Australian Government
Department of Health, Disability and Ageing
Office of the Gene Technology Regulator

April 2026

Risk Assessment and Risk Management Plan (Consultation version) for

DIR 220

Commercial supply of multivalent cat vaccines containing a genetically modified component for the prevention of feline leukemia virus infection

Applicant: Intervet Australia Pty Ltd

This RARMP is open for consultation until 2 June 2026.

Written comments on the risks to human health and safety and the environment posed by this proposed supply of the vaccine containing a GMO are invited. You may make your submission.

Via the consultation hub:	https://consultations.health.gov.au/ogtr/dir-220-consultation
via mail to:	The Office of the Gene Technology Regulator, MDP 54 GPO Box 9848, Canberra ACT 2601
or via email to:	ogtr@health.gov.au.

Please note that issues regarding food safety and labelling, the use of agricultural chemicals, benefits, and marketing and trade implications **do not** fall within the scope of these evaluations as they are the responsibilities of other agencies and authorities.

Summary of the Risk Assessment and Risk Management Plan (Consultation version) for Licence Application DIR 220

Introduction

The Gene Technology Regulator (the Regulator) has received a licence application (DIR 220) for the import, transport, storage and disposal of a multivalent vaccine containing a genetically modified (GM) Venezuelan Equine Encephalitis Virus (VEEV) that produces the glycoprotein from Feline leukemia virus (FeLV), as part of its commercial supply to vaccinate cats. These activities are classified as Dealings involving the Intentional Release (DIR) of genetically modified organisms (GMOs) into the Australian environment under the *Gene Technology Act 2000*.

Before vaccines containing the GMO can be used, Intervet Australia Pty Ltd must also obtain regulatory approval from the Australian Pesticide and Veterinary Medicines Authority (APVMA). The APVMA administers the *Agricultural and Veterinary Chemicals Code Act 1994* (the Agvet Code) to regulate agricultural and veterinary chemical products, including veterinary vaccines. For commercial products, the standard form of approval is through registration. The APVMA can impose conditions on the use of veterinary products via registrations and permits.

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 negligible risks to 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

Project title	Commercial supply of multivalent cat vaccines containing a genetically modified component for the prevention of feline leukemia virus infection[1]
Parent organism	Venezuelan Equine Encephalitis Virus (VEEV) vaccine strain TC-83
Genetic modifications	**Deleted genes**: - Viral structural genes - to render the GMO unable to produce new viral particles **Introduced gene**: - Feline leukemia virus glycoprotein gene – trigger an immune response against the feline leukemia virus and protect animals against later infection
Previous releases	The GMO in the vaccine has not been previously approved for release in Australia
Current approvals	The GMO and the vaccine are currently approved for use by the United States Department of Agriculture and are under review by the European Medicines Agency.

[1] The title for the licence application submitted by Intervet Australia Pty Ltd is “Commercial DIR application for Nobivac NXT HCPChFeLV Live Vaccine for cats, plus fall out vaccine product Nobivac NXT HCPFeLV Live Vaccine for cats”.

Proposed locations	Australia-wide
Primary purpose	Commercial supply of the multivalent vaccines to protect against infectious diseases in cats.

Risk assessment

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 the potential exposure of people to the GMO; the potential exposure of animals to the GMO; and the potential for the GMO to recombine with other similar viruses. The potential for the GMO to be released into the environment and its effects were also considered.

The risk assessment concludes that risks to the health and safety of people are negligible and the risks to the environment from the proposed supply of this vaccine are negligible. Specific measures are included in the licence to maintain the risk context.

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

- The GMO is unable to produce new viral particles and is unlikely to cause disease in cats, horses or other susceptible mammalian species;
- The likelihood of accidental exposure to the GMO by people and the environment would be minimised due to well-established transport, storage and disposal procedures that are regulated by each State and Territory; and local councils;
- The GMO would be imported under a DAFF import permit, that requires specific import conditions to manage biosecurity risks;
- The GMO would need to be registered with the APVMA, who would impose conditions on the use, transport, storage and disposal of the vaccine; and
- Recombination of the GMO with other alphaviruses is highly unlikely due to superinfection exclusion mechanisms.

Risk management

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. Draft licence conditions are detailed in Chapter 4 of the RARMP.

The risk management plan concludes the negligible risks can be managed to protect the health and safety of people and the environment. The product is not currently registered by the APVMA and registration with the APVMA is required prior to commercial use. The draft licence requires the Regulator to be notified of the APVMA registration of the product and any amendments to the registration (see Chapter 4).

