

## **Questions & Answers on licence application DIR 126 – Clinical trial of a genetically modified (GM) vaccine against cholera**

### **What does this licence allow?**

PaxVax Australia Pty Ltd (PaxVax) has received approval to conduct a clinical trial with a genetically modified vaccine against cholera. The trial will take place in clinical facilities in Queensland, SA, Victoria and WA. The trial is expected to be completed within one year.

As this will be a clinical trial involving the use of a therapeutic product, it must also meet Therapeutic Goods Administration (TGA) requirements (<http://www.tga.gov.au/industry/clinical-trials.htm>), and will require approval from, and oversight by, a human research ethics committee.

### **What is the purpose of the proposed clinical trial?**

The purpose of the trial is to verify the effectiveness of this single dose oral vaccine for protecting against cholera infection. Ultimately, the vaccine is being developed for vaccination of travellers to areas outside Australia where cholera is an endemic disease, as well as for use in developing countries in response to cholera outbreaks.

### **Who will be vaccinated and how will they be vaccinated?**

Up to 1000 healthy volunteers, covering different age groups, will participate in this clinical trial. All volunteers will be given extensive information about the GM vaccine prior to consenting to participate in the trial.

The vaccine will be administered by qualified health professionals in clinical facilities. Clinical trial participants will be given the vaccine as a drink. The vaccine will not be injected into participants and it will not be sprayed into the air.

### **Has this GM vaccine been previously tested or used?**

This same vaccine strain was previously approved and marketed in several different countries, including Australia, under the brand name “Orochol” or “Mutacol”. Orochol<sup>®</sup> was registered in Australia as a prescription medicine by the Therapeutic Goods Administration, after undergoing extensive evaluation of its safety, quality and efficacy, and it was licensed by the Gene Technology Regulator in 2003. Since the manufacturer of Orochol<sup>®</sup> ceased production of this vaccine, they voluntarily surrendered the licence in 2010.

PaxVax is developing this GM vaccine as a new commercial product. Although it is the same vaccine strain, it is manufactured in different facilities. Therefore, clinical trials are required to confirm the safety and efficacy of the newly manufactured product.

### **Why is this clinical trial being conducted in Australia?**

The clinical trial being conducted in Australia is part of a larger international study and similar clinical trials are being conducted in the USA and Canada. The purpose of the trial is to test the safety and efficacy of the vaccine. In order to produce clearer efficacy data it is preferred that the study is conducted in locations where cholera is not endemic or is present only at low levels (such as USA, Canada and Australia). Conducting the clinical trial in these locations is likely to produce clearer efficacy data than that produced in cholera endemic areas.

## **How has the vaccine been genetically modified?**

The GM vaccine contains live GM cholera bacteria, *Vibrio cholerae*, genetically modified so that they cannot cause disease. Unmodified cholera bacteria produce a toxin and a protein (haemolysin) which can break open blood cells. The vaccine strain has been produced by removing a part of the toxin gene and disrupting the haemolysin gene. As a result of the genetic modification, the GM vaccine strain cannot produce the cholera toxin molecule or the protein which breaks open red blood cells. The vaccine cannot cause cholera.

## **What controls are proposed for this trial?**

The Risk Assessment and Risk Management Plan (RARMP) for this application concluded that the proposed trial poses negligible risks to people or the environment. However, a range of licence conditions would limit the scale and scope of the clinical trial and restrict spread or persistence of the GM bacteria. Control measures include conditions which provide for secure transport and storage of the GM vaccine, administration of the vaccines only by trained clinical staff, exclusion of individuals who could be at risk of adverse effects, fully informing volunteers participating in the trial, and appropriate disposal of trial waste. The trial would also need to comply with TGA requirements for clinical trials of therapeutic products.

## **Want more information?**

A number of documents relating to this decision are available on the DIR 126 page of the OGTR website or via Freecall 1800 181 030. These documents include the finalised RARMP, a summary of the RARMP and the licence.

**The Office of the Gene Technology Regulator**  
**Tel: 1800 181 030      E-mail: [ogtr@health.gov.au](mailto:ogtr@health.gov.au)**  
**Website: <http://www.ogtr.gov.au>**