



## **CONSULTATION DOCUMENT ON APPLICATION OF LIVING CELL TECHNOLOGIES TO CONDUCT A TRIAL OF PIG CELL TRANSPLANTATION IN 8 PATIENTS WITH TYPE 1 DIABETES**

### **About this consultation**

The National Health Committee (NHC) provides the Minister of Health with independent advice on a broad spectrum of health and disability issues. It is a statutory committee that was first established in 1992, and now derives its mandate from section 13 of the New Zealand Public Health and Disability Act 2000. Members are appointed by the Minister of Health.

The Minister of Health has asked the NHC to provide him with independent advice on an application by Living Cell Technologies (LCT) to conduct a clinical trial of pig cell transplantation in New Zealand.

The trial involves inserting pancreatic cells from pigs into 8 people with type 1 diabetes, to test whether the cells will produce insulin, thus reducing or eliminating the need for these people to use injected insulin. This trial is limited to testing the safety of the procedure for the patients, and will give early indications of whether the treatment is likely to be effective in humans. If it proves to be safe and looks likely to be effective, a further trial would be required to establish that the treatment is effective enough to be made available to other people with type 1 diabetes. This would require a separate application process.

The NHC is undertaking a public consultation on LCT's application, and the submissions received will be taken into account in its advice to the Minister of Health. The NHC is particularly interested to receive submissions from people with type 1 diabetes, and anyone with expertise in the field of xenotransplantation and related fields.

The Minister of Health has asked the NHC to provide him with advice by 8 August 2008. To meet that deadline, the closing date for public submissions will be **Friday 25 July 2008**.

## Focus of the consultation

The NHC has been asked to provide advice on whether the trial meets the five criteria under Section 96E(1) of the Medicines Act 1981, which are that:

1. the conduct of the procedure or class of procedure does not pose an unacceptable risk to the health or safety of the public
2. any risks posed by the conduct of the procedure or class of procedure will be appropriately managed
3. any ethical issues have been adequately addressed
4. any cultural issues have been adequately addressed
5. any spiritual issues have been adequately addressed.

## Consultation question

The NHC is therefore inviting public submissions on the question:  
***“Do you think the proposed trial meets these five criteria?”***

## Summary of information

The following information may be useful for those wishing to make a submission:

- what is xenotransplantation? (page 2)
- what is type 1 diabetes? (page 3)
- the proposed trial (page 3)
- the application process (page 4)
- the NHC’s process (page 6)
- how to make a submission (page 6)
- Appendix 1 - further information (page 7)

## What is xenotransplantation?

Xenotransplantation is any medical procedure that involves the insertion or injection into a human being of any material that consists of, or includes, living biological material from an animal.

It includes:

- organ transplantation (ie, transplantation of whole or partial animal organs into humans)
- cell therapies (ie, insertion of animal cells into humans)
- external therapies (ie, animal and human cells come into contact outside the human body, and the resulting product is administered to a person (eg, skin grafts grown on a layer of animal cells).

There have been many attempts over the past hundred or so years to carry out xenotransplantation procedures. The practical problems associated with

transplantation of animal organs into humans (most notably rejection<sup>1</sup>) have proved so considerable that this form of xenotransplantation is unlikely to be feasible any time soon. However cell therapies and external therapies are technically feasible, and represent the most likely direction for xenotransplantation to develop in the immediate future.

The main reason that xenotransplantation has been investigated is because there is a shortage of suitable tissue from humans. Demand for human tissue far outstrips tissue available from human donors. Xenotransplantation (along with stem cell research) represents a possible answer to this problem.

However, there are potential down sides. Some people have ethical objections to the use of living cells and tissue from animals in this way. But perhaps the most significant concern that people have had is about the risk of transmission of novel infections from animals to individuals, who might then transmit them to the wider population. One of the main safety concerns with pig cell xenotransplantation, for this particular trial, is the existence of Porcine Endogenous Retrovirus ("PERV") in pig DNA. While there is no evidence to date of human infection of PERV arising from pig transplantations, the possibility, however small, cannot be ruled out entirely.