General conditions were also included in the draft licence to ensure that there is ongoing oversight of the GM vaccine. Conditions were included requiring the applicant to report any new information obtained after release of the GMO to allow the collection of information to verify the findings of the RARMP. Post-market surveillance of veterinary vaccines is carried out in an ongoing capacity by State and Territories. The draft licence also contains a number of general conditions relating to ongoing licence holder suitability, auditing

and monitoring, and other reporting requirements, which include an obligation to report any unintended effects.

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Abbreviations

ACT	Australian Capital Territory
AgVet Code	*Agricultural and Veterinary Chemicals Code Act 1994*
AHA	Animal Health Australia
APVMA	Australian Pesticides and Veterinary Medicines Authority
DAFF	Department of Agriculture, Fisheries and Forestry
DIR	Dealings involving Intentional Release
DNA	Deoxyribonucleic acid
EPA	Environment Protection Authority
FeLV	Feline Leukemia Virus
GLP	Good Laboratory Practice
GM	Genetically modified
GMP	Good Manufacturing Practice
GMO	Genetically modified organism
GTTAC	Gene Technology Technical Advisory Committee
HGT	Horizontal gene transfer
IR	Internal repeat
kb	Kilobase pair of DNA
LGA	Local government area
ml	Milli litre
NSW	New South Wales
NT	Northern Territory
OGTR	Office of the Gene Technology Regulator
Orf	Open reading frame
PCR	Polymerase chain reaction
QLD	Queensland
RARMP	Risk Assessment and Risk Management Plan
RNA	Ribonucleic acid
SA	South Australia
sa-mRNA	Self-amplifying mRNA
TAS	Tasmania
the Act	The *Gene Technology Act 2000*
the Regulations	The Gene Technology Regulations 2001
the Regulator	The Gene Technology Regulator
USA	United States of America
VEEV	Venezuelan Equine Encephalitis Virus
VIC	Victoria
WA	Western Australia

Chapter 1 Risk assessment context

Section 1 Background

1. An application has been made under the *Gene Technology Act 2000* (the Act) for Dealings involving the Intentional Release (DIR) of genetically modified organisms (GMOs) into the Australian environment.

2. The Act and the Gene Technology Regulations 2001 (the Regulations), together with corresponding State and Territory legislation, comprise Australia's national regulatory system for gene technology. Its objective is to protect the health and safety of people, and to protect the environment, by identifying risks posed by or as a result of gene technology, and by managing those risks through regulating certain dealings with GMOs.

3. Section 50 of the Act requires that the Gene Technology Regulator (the Regulator) must prepare a Risk Assessment and Risk Management Plan (RARMP) in response to an application for release of GMOs into the Australian environment. Sections 50, 50A and 51 of the Act and sections 9 and 10 of the Regulations outline the matters which the Regulator must take into account and who must be consulted when preparing the RARMP.

4. The *Risk Analysis Framework* (RAF) (OGTR, 2013) explains the Regulator's approach to the preparation of RARMPs in accordance with the Act and the Regulations. The Regulator has also developed operational policies and guidelines that are relevant to DIR licences. These documents are available from the Office of the Gene Technology Regulator (OGTR website).

5. Figure 1 shows the information that is considered, within the regulatory framework above, in establishing the risk assessment context. This information is specific for each application. Risks to the health and safety of people or the environment posed by the proposed supply are assessed within this context. Chapter 1 describes the risk assessment context for this application.

