Australian Government
Department of Health
Office of the Gene Technology Regulator

June 2020

Summary of the Risk Assessment and Risk Management Plan

for

Licence Application No. DIR 171

Decision

The Gene Technology Regulator (the Regulator) has received a licence application to conduct a clinical trial using a genetically modified organism (GMO). It qualifies as a DIR licence application under the *Gene Technology Act 2000* (the Act). The applicant, Clinical Network Services (CNS) Pty Ltd proposes to conduct a clinical trial to assess the efficacy and safety of GM influenza vaccines for protection of people from Influenza A virus infection.

Influenza (flu) viruses are highly infectious pathogens which are endemic in Australia. Influenza is predominately transmitted through aerosol droplets generated when an infected person coughs or sneezes, and influenza infections peak during the winter months. Symptoms usually present as a sudden onset of mild respiratory illness. In healthy individuals, infection normally resolves in under two weeks but the elderly, young children, pregnant women and the immunocompromised can suffer more severe symptoms.

The proposed GM vaccine is predicted to provide increased protection against influenza A virus infection. The GM vaccine would be manufactured overseas and imported into Australia. It would be administered by intranasal spray to a limited number of healthy children at clinical facilities located in Perth, Adelaide, Melbourne, Sydney or Brisbane.

Clinical trials in Australia are conducted in accordance with requirements of the *Therapeutic Goods Act 1989*, which is administered by the Therapeutic Goods Administration (TGA). Therefore, in addition to approval by the Regulator, CNS would require authorization from TGA before the trial commences. Clinical trials conducted in Australia must also be conducted in accordance with the *National Statement on Ethical Conduct in Human Research* and with the *Guidelines for Good Clinical Practice* of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

CNS would also require approval from the Department of Agriculture, Water and the Environment for import of the GM vaccine.

The Regulator has prepared a Risk Assessment and Risk Management Plan (RARMP) for this application, which concludes that the proposed clinical trial poses negligible risks to human health and safety and the environment, and that any risks posed by the dealings can be managed by imposing conditions on the trial.

The application

Project Title	Clinical trial of genetically modified Influenza vaccine (H3N2 M2SR)[1]
Parent organism	*Influenza A virus*
Principal purpose	To assess the safety and efficacy of GM influenza vaccine in a clinical trial
Genetic modifications	**Modified *Influenza A virus* gene conferring replication incompetence:** • *Insertion of two stop codons in M2 gene* – prevents virus assembly • *Deletion in M2 gene* – prevents virus assembly **Substituted *Influenza A virus* genome segments encoding antigens:** • *Hemagglutinin subtype 3* – Influenza virus surface protein • *Neuraminidase subtype 2* – Influenza virus surface protein
Previous clinical trials	One completed phase 1 clinical trial in the United States Two ongoing phase 1 clinical trials in the United States One ongoing phase 2 clinical trial in Belgium
Proposed limits and controls	
Proposed duration	3 years
Proposed trial size	Up to 240 clinical trial participants
Proposed locations	Up to four clinical facilities, which would be located in Adelaide, Brisbane, Melbourne, Perth or Sydney

Risk assessment

The risk assessment concludes that risks to the health and safety of people and the environment from the proposed clinical trial are negligible. No specific risk treatment measures are required to manage these negligible risks.

The risk assessment process considers how the genetic modifications and proposed activities conducted with the GMO might lead to harm to people or the environment. Risks are characterised in relation to both the seriousness and likelihood of harm, taking into account information in the application (including proposed controls), relevant previous approvals and current scientific/technical knowledge. Both the short and long term impact are considered.

Credible pathways to potential harm that were considered included exposure of people or animals to the GMOs and whether there is the potential for reassortment with other viruses. Potential harms that were considered in relation to these pathways included ill health and increased disease in people or animals.

Important factors in reaching the conclusions of the risk assessment included: that the GM vaccine is replication incompetent; the inability of GMO progeny to be shed by the inoculated trial participants, and unintended exposure to the GMOs would be minimised by the limits and controls.

[1] The title of the project as supplied by the applicant is 'Clinical trials with a prophylactic influenza A/H3N2 live, M2-deleted, intranasal vaccine (H3N2 M2SR)'.

As risks to the health and safety of people, or the environment, from the proposed trial of the GM viruses have been assessed as negligible, the Regulator considers that the dealings involved do not pose a significant risk to either people or the environment.

Risk management plan

The risk management plan describes measures to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan is given effect through licence conditions.

As the level of risk is considered negligible, specific risk treatment is not required. However, since this is a clinical trial, the licence includes limits on the size, location and duration of the trial, as well as a range of controls to minimise the potential for the GMO to spread in the environment. In addition, there are several general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements which include an obligation to report any unintended effects.