



World Health Organization

First WHO Global Consultation on Regulatory Requirements for Xenotransplantation Clinical Trials

Changsha, China, 19-21 November 2008

The Changsha Communiqué¹

Principles

1. Successful xenotransplantation has the potential to treat a wide range of serious diseases such as diabetes, heart and kidney disease. Successful xenotransplantation could provide transplants for people who currently would not get a transplant.
2. Potentially animals could provide a plentiful supply of readily available, high quality cells, tissues and organs for transplantation. Genetic modification of the animals may improve the effectiveness of such xenotransplant material. Animals used in xenotransplantation should be from a closed herd bred for the purpose and housed in a well-controlled, pathogen-free environment with high standards of animal welfare. Source animals should be extensively tested to ensure freedom from known pathogens with appropriate biosecurity and surveillance in place to ensure continued freedom from infectious disease.
3. Xenotransplantation is a complex process which carries risks, including graft rejection, inadequate graft function and transmission of recognized or unrecognized infectious diseases to the recipient. There is the risk of developing serious or novel infections which could infect not just the transplant recipient but also close contacts or the wider human or animal populations.
4. Because of these wider community risks, xenotransplantation clinical trials and procedures need to be effectively regulated. There should be no xenotransplantation in the absence of effective regulation by the government of the country. Regulation should have a legal basis with powers to ban unregulated procedures and enforce compliance with regulatory requirements. The regulatory system should be transparent, must include scientific and ethical assessment and should involve the public.
5. Because of the community risk, in proposed clinical trials of xenotransplantation there should be a high expectation of benefit to balance the risk. The level of this expectation should be in proportion to the level of the risk. The level of safety and efficacy should conform to recommendations from the international scientific community, when available, and requires rigorous pre-clinical studies using the most relevant animal models. Proposers of trials must provide all the information required by the regulatory authority to assess the risks and determine how the risks can be minimised.

¹ Disclaimer: These are the conclusions of the above meeting for which WHO was the Secretariat. These conclusions do not necessarily represent the decisions and policies of WHO.

6. Proposers of xenotransplantation clinical trials must be able to clearly justify carrying out a particular trial on a specific patient population. Patient selection should be on the basis of informed consent from motivated patients willing to accept the special conditions that will be required by the trial. Patients and close contacts should be effectively educated about their treatment to encourage compliance, and to minimize risks for themselves and for society.
7. Participation in xenotransplantation will usually require the long term storage of animal and patient samples, pre- and post-treatment, as well as records. It will require life-long follow up of recipients and possibly their close contacts. There must be rigorous analysis of trial outcomes. Xenotransplant product recipients must be registered in an appropriate database with traceability to the donor animal, while ensuring that patient privacy is protected. If anything happens to prevent the proposers from continuing the trial, there must be an adequate provision for all records, data and archived samples such as their transfer to the regulatory authority or other designated organization.
8. Medical teams must have appropriate expertise and understand the risks to the patients, themselves and the community. Because of the risk of infectious disease for the community, there must be a system in place for vigilance and surveillance with contingency plans to identify and respond to any indication of xenotransplantation-related infection in a timely manner.
9. There needs to be a global system for exchanging information, preventing unregulated xenotransplantation, providing support for states and coordinating xenotransplantation vigilance, surveillance and response to suspected infections.
10. Because of the potential benefits of successful xenotransplantation, consideration should be given from the beginning to future equitable access to this therapy and the public sector should be encouraged to support xenotransplantation research and development.

Key Recommendations

To WHO

1. WHO should have a dedicated resource to develop and support a plan for global action for xenotransplantation.
2. WHO should inform Member States of the need to assess xenotransplantation practices in their territories.
3. WHO should encourage and, if requested, support Member States to the extent possible in assessing their capacity to regulate xenotransplantation and in identifying xenotransplantation practices in their territories.
4. WHO should promote public awareness of the potential benefits of successful xenotransplantation and of the dangers of unregulated xenotransplantation, including xenotourism.

5. WHO should have in place a system for the identification of and response to any xenotransplantation infectious disease outbreak in a timely manner.
6. WHO should continue its support to the database of worldwide xenotransplantation practices.
7. WHO should maintain a register of xenotransplantation trials and a list of experts who can advise Member States on aspects of xenotransplantation and of specialized laboratories able to test for xenotransplantation-related pathogens.
8. WHO should promote future equitable access to successful xenotransplantation products.

To Member States

1. Member States should take immediate steps to identify any xenotransplantation practices in their territories and ban those that are unregulated. They should promote public awareness of these practices and their risks.
2. Member States should ensure that public health officials are aware of the infection risks of xenotransplantation, including those associated with patients travelling to receive xenotransplantation products outside their territories and have plans in place to timely identify and respond to any such infection.
3. Member States should review their laws to determine whether they have adequate authority to regulate xenotransplantation, ban unregulated xenotransplantation and provide appropriate sanction for failure to comply.
4. Member States should assess whether they have the resources and capacity to regulate xenotransplantation effectively. If they do not have such resources and capacity, they should ban xenotransplantation in their territories.
5. If a Member State has the capacity to regulate xenotransplantation and believes xenotransplantation should be carried out, it should ensure there is an effective national registry and regulatory process in place.

To investigators and proposers of clinical trials using xenotransplantation products

1. Investigators must ensure that source animals are bred for the purpose and as safe as possible, using a closed colony of consistently known specific pathogen-free animals housed in a well controlled pathogen-free environment with high levels of biosecurity.
2. Investigators must provide clear justification for the trial, including adequate pre-clinical data on safety and efficacy, usually from non-human primate testing.
3. Investigators should select trial participants for whom there is no adequately effective alternative therapy available and who understand the risks and consequences of the procedure, including the need for compliance with life-long follow up and who are motivated to modify their behaviour accordingly.

4. Investigators must provide appropriately trained and experienced personnel to provide the transplant material and conduct the clinical trial and surveillance.
5. Investigators must have a comprehensive plan for effective communication with public health authorities overseeing the trial.
6. Investigators must have a comprehensive plan for post-transplant long-term patient follow up and timely identification, reporting, and management of possible xenotransplant-related infection episodes.
7. Investigators must ensure storage of appropriate pre- and post-procedure specimens and maintain both the specimens and records in accordance with national regulatory guidelines (normally for 30 to 50 years).