Xenotransplantation

<table>
<thead>
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<th>What is xenotransplantation?</th>
<th>Xenotransplantation refers to the transplantation of living cells, tissues, and organs from one species to another. In this document it is used principally to describe animal-to-human transplants. An example is the transplant of a kidney from a pig into a human.</th>
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<td>What are the potential benefits of xenotransplantation?</td>
<td>The main reason for medical scientists to explore the potential of xenotransplantation is to find alternatives for human organ and tissue transplants. Although many human transplant operations are highly successful, there is always a severe shortage of suitable donated organs and tissues. The greatest benefit would be to increase the supply available for transplantation.</td>
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<td>How can it help cure diseases or decrease health problems?</td>
<td>Possible new therapies from xenotransplantation include the treatment of life-threatening or chronic debilitating illnesses. One example is diabetes - primarily caused by the destruction of islet cells which produce insulin in human bodies. Pre-clinical research is now exploring the possibility of pig islets transplanted into a patient which may control his/her blood sugar levels.</td>
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<td>Have animal organs or tissues been used for transplants before?</td>
<td>Other procedures, some of which are being investigated in early clinical trials in other countries, explore the use of cells or tissues from other species to treat life-threatening illnesses such as liver failure and Parkinson’s disease. Medical science already uses animal parts for various therapeutic reasons, such as replacement heart valves from pigs. However, these therapeutic products have been chemically treated and are not functional, living tissue. This distinguishes them from the viable organs used in xenotransplantation.</td>
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What are the risks of xenotransplantation to the patient?

No medical procedure is without risk. It is natural for a person’s immune system to reject foreign tissues. The rejection of a transplanted organ or tissue is the biggest risk to the patient, and this already occurs when human organs are used. However, in the case of xenografts, the organ rejection may be more severe since the differences between animal and human cells are greater.

Another possible risk is that animal disease agents, such as viruses, may be transmitted to the patient.

Xenotransplants pose a risk to the general public because they may cause new types of infectious diseases.

As stated above, animal disease agents may be transmitted to humans through transplanted cells, tissues, or organs. Some of these agents, such as the ones that cause rabies, malaria, Lyme disease, and anthrax are known and can be detected. However, there are other agents present in animal tissues of which very little is known and possibly others that have not been identified. One example is a pig virus known as porcine endogenous retrovirus (PERV) that is found in the genetic material of every pig. PERVs cannot be eliminated or screened out and laboratory experiments have shown that they can infect human cells. However, it is not yet known if PERVs can be transmitted through a xenotransplant.

Some of these infectious agents do not seem to cause disease in the animals themselves, but they may cause disease in the transplant recipient. There is also the possibility that the agent may then be transmitted to those in close contact with the patient and the larger community.

What are the potential risks to the public?

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What is the regulatory status of xenotransplantation in Canada?

Xenografts - the live cells, tissues, and organs from animal sources - are considered therapeutic products (drugs or medical devices) and are subject to the requirements of the *Food and Drugs Act and Regulations*. Companies wishing to undertake clinical trials involving xenografts must obtain the approval of the Therapeutic Products Programme (TPP) of Health Canada before they may proceed.

What is a clinical trial?

A clinical trial is medical research undertaken with informed and consenting human subjects in a controlled environment. The intent of a clinical trial is for the sponsoring company or research institute to gather information on the safety and effectiveness of new drugs or therapies prior to seeking approval of a procedure or product for use by the Canadian public.

How soon could xenotransplants be carried out in Canada?

To date, no requests for clinical trials involving xenografts have been received or approved by Health Canada.

What animals would be used for xenotransplants?

While it may seem logical to choose animals that are genetically similar to humans, such as apes or baboons, it is becoming clear that more distant mammals may be preferred. Researchers are suggesting that the pig is a more suitable species, for several reasons: pigs are available in large numbers; their organs are of a size suitable for use in adult patients; and they can also be genetically manipulated to reduce the possibility and severity of transplant rejection. The pigs would be raised in specially designed facilities and would be used only for transplantation procedures.

What have other countries done about xenotransplantation?