### **What is type 1 diabetes?**

Diabetes is the result of the body not producing enough insulin to keep blood glucose levels in the normal range. About 10% of people with diabetes (around 15,000 people in New Zealand) have type 1 diabetes. Type 1 diabetes is an auto-immune condition, where the body attacks the cells within it that make insulin. These cells are called beta islet cells and are located in the pancreas.

Type 1 diabetes most often begins in childhood, although it can occur at any age. It is progressive, in that a person recently diagnosed with type 1 diabetes will still have some insulin being produced in their body. But, over time their own insulin production becomes less and less, and finally most people with type 1 diabetes are producing none of their own insulin.

People with type 1 diabetes currently require injections of insulin to replace the insulin no longer being produced by their bodies. They also need to control their diet.

### **The proposed trial**

Living Cells Technologies (LCT) is an international biotechnology company with offices in New Zealand. It specialises in researching therapies that use animal cells to replace missing cells in humans, a form of xenotransplantation.

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<sup>1</sup> When the body's immune system recognises and attacks foreign cells. This is a significant issue with any form of transplantation of foreign cells, including human-to-human organ transplantation. Addressing it requires the use of drugs to suppress the patient's immune system, which leaves them vulnerable to infection.

LCT has applied to carry out a trial of an animal cell therapy at Middlemore Hospital. It involves inserting non-genetically modified pig pancreatic cells encapsulated in a seaweed-based gel into the abdomens of 8 people with type 1 diabetes. If successful, the pig cells would secrete insulin in response to the body's demands, reducing or perhaps even eliminating the need for injected insulin.

The seaweed gel is intended to shield the pig cells from the patients' immune systems, meaning that drugs to suppress the immune system would not be required. Such drugs are generally required when performing transplants, but patients then have a greater risk of infection.

The pigs being used are descended from pigs that were isolated on the Auckland Islands. These pigs are freer from common pig infections than other pigs, and will be extensively tested and monitored for common pig diseases throughout the trial. If the trial goes ahead, LCT's premises and processes would also be regularly monitored by Medsafe. LCT would also be obliged to report any adverse events (including an infectious outbreak) to Medsafe.<sup>2</sup>

The current application is for a phase I/IIa trial, which means that it is only testing the safety and preliminary efficacy of the procedure for the recipients. If the procedure proves to be safe and there is sufficient preliminary evidence that the treatment is effective, a further trial would be required to establish that the treatment is effective enough to be made available to the wider population of people with type 1 diabetes. This would require a separate application process. A similar trial is being conducted by LCT in Russia (see LCT's website link in Appendix 1 of this document for more information).

### **The application process**

Applications for clinical trials involving xenotransplantation in humans have to go through three steps: a scientific assessment, then an ethics assessment, then advice from the Ministry of Health to the Minister, before the Minister gives final approval.

LCT applied to the Ministry of Health in August 2006 to conduct a clinical trial of their pig pancreatic cell procedure. The encapsulated pig cells were considered to meet the definition of a medicine under the Medicines Act, so the application was originally made and considered under Section 30 of the Medicines Act, which covers clinical trials of medicines.

As with other applications under Section 30, LCT's application required approval from both the Health Research Council (HRC) and an appropriately accredited ethics committee.

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<sup>2</sup> Medsafe, the New Zealand Medicines and Medical Devices Safety Authority, is a business unit of the Ministry of Health and is the authority responsible for the regulation of therapeutic products in New Zealand.

### *Scientific assessment*

The Gene Technology Advisory Committee (GTAC) is a committee of the HRC that assesses the scientific merit of New Zealand applications to produce new medical therapies through the transfer of genes from another species to humans, and between species. Part of GTAC's Terms of Reference is to review Section 30 applications that involve xenotransplantation. GTAC assessed the proposal and concluded that there was sufficient evidence that the proposed therapy was safe and had the potential to be effective to allow the trial to proceed.

