Australian Government
Department of Health
Office of the Gene Technology Regulator

24 May 2022

Summary of Licence Application DIR 192

Medpace Australia Pty Ltd has made an application under the *Gene Technology Act 2000* (the Act) to conduct a Phase I clinical trial using a genetically modified organism (GMO).

Project Title	Clinical trial of a genetically modified (GM) chimeric Orthopoxvirus (CF33-hNIS) as a cancer treatment[1]
Parent organism	Chimeric Orthopoxvirus (CF33).
Genetic modifications	• Deletion of *J2R* gene – leading to preferential viral multiplication in cancer cells. • Insertion of the human sodium-iodide symporter (hNIS) gene – to facilitate the visualisation of the virus within a living organism by medical imaging.
Principal purpose	The proposed trial is a Phase 1 study designed to evaluate the safety and efficacy of a GM chimeric Orthopoxvirus, alone and in combination with an existing cancer therapy, for the treatment of Australian patients with metastatic or advanced solid cancerous tumours.
Previous clinical trials	The proposed study is the first clinical trial to be conducted with CF33-hNIS.
Proposed limits	
Proposed duration	5 years
Proposed number of participants	Up to 18 participants would be enrolled in the trial in Australia.
Proposed location/s	This clinical trial would be conducted within clinical trial sites and hospitals in Australia. The number of sites and specific locations are yet to be determined.
Proposed controls	• The GMO would be administered to trial participants within a suitable medical facility. • Staff preparing and administering the GMO would use personal protective equipment. • Import, transport and storage of the GMO would be carried out according to the OGTR *Guidelines for the* T*ransport, Storage and Disposal of* GMOs. • Waste that may contain the GMO would be disposed of as infectious material (e.g. via the clinical waste stream).

[1] The title of the project as supplied by the applicant is "A Phase I, Dose Escalation Safety and Tolerability Study of VAXINIA (CF33-hNIS), Administered Intratumorally or Intravenously as a Monotherapy or in Combination with Pembrolizumab in Adult Patients with Metastatic or Advanced Solid Tumors (MAST)"

The application

Oncolytic viral therapy is a relatively new strategy that uses viruses as a treatment for cancer. Oncolytic viruses (OVs) can occur naturally or consist of a genetically modified virus that can preferentially infect, replicate, and destroy cancer cells. OVs can also stimulate the immune system, which is often suppressed within tumours, to aid in the clearance of the tumours.

Medpace Australia Pty Ltd is seeking approval for a clinical trial with a GM Orthopoxvirus, known as CF33-hNIS. The GMO was modified from the oncolytic virus CF33, which is a chimeric Orthopoxvirus strain which has been shown to target cancer cells. The genetic modifications lead to higher levels of viral replication in cancer cells compared to normal cells. Additionally, the genetic modifications facilitate the visualisation of the GMO after administration to patients by medical imaging.

The clinical trial will evaluate the safety and efficacy of the GMO in adults with solid cancers that are locally advanced or have spread throughout the body. Up to 18 participants in Australia would receive multiple doses of the GMO treatment over a period of 2 years.

The application is for limited and controlled release under section 50A of the Act, as the Regulator is satisfied that its principal purpose is to enable the applicant to conduct the trial, and the proposed limits and controls are such that consultation with prescribed experts, agencies and jurisdictions is not required at this stage. The proposed clinical trial must meet Therapeutic Goods Administration (TGA) requirements and would need approval from a registered Human Research Ethics Committee prior to commencement.

Next steps

The Gene Technology legislation sets out what the Regulator must do, as well as what the Regulator can or must consider, before deciding whether or not to issue a licence for this application.

The Regulator's staff will prepare a consultation version of the Risk Assessment and Risk Management Plan (RARMP) considering aspects of the application including the proposed limits and controls in accordance with the legislation.

The Regulator will seek comments on the consultation RARMP from the public, as well as a wide range of experts, agencies and authorities. The public and experts will be invited to provide submissions on the risks to human health and safety, and on risks to the environment from the proposed clinical trial.

At this stage, the consultation RARMP is expected to be released for comments in **July 2022**.

After consultation, the Regulator's staff will finalise the RARMP, taking into account advice on relevant matters. The finalised RARMP will form the basis of the Regulator's decision whether or not to issue a licence. The consultation and final versions of the RARMP and associated documents will be available on the OGTR website when they are released.

Other information available from the OGTR website:

- information on Australia's national scheme for regulation of gene technology and
- information on the DIR application process.

Please use the contact details below, if you

- would like a copy of the application. Please include the identifier DIR 192.
- have any questions about the application or the legislated evaluation process or
- wish to register on the mailing list.

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