Xenotransplantation 2005: 12: 255–257
Printed in Singapore. All rights reserved
doi: 10.1111/j.1399-3089.2005.00233.x

Draft reports for public comment from the US Secretary's Advisory Committee on Xenotransplantation

The US Department of Health and Human Services Secretary's Advisory Committee on Xenotransplantation (SACX) recently produced two reports in draft form, for which public comment was requested. The first report considered the topic of *Informed Consent in Clinical Research Involving Xenotransplantation*, and the second was on the *State of the Science in Xenotransplantation*. A very brief summary of each report is presented below, including the recommendations of the SACX in full. Attention to these reports was drawn in the *Federal Register* of 9 March 2005, and the deadline for comment was 31 March 2005.

The full reports can be found on the SACX website at http://www4.od.nih.gov/oba/sacx.htm. A paper or electronic copy of each report can also be requested by calling the NIH Office of Biotechnology Activities at +1 301 496 9838 or by e-mailing Mary Groesch at groeschm@od.nih.gov. (Mary Groesch, PhD, Executive Director, Secretary's Advisory Committee on Xenotransplantation, Office of Biotechnology Activities, Office of Science Policy, National Institutes of Health, 6705 Rockledge Drive, Suite 750, MSC 7985, Bethesda, MD 20892 7985; Tel.: +1 301 496 9838; Fax: +1 301 496 9839).

Informed consent in clinical research involving xenotransplantation

This report considered the ethical foundations and functions of informed consent, the components of informed consent, the informed consent process as it pertains to xenotransplantation, the nature of informed consent forms, and the special issues raised by xenotransplantation.

The SACX made the following recommendations.

1. The informed consent process used with respect to competent adults in clinical research involving xenotransplantation should ensure that (a) information disclosed is sufficiently complete, (b) the participant comprehends the information disclosed, and (c) the participant's consent to participate is voluntary.
2. The goals of the informed consent process should be facilitated by the following:
   (i) involving a "consent team" comprising (at a minimum) the principal investigator, a researcher team member who is knowledgeable about post-transplant care and the long-term responsibilities of recipients, and an individual(s) who has expertise in the social, psychological, and financial implications of xenotransplantation;
   (ii) holding a series of face-to-face discussions with the prospective xenotransplantation recipient in a setting that affords privacy and comfort, and using comprehensible language; and
   (iii) using an informed consent form that includes specific elements required by the Common Rule as well as information recommended by the PHS (US Public Health Service), the DHHS (US Department of Health and Human Services), and the FDA (US Food and Drug Administration) and that is written in a manner that will help ensure understanding.
3. To protect against the potential spread of new diseases, the informed consent process should include the prospective participant's understanding and agreement to comply with public safety measures (including lifelong monitoring, temporary isolation if indicated, and autopsy) and to inform family members, current and future intimate contacts, and health care personnel about the possibility of transmission of xenogeneic infection.
4. Public health authorities should maintain good communication with physicians and other health care providers who are likely to serve as the first line of defence against the spread of potential pathogens detected in xenotransplantation recipients.
5. Legislatures should evaluate the effectiveness of current public health laws to address situations in which an asymptomatic

xenotransplantation recipient fails to comply with surveillance instructions, and they should consider appropriate amendments to those laws if needed.