### *Ethics assessment*

The application then went to the Northern X Regional Ethics Committee, one of the seven independent health and disability ethics committees established under the New Zealand Public Health and Disability Act 2000. The Ethics Committee suggested some changes to the trial design and documentation, which LCT made to the Committee's satisfaction. The Ethics Committee approved the trial in September 2007, subject to the following issues being addressed by the Minister of Health:

1. "The Minister is assured that there are powers he can immediately use to contain a public health emergency, should one arise as a result of this clinical trial",
2. "... that a national register and archive will be in place before the end of 2008"; and
3. Consideration of whether the Minister is satisfied that, should an injury be suffered by a participant many years after the trial when the sponsor company is not going to market with the products under trial or if for any reason the company is wound up, "an appropriation will be made available from the public purse to cover such compensation".

### *Ministry of Health advice and approval by the Minister of Health*

In New Zealand, xenotransplantation trials are possible within the regulatory framework contained in Part 7A of the Medicines Act 1981 (which was inserted into the Medicines Act in 2002). The current application is the first one to be considered under Part 7A. Xenotransplantation can only occur upon written authorisation by the Minister of Health. The Minister of Health may only give such authorisation if satisfied that the proposed procedure meets the five criteria (see page 2 of this document).

The Minister is also able to seek further independent advice, and in this case, has asked the National Health Committee to provide such advice, before making his decision.

## **The NHC's process**

Pursuant to Section 96F(2) of the Medicines Act, the NHC will provide advice after it has given interested parties and members of the public a reasonable opportunity to make submissions, and after it has taken those submissions into account. At some point after the NHC has provided its advice to the Minister, and the Minister has made his decision on the application, the Committee's report will be made publicly available. A summary of submissions will also be made publicly available.

## **How to make a submission**

If you wish to make a submission, you can do any one of the following by the closing date of 25 July 2008:

Post your submission to:

LCT Application Submission  
National Health Committee  
PO Box 5013  
WELLINGTON.

Hand deliver your written submission, in an envelope marked

"LCT Application Submission, National Health Committee"  
to  
Ministry of Health offices  
Level 2  
No 1 The Terrace  
WELLINGTON.

Email your submission, with the title reading "LCT Application Submission" to [nhc\\_info@nhc.govt.nz](mailto:nhc_info@nhc.govt.nz)

Fax your submission to: (04) 496 2191, attention "National Health Committee".

If for any reason you are unable to make a written submission, but would like your views to be conveyed to the NHC, please call toll free on 0800 990 028 as soon as possible.

Please note that any submissions made may be subject to a request, and subsequently released, under the Official Information Act 1982.

## **Appendix 1          Further information**

A range of public information is available that gives information on xenotransplantation. Some of it is listed on the NHC's website, with links so that you can download further information if you wish.

### **1. Bioethics Committee Website**

The Cultural, Ethical and Spiritual Aspects of Animal-to-Human Transplantation - A report on xenotransplantation by Toi te Taiao: the Bioethics Council

<http://www.bioethics.org.nz/publications/xeno-final-report-aug05/index.html>

The Cultural, Spiritual and Ethical Aspects of Xenotransplantation: Animal-to-Human Transplantation - a discussion document

<http://www.bioethics.org.nz/publications/xeno-discussion-jan05/>

Whakapapa & xenotransplantation: animal-to-human transplantation

<http://www.bioethics.org.nz/publications/xeno-whakapapa-jan05/index.html>

The Bioethics Committee conducted a public consultation on the issue of xenotransplantation in 2005. The discussion document, report and the publication on whakapapa talk about ethical, cultural and spiritual issues.

