. Significantly shifting research dollars from curing illness to preventing disease.
- Serious investment into education, promotion, and incentives for preventive health care!
 - a) A low fat, plant-based diet
 - b) Regular exercise program
 - c) Stress reduction and management

- Increase public debate by making it a priority to invite participation from a broader community than the "insiders" that are currently involved. Obviously, the scientists and physicians who have extensive knowledge of infectious disease and transplantation are key to the process. But xenotransplantation has much broader significance to public health and allocation of health care services. The new Secretary's Advisory Committee on Xenotransplantation (SACX) that is being established needs to reflect this diversity.

Xenotransplantation is not the answer, despite all the rosy pictures over-optimistic researchers, genetic engineers, and pharmaceutical companies paint of readily available animal organs. We need to first establish priorities by increasing the supply of human organs and decreasing the need for human organs through preventive medicine. There may be better alternatives to xenotransplantation in which the benefits will outweigh the costs.

As always, I appreciate the opportunity to present my views on this very important issue.

Sincerely,



Alan H. Berger
Executive Director



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