6. Health care workers who will be involved in xenotransplantation procedures should be informed in advance of the known and potential risks of xenogeneic infections posed by the procedure, behaviours known to transmit infectious agents, methods to minimize that risk, the need to report significant unexplained illness, and the plans of the sponsor and/or the center where the procedure is performed for monitoring health care workers and for post-exposure evaluation and management.
7. The sponsor or institution where the xenotransplantation procedure is performed should produce and periodically update plans for monitoring involved health care workers and plans for post-exposure evaluation and management and should ensure that infection control measures are adhered to.
8. The SACX (or another appropriately constituted advisory committee) should continue to serve as a mechanism for ensuring education and discourse in the lay community about public health concerns, as well as other social, medical and ethical issues raised by xenotransplantation clinical research, through the following:
   (i) providing a forum for public discussion of xenotransplantation issues, as appropriate, and ensuring that the members of the advisory body are available for interviews;
   (ii) being informed about xenotransplantation protocols so that it can knowledgeably communicate with the community about pertinent social, public health, medical and ethical issues;
   (iii) developing and making available informational resources on xenotransplantation;
   (iv) making recommendations to the DHHS Secretary on policy and procedures, following consensus developed by the committee's multidisciplinary membership; and
   (v) developing closer relationships with relevant groups in other nations.
9. At present, enrolment of incapacitated adults into xenotransplantation protocols should be limited to situations in which:
   (i) the individual's mental capacity is likely to be restored by the procedure;
   (ii) the individual's legally authorized surrogate decision maker determines that the individual's enrolment in the protocol accords with the individual's likely preferences under the circumstances, or if these preferences are unknown, that enrolment would promote the individual's best interests;
   (iii) the individual's legally authorized surrogate represents that the individual is a responsible person and is likely to adhere to lifelong follow-up responsibilities; and
   (iv) there are plans for assistance with life-long follow-up requirements in the event that such assistance is needed.
10. At this time, as a general matter, children should not participate in xenotransplantation protocols. There may be special circumstances, however, in which the possibility of benefit to a child is high, given available alternatives. Researchers and institutions should consider these situations on a case-by-case basis and should pursue further study of this issue.

State of the science in xenotransplantation

This report reviewed the potential impact of xenotransplantation on the US chronic disease burden, the types of xenotransplantation procedures, the potential source animals, the scientific challenges, the current approaches to these challenges, the infectious disease risks, "xenotourism," knowledge gaps and resource limitations, and parallel or alternative strategies to xenotransplantation.

The SACX made the following recommendations for pursuing xenotransplantation as a strategy for treating a variety of medical disorders:

1. Continue to evaluate pigs as a suitable source animal for xenotransplantation. Due to heightened risks and ethical concerns apparent with nonhuman primates, these animals should not be considered as source animals for xenotransplantation. The establishment of closed colonies of pigs will ultimately be needed to raise animals for clinical trials.
2. Support existing federal guidelines on source animals for xenotransplantation.
3. Further development of diagnostic tools, including antibody and nucleic acid-based assays, to detect known and unrecognized porcine pathogens that might pose a risk to humans should be supported. Continue(d) research on the risks of zoonotic infection in xenotransplantation recipients and gauging the potential for new emerging diseases is needed.
4. Initiate research studies that will use the new tools of molecular biology and genetics to reveal physiological and immunological

incompatibilities between source animals and humans.

5. Develop facilities where pig-to-non-human primate models could be used to gauge the efficacy of xenotransplantation of pig organs, tissues, and cells to humans.
6. Encourage scientists from diverse disciplines to apply their expertise in the discovery of solutions for successful xenotransplantation.
7. Establish repositories in which reagents, genetically modified pigs, and other valuable materials can be maintained and distributed to researchers and laboratories engaged in xenotransplantation research.
8. Build government-industrial-academic partnerships that ensure the sharing of reagents and research animals.
9. Provide counselling to industry early in their development of xenotransplantation products on issues related to compliance with federal regulatory and safety issues.
10. The problem of broad liability for the consequences of possible zoonotic infections is perceived by some as a deterrent to participation by industry in xenotransplantation research. Investigate this issue and identify solutions.
11. Periodically re-evaluate federal guidelines on xenotransplantation and institute a system of review and oversight of regulations.
12. Investigate the scope of xenotransplantation in countries lacking stringent oversight and the extent of risks posed by entry into the US of persons receiving xenotransplants in such countries. Appropriate federal agencies should consider the need for adjustments to immigration policy and questionnaires to protect the public health.
13. Educate US residents about the risks of unregulated xenotransplantation procedures and discourage their participation in those lacking regulatory oversight as stringent as that in the US.
14. Work closely with international health agencies to promote regulations and guidelines for xenotransplantation that are as rigorous as those developed by the PHS and assist other countries in implementing them.

D.K.C. Cooper
Editor-in-Chief
(E-mail: cooperdk@upmc.edu)