Australian Government
Department of Health
Office of the Gene Technology Regulator

18 December 2020

Summary of the Risk Assessment and Risk Management Plan

(Consultation Version) for

Licence Application DIR 180

Introduction

The Gene Technology Regulator (the Regulator) has received a licence application (DIR 180) for import, transport, storage and disposal of a genetically modified (GM) COVID-19 vaccine, as part of its commercial supply as a human vaccine. These activities are classified as Dealings involving the Intentional Release (DIR) of genetically modified organisms into the Australian environment under *the Gene Technology Act 2000*.

Before the GM vaccine can be used, AstraZeneca must also obtain regulatory approval from the Therapeutic Goods Administration (TGA). Therapeutic goods for sale in Australia must be included in the Australian Register of Therapeutic Goods (ARTG) under the *Therapeutic Goods Act 1989*. The TGA would assess patient safety and the quality and efficacy of the vaccine prior to including the GM vaccine on the ARTG. In addition, approval from the Department of Agriculture, Water and the Environment will also be required 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 supply of the GM vaccine poses negligible risks to human health and safety and the environment. Licence conditions have been drafted for the proposed supply. The Regulator invites submissions on the RARMP, including draft licence conditions, to inform the decision on whether or not to issue a licence.

The application

Application number	DIR-180
Applicant	AstraZeneca Pty Ltd
Project title	Commercial supply of a genetically modified COVID-19 vaccine[1]
Parent organism	Chimpanzee adenovirus Y25

Introduced gene and modified trait	• Deletion of:
	  ○ E1 gene (renders virus unable to multiply)
	  ○ E3 gene (increases immune response to virus and virus production during manufacture)
	• Partial substitution of E4 gene with the corresponding gene from the human adenovirus 5 (improves virus yield during manufacture)
	• Insertion of a gene encoding codon-optimised full length SARS-CoV-2 spike protein (expresses spike protein)

Previous clinical trials	Phase 1/2 clinical trial with the GM vaccine ChAdOx1-S [recombinant] (also known as AZD1222, ChAdOx1 nCoV-19) was conducted and completed in the United Kingdom (UK) to test the safety of the vaccine in adults aged 18-55 years.

[1] The title of the licence application submitted by AstraZeneca is "Commercial release of a COVID-19 vaccine AstraZeneca to Prevent Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)".

Current approvals	• Clinical trials with the GM vaccine ChAdOx1-S [recombinant] (also known as AZD1222, ChAdOx1 nCoV-19) are approved and are currently ongoing in several overseas jurisdictions including the UK, the United States (US), Brazil, South Africa, Argentina, Chile, Colombia, Japan, Peru and the Russian Federation. • The GM vaccine may be manufactured in Australia under Dealings Not involving Intentional Release (DNIR) of a GMO into the environment (DNIR-630 and DNIR-632) or imported under a Notifiable Low Risk Dealing. • The GM vaccine is currently not approved for commercial supply in any region or country.
Proposed locations	Australia-wide
Primary purpose	Commercial supply of the GM COVID-19 vaccine

Risk assessment

The risk assessment concludes that risks to the health and safety of people or the environment from the proposed supply, either in the short or long term, are negligible. No specific risk treatment measures are required to manage these negligible risks.

The current assessment focuses on risks posed to people other than the intended vaccine recipient and to the environment, including long term persistence of the GMOs, which may arise from the import, transport, storage or disposal of the GMO. The risk assessment process considers how the genetic modification and activities conducted with the GM vaccine in the context of import, transport, storage and disposal 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, relevant previous approvals, current scientific knowledge and advice received from a wide range of experts, agencies and authorities consulted on the preparation of the RARMP. Both the short and long term risks were considered.

Credible pathways to potential harm that were considered included: whether people and animals can be exposed to the GMO and whether there is a potential for the GMO to recombine with other similar viruses or to get genes from those viruses. The potential for GMO to be released into the environment and its effects was also considered.

The principal reasons for the conclusion of negligible risks associated with import, transport, storage and disposal of the GMO are:

- The GMO is replication incompetent which will prevent it from multiplying in other cells;
- The GMO would be restricted to the site of injection and/or draining lymph nodes and would not be shed from the vaccine recipients;
- The GMO does not cause disease in humans and other organisms other than great apes;
- The likelihood of accidental exposure to the GMO in people not being vaccinated (non-vaccinees) would be minimised due to well-established import, transport, storage and disposal procedures; and
- The likelihood of complementation and recombination of GMO with other adenoviruses is very low.

Risk management

The risk management plan concludes that risks from the proposed dealings can be managed so that people and the environment are protected by imposing general conditions to ensure that there is ongoing oversight of the vaccine containing the GMO.

Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan evaluates and treats identified risks and considers general risk management measures. The risk management plan is given effect through licence conditions.

As the level of risk was assessed as negligible, specific risk treatment is not required. However, the Regulator has drafted licence conditions regarding post-release review (post-market surveillance) to ensure that there is ongoing oversight of the supply of the GM COVID-19 vaccine and to allow the collection of ongoing information to verify the findings of the RARMP. The draft licence, detailed in Chapter 4 of the consultation RARMP, also contains a number of general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements, which include an obligation to report any unintended effects.