



Summary of the Risk Assessment and Risk Management Plan for Licence Application DIR 184

Decision

The Gene Technology Regulator (the Regulator) has received a licence application to conduct a clinical trial using a genetically modified (GM) COVID-19 vaccine. It qualifies as Dealings involving the Intentional Release (DIR) of genetically modified organisms into the Australian environment under the *Gene Technology Act 2000*.

The applicant, Avance Clinical Pty Ltd (Avance) proposes to conduct a clinical trial to evaluate the safety and tolerability of genetically modified human adenovirus serotype 6 (HAdV-C6) as a GM vaccine to treat COVID-19 in adults. This clinical trial involves the intranasal administration of the GM vaccine, which is different to the intramuscular (IM) administration of current COVID-19 vaccines.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus discovered in December 2019 in Wuhan, China and is the cause of the COVID-19 disease. The World Health Organization (WHO) declared the outbreak a pandemic on 11th March 2020 and as of 14th June 2021, there have been over 3.8 million deaths reported worldwide.

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, Avance will require authorisation 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.

Avance will also require approval from the Department of Agriculture, Water and the Environment for import of the GMO.

The Regulator has prepared a Risk Assessment and Risk Management Plan (RARMP) for this application, which concludes that the proposed supply of the GM vaccine 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 clinical trial.

The application

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| Application number | DIR-184 |
| Applicant | Avance Clinical Pty Ltd |
| Project title | Clinical trial with a genetically modified human adenovirus COVID-19 vaccine ¹ |

¹ The title of the licence application submitted by Avance Clinical Pty Ltd is “Clinical development of an Adenovirus Vector SARS-CoV-2 vaccine (SC-Ad6-1-002) given by intranasal administration to prevent COVID-19”.

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| Parent organism | Human adenovirus 6 (HAdV-C6) |
| Introduced gene and modified trait | <ul style="list-style-type: none"> • Deletion of: <ul style="list-style-type: none"> ○ <i>Illa</i> gene (stops virus multiplying) ○ Large portions of E3 gene (increases immune response to virus) ○ E4 UXP ORF (reduce virus growth) • Insertion of a gene encoding the SARS-CoV-2 spike protein (expresses spike protein) |
| Principle purpose | The proposed trial is a phase I study designed to evaluate the safety, tolerability, immunogenicity and efficacy of SC-Ad6-1 as a second generation, prophylactic vaccine to prevent COVID-19. |
| Previous clinical trials | This is a first in human clinical trial using an intranasal route. |
| Proposed locations | Clinical trials will be conducted at clinical trial sites and hospitals within Australia. |
| Proposed limits and controls | <ul style="list-style-type: none"> • Import, transport and storage of the genetically modified organism (GMO) will be carried out according to Regulator's <i>Guidelines for the Transport, Storage and Disposal of GMOs</i> appropriate for PC1 GMOs • The GMO will be administered to trial participants in a suitable medical facility setting. • Staff handling the GMO will be trained and use personal protective equipment. • Waste that may contain the GMO will be disposed of via the clinical waste stream. • Participants will be held at clinical trial site for at least 4 hours after administration and sent home with detailed instructions post-treatment. • The clinical trial would enrol a limited numbers of trial participants (up to 1000 healthy volunteers in Australia at multiple sites). |

Risk assessment

The risk assessment concludes that risks to the health and safety of people or 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 include: the potential exposure of people and animals to the GMO; the potential for the GMO to recombine with other similar viruses or to get genes from those viruses; and the potential for the GMO to integrate into the host genome. The potential for the GMO to be released into the environment and its effects were also considered.

Important factors in reaching the conclusions of the risk assessment included:

- The GMO is unable to form infectious viral particles, which will prevent it from multiplying in other cells and is very unlikely to be shed from the vaccine recipient;

- The likelihood of accidental exposure to the GMO in people not being vaccinated (non-vaccinees) would be minimised due to appropriate limits and controls, well-established import, transport, storage and disposal procedures; and
- The likelihood of complementation and recombination of GMO with other adenoviruses is very low.

As risks to the health and safety of people, or the environment, from the proposed trial of the GM vaccine 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

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 number of trial participants, locations limited to hospitals and clinical trial sites, limits on the 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.