Discussions on the benefits and risks of xenotransplantation have begun in several countries. In the United States, the regulatory responsibility lies with the Food and Drugs Administration (FDA) which is updating “The Public Health Service Guidelines on Infectious Disease Issues in Xenotransplantation” that
was first released in September 1996. Clinical trials have been approved by the FDA.

In the United Kingdom, clinical trial applications may now be submitted for review to the United Kingdom Xenotransplantation Interim Regulatory Authority (UKXIRA). UKXIRA was established in May 1997 to advise the UK Health departments on actions necessary to regulate xenotransplantation and to advise on the acceptability of clinical trial applications. UKXIRA has not approved any clinical trials to date.

The World Health Organization, in its efforts to foster international consensus on issues related to human health, hosted a consultation with international experts and published guidelines in 1998 on preventing and managing infectious diseases associated with xenotransplantation.

In January 1999, the Council of Europe’s Parliamentary Assembly called for a moratorium on xenotransplantation until this new technology is evaluated and guidelines are established and agreed. The Assembly also asked the Council of Europe Public Health and Bioethics Committees to work hand in hand with the World Health Organisation on a strategy which balances ethical, medical, scientific, legal, social and public health issues before human clinical trials continue.

Have there been xenotransplants in other countries?

Clinical trials have taken place in the United States and Sweden, and include the transplantation of fetal pig neural cells into patients with Parkinson’s disease; fetal pig islet cells transplanted into diabetic patients; and genetically modified pig livers used to temporarily
treat patients with severe liver failure. These controlled trials involve a small number of patients and will provide information on whether this procedure is safe and effective.

A national discussion on the risks and benefits of xenotransplantation and its role in human medicine is underway. Health Canada will be leading and coordinating this discussion. In the meantime, the Therapeutic Products Programme (TPP) is developing strategies for improving the availability, safety and equitable distribution of human organs and tissues for transplantation and mechanisms to control and regulate xenotransplantation until society has reached a consensus on its place in human medicine.

The TPP has established an Expert Working Group comprised of transplant experts, bioethicists, legal experts, consumers and other stakeholders to develop safety standards for organs and tissues for transplantation. A consultation process has now begun to incorporate these as National Standards of Canada.

In consideration of the potential benefits and risks of xenotransplantation, experts are also drafting guidelines and safety standards specifically for xenotransplantation that can be used if and when the procedure is approved in Canada.

The TPP also sponsored a National Forum on Xenotransplantation in Ottawa on November 6-8, 1997. This Forum represented the first national consultation on the scientific, ethical, and regulatory issues surrounding xenotransplantation. Participants included professional associations, transplant recipients, scientists, health professionals and specialists in the area of transplantation, disease transmission, ethics, law, animal rights, and veterinary medicine.
The release of the Forum report in December 1998 represents the TPP’s next step in broadening discussions with Canadians. It makes several important recommendations, such as the need to inform the public about xenotransplantation; to involve the public in the policy development process; and to develop safety standards that can be used to regulate xenografts if and when they are approved for use in Canada.

What are the next steps?

The TPP intends to develop policy to address the safety, efficacy, ethical, and regulatory issues surrounding the potential use of xenografts. The policy framework will encompass the views of Canadians and the shared responsibilities of Health Canada, the provinces, health institutions, industry, and the public. To achieve this goal, the TPP will continue to involve Canadians in the discussion on xenotransplantation.

The TPP is committed to providing Canadians with information about the benefits and risks of this new technology and involving them in the development of policy.

How can you participate?

Persons interested in the issue of xenotransplantation are invited to read the Forum report or the summary of the report and send their comments to the TPP. In addition, there will be an opportunity to participate in upcoming public consultations on xenotransplantation. Those wishing to participate are asked to notify the TPP.
To forward comments or request further information

Write: Policy Division
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     Therapeutic Products Programme
     Health Canada
     1600 Scott St., Tower B, 2nd Floor
     A.L. 3102C5
     Ottawa, Ontario K1A 1B6

     Fax: (613) 941-6458

or visit our website:

www.hc-sc.gc.ca/hpb-dgps/therapeut/htmleng

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The Therapeutic Products Programme is the national authority that evaluates and monitors the safety, effectiveness, and quality of drugs, medical devices and other therapeutic products available to Canadians; and plays a national role in the control of illicit drugs and related substances in Canada.