Checklist for Institutional Review Boards Reviewing a First-in-Human Pig Kidney Xenotransplant Clinical Trial Protocol

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Introduction: Xenotransplantation is a novel experimental treatment that involves transplanting organs from nonhuman animals into humans. Several pig kidney xenotransplants have already been performed. In the research context, pig kidneys from genetically modified source pigs have been transplanted into deceased humans. Additionally, several living humans have received genetically modified pig kidneys via the U.S. Food and Drug Administration's (FDA's) Expanded Access/Compassionate Use pathway, which allows patients with a serious or immediately life-threatening condition to gain access to an investigational medical treatment outside of a clinical trial setting.

Historical Context: At least one company has obtained approval from the FDA to initiate a first-in-human pig kidney xenotransplant clinical trial (henceforth referred to as pig kidney clinical trials) using genetically modified pig kidneys. Other companies that have developed source pigs with different types of genetic modifications may also be applying to the FDA to initiate pig kidney clinical trials.

Checklist Purpose: The purpose of this checklist is to assist Institutional Review Board (IRB) members reviewing protocols and informed consent forms for pig kidney clinical trials. This checklist is designed to supplement existing procedures used by IRB members to review study protocols. This checklist focuses on unique features and nuances of pig kidney clinical trials that require additional IRB oversight.

Checklist Development: The checklist was developed with input from former and current IRB members and chairs, and from a 17-member multidisciplinary Advisory Committee composed of transplant clinicians, transplant recipients, a living donor, xenotransplant researchers, transplant regulators, transplant health services researchers, and experts in human research ethics.

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I. FIRST-IN-HUMAN PIG KIDNEY XENOTRANSPLANT CLINICAL TRIAL PROTOCOL

A. Scientific Justification and Clinical Trial Description	Yes	No	N/A
A1. Does the protocol adequately describe the societal relevance of a pig kidney clinical trial? *(e.g., to reduce the organ shortage and thereby save patients' lives)*			
A2. Does the information supplied in the protocol provide sufficient scientific justification for a pig kidney clinical trial?			
A3. Is the study design sufficient to answer the research question(s)?			
A4. Does the protocol adequately describe the endpoints of the trial?			

B. Source Pig	Yes	No	N/A
B1. Does the protocol describe the genetic modifications that were made to the source pig?			
B2. Does the protocol explain the purpose or associated rationale for the genetic modifications made to the source pig?			
B3. Does the protocol sufficiently document the general conditions and certifications assuring that the source pig is free of known pathogens?			
B4. Does the protocol sufficiently explain the process of procurement of the pig kidney?			
B5. Does the protocol sufficiently explain the process of transportation of the pig kidney to the transplant center?			
B6. Does the protocol sufficiently document the general conditions and certifications required by the FDA for the kidney to leave the animal facility?			
B7. Does the protocol describe what steps, if any, were taken to minimize suffering and ensure ethical treatment of the donor pig prior to organ procurement?			

C. Study Risks and Benefits	Yes	No	N/A
C1. Are the risks of receiving a pig kidney transplant adequately described in the protocol? **These may include:**			
i. Physical risks *(e.g., infections, surgical complications, graft rejection)*			
ii. Psychological risks *(e.g., unease with an animal organ in body)*			

iii. Social risks *(e.g., stigma associated with having an animal organ in body)*			
iv. Privacy risks *(e.g., unauthorized news coverage about the xenotransplant)*			
v. Economic risks *(e.g., post-transplant medical treatment expenses that may not be covered by the recipient's medical insurance carrier)*			
C2. If participants will receive immunosuppressive or other drugs as part of the study, does the protocol adequately describe the risks of taking said drugs?			
C3. Does the protocol state whether any immunosuppressive or other drugs used as part of the study are not FDA-approved?			
C4. Does the protocol describe known infections the pig kidney might transmit to research participants?			
C5. Does the protocol acknowledge the possibility of unknown infections the pig kidney might transmit to research participants?			
C6. Does the protocol describe provisions for monitoring recipients for potential transmission of pig infectious diseases to the recipient?			
C7. Does the protocol describe the possibility that known and unknown pig infections could be transmitted to research participants' close contacts?			
C8. Does the protocol define 'close contacts'?			
C9. Are the risks of receiving a pig kidney transplant reasonable in relation to any potential benefits to participants?			
C10. Are the risks of receiving a pig kidney reasonable in relation to the importance of the knowledge that may reasonably be expected to result from the study?			