Mail Address:

Toi te Taiao: the Bioethics Council  
PO Box 10362  
Wellington  
New Zealand

Phone: (04) 439 7673

### **2. Gene Technology Advisory Committee Website**

Guidelines for Preparation of Applications Involving Clinical Trials of Xenotransplantation

[http://www.hrc.govt.nz/root/Publications/Guidelines\\_directories\\_and\\_handbooks.html](http://www.hrc.govt.nz/root/Publications/Guidelines_directories_and_handbooks.html)

These guidelines give some idea about what the GTAC looks for when considering whether to recommend approval of a trial that involves xenotransplantation.

Mail Address:

PO Box 5541  
Wellesley Street  
Auckland, 1141  
New Zealand

Phone: (9) 303 5200

### **3. New Zealand Health and Disability Ethics Committees**

[http://www.ethicscommittees.health.govt.nz/moh.nsf/indexcm/ethics-forms-nationalapplication?Open&m\\_id=5.1](http://www.ethicscommittees.health.govt.nz/moh.nsf/indexcm/ethics-forms-nationalapplication?Open&m_id=5.1)

Part 8 of the National Application Form for Ethical Review of a Research Project gives an indication of the type of information Ethics Committees require when assessing a xenotransplantation application on ethical grounds.

Mail Address:

Sally Cook  
National Co-ordinator of Ethics Committees  
Ministry of Health  
1 - 3 The Terrace  
PO Box 5013  
Wellington

Phone: (04) 496 2053

### **4. Living Cell Technologies Website**

<http://www.lctglobal.com>

Information about LCT and the work it does can be found here. Note that this website presents the views of LCT, but not necessarily the views of the NHC.

Mail Address:

PO Box 3014  
Auburn VIC 3123  
Australia

Phone: 0061 3 9886 0247

### **5. Relevant Legislation in New Zealand**

Health Act 1956

[http://www.legislation.govt.nz/act/public/1956/0065/latest/DLM305840.html?search=ts\\_act\\_health+act&sr=1](http://www.legislation.govt.nz/act/public/1956/0065/latest/DLM305840.html?search=ts_act_health+act&sr=1)

Refer to Part 3 of the Health Act 1956, especially Section 79, which describes what action can be taken in relation to infectious and notifiable diseases.

Medicines Act 1981

[http://www.legislation.govt.nz/act/public/1981/0118/latest/DLM53790.html?search=ts\\_act\\_Medicines&sr=1](http://www.legislation.govt.nz/act/public/1981/0118/latest/DLM53790.html?search=ts_act_Medicines&sr=1)

Section 30 of the Medicines Act outlines the process for applications classified as medicines – the section under which the LCT application for this trial was originally lodged. Part 7A covers the process for applications involving a xenotransplantation procedure.

## **6. Australian Website**

<http://www.nhmrc.gov.au/media/media/rel02/xenofaq.htm>

This link is a media release on the Australian National Health and Medical Research Council website covering frequently asked questions on xenotransplantation.

## **7. UK Website**

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_063075](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_063075)

This website provides information on the United Kingdom Department of Health's policy position on xenotransplantation, describes approval processes and points to appropriate sources of expertise and advice for further information and support.

## **8. UK Parliament discussion in Hansard**

<http://www.publications.parliament.uk/pa/cm/cmtoday/cmwms/archive/061212.htm>

Look under health then copy the link given in Hansard.

## **9. Health Canada**

[http://www.hc-sc.gc.ca/dhp-mps/brgtherap/activit/fs-fi/xeno\\_fact-fait-eng.php](http://www.hc-sc.gc.ca/dhp-mps/brgtherap/activit/fs-fi/xeno_fact-fait-eng.php)

This link goes to Health Canada's factsheet on xenotransplantation.

## **10. World Health Organisation**

<http://www.who.int/transplantation/xeno/en/>

This link goes to the World Health Organisation website, which includes the World Health Assembly resolution on xenotransplantation.