II. INFORMED CONSENT FORM FOR A PIG KIDNEY XENOTRANSPLANT CLINICAL TRIAL

D. Explanation of Research	Yes	No	N/A
D1. Does the informed consent form adequately describe the societal relevance for a pig kidney clinical trial? *(e.g., to reduce the organ shortage and thereby save patients' lives)*			
D2. Does the informed consent form describe the genetic modifications that were made to the source pig and explain the associated rationale for those modifications?			

D3. Does the informed consent form describe the outcomes of animal studies that used pig kidneys with the same genetic modifications as the pig kidneys for this study?			
D4. Does the informed consent form clearly state that xenotransplantation is experimental and not standard of care?			
D5. Does the informed consent form clearly distinguish which procedures are experimental?			

E. Risks	**Yes**	**No**	**N/A**
E1. If participants will receive immunosuppressive or other drugs as part of the study, does the informed consent form adequately describe the risks of taking said drugs?			
E2. Does the informed consent form state whether any immunosuppressive or other drugs used as part of the study are not FDA-approved?			
i. If yes, does the informed consent form explain whether drugs not approved by the FDA are being tested in studies to determine if they are safe and effective?			
E3. Are the risks of receiving a pig kidney transplant well described in the informed consent form? **These may include:**			
i. Physical risks *(e.g., infections, surgical complications, graft rejection)*			
ii. Psychological risks *(e.g., unease with an animal organ in body)*			
iii. Social risks *(e.g., stigma associated with having an animal organ in body)*			
iv. Privacy risks *(e.g., unauthorized news coverage about the xenotransplant)*			
v. Economic risks *(e.g., post-transplant medical treatment expenses that may not be covered by the recipient's medical insurance carrier)*			
E4. Does the informed consent form describe the risks of known infections the pig kidney might transmit to research participants?			
E5. Does the informed consent form explain that there may be unknown pig infections that could be transmitted to research participants?			
E6. Does the informed consent form describe the possibility that known and unknown pig infections could be transmitted to research participants' close contacts?			
E7. Does the informed consent form define 'close contacts'?			

E8. Does the informed consent form adequately describe the symptoms that a participant might experience from a potential pig infection?			
E9. Does the informed consent form describe whether treatment options are available if a pig infection is transmitted to study participants?			
E10. Does the informed consent form describe whether treatment options are available if a pig infection is transmitted to study participants' close contacts?			
E11. Does the informed consent form describe post-transplant outcomes that will be monitored by the research team? *(e.g., infectious disease transmission, organ function, patient satisfaction, quality of life, mental health, etc.)*			
E12. Does the informed consent form describe participant requirements for post-transplant monitoring? *(e.g., procedures for monitoring, the duration of monitoring, type of monitoring required, etc.)*			
E13. Does the informed consent form explain that participants' close contacts may need to be monitored if the participant tests positive for an infection that was transmitted by the pig kidney?			
i. If yes, does the informed consent form describe requirements for post-transplant monitoring of close contacts? *(e.g., procedures for monitoring, the duration of monitoring, type of monitoring required, etc.)*			
E14. Does the informed consent form explain that there may be other unknown risks associated with the xenotransplant, which cannot be anticipated by the research team?			

F. Participation and Withdrawal	**Yes**	**No**	**N/A**
F1. Does the informed consent form state that participants can withdraw from the study?			
F2. Does the informed consent form describe the consequences of withdrawing from the study? **Consequences of withdrawal may include:**			
i. Potential health consequences to participants if they are no longer monitored			
ii. Use of study data collected prior to participant withdrawal			
iii. Use of biospecimens collected prior to participant withdrawal			
F3. Overall, does information in the informed consent form support an informed consent process that minimizes the possibility of coercion or undue influence to participate?			
F4. Does the informed consent form describe what options are available for treatment if the pig kidney stops working?			

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