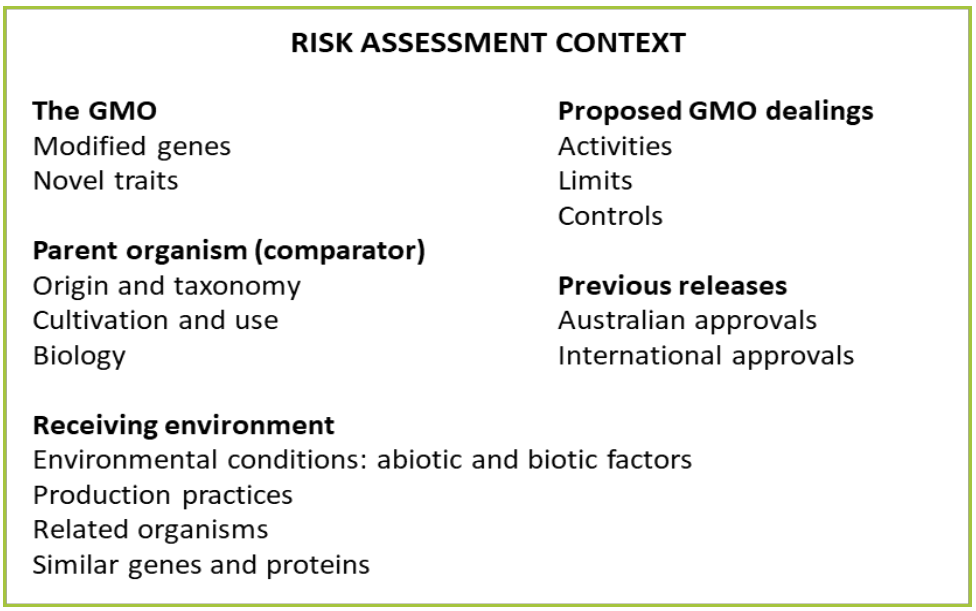

Figure 1. Summary of parameters used to establish the risk assessment context, within the legislative requirements, operational policies and guidelines of the OGTR and the RAF.

6. Since this application is for commercial purposes, it does not meet the criteria for a limited and controlled release application under section 50A of the Act. Therefore, under section 50(3) of the Act, the Regulator was required to seek advice from prescribed experts, agencies and authorities on matters relevant to the preparation of the RARMP. This first round of consultation included the Gene Technology Technical Advisory Committee (GTTAC), State and Territory Governments, Australian Government

authorities and agencies prescribed in the Regulations and the Minister for the Environment. A summary of issues contained in submissions received is provided in Appendix A.

7. Section 52 of the Act requires the Regulator to seek comment on the RARMP from the experts, agencies and authorities outlined above, as well as the public, through a second round of consultation.

1.1 Interface with other regulatory schemes

8. Gene technology legislation operates in conjunction with other regulatory schemes in Australia. The GMOs and any proposed dealings conducted under a licence issued by the Regulator may also be subject to regulation by other Australian government agencies that regulate GMOs or GM products, including the Australian Pesticides and Veterinary Medicines Authority (APVMA) and the Department of Agriculture, Fisheries and Forestry (DAFF). These dealings may also be subject to the operation of State legislation declaring areas to be GM, GM free, or both, for marketing purposes.

9. The APVMA provides a national registration and permit scheme for agricultural and veterinary chemical products. It administers the provisions of the *Agricultural and Veterinary Chemicals Code Act 1994* (AgVet Code). For registration, the APVMA assesses whether a new veterinary vaccine meets the criteria set out in the AgVet Code before it is registered in the Register of Agricultural and Veterinary Chemical Products. A new veterinary vaccine that is not registered may be legally used for animal trials by obtaining a permit from the APVMA.

10. As part of the registration process, the APVMA must first approve the new active constituent and then assess the quality, safety and efficacy of the vaccine. Quality aspects could include batch-to-batch consistency in vaccine composition, purity and potency. The product must also be manufactured in premises that comply with Good Manufacturing Practice (GMP), which is also audited by the APVMA. Safety aspects include the toxicological profile of the vaccine and its residues, including metabolites and degradation products. The APVMA approves the label, which includes instructions for the handling and storage, and directions for supply of veterinary vaccines, to ensure safe use. The APVMA would also carry out an environmental risk assessment to minimise environmental risks. The States and Territories are responsible for the enforcement of the conditions associated with an APVMA registration and carry out post-market surveillance.

11. The applicant has proposed importing the vaccines into Australia. DAFF regulates products imported into Australia to protect Australia from biosecurity risks. Under the *Biosecurity Act 2015*, the importation of biological material such as live GM vaccines and treatments requires a permit from DAFF.

12. Venezuelan equine encephalitis virus (VEEV) is listed as a national notifiable equine disease (National list of notifiable animal diseases - DAFF). It is also listed as a prohibited matter under the New South Wales (NSW) *Biosecurity Act 2015,* Queensland *Biosecurity Act 2014*, Tasmanian *Biosecurity Act 2019*, and is a declared notifiable exotic disease in South Australia, pursuant to Section 4 of the *Livestock Act 1977*. VEEV is a reportable animal disease in Western Australia (WA) under the *Biosecurity and Agricultural Management Act 2007* and in Victoria under the *Livestock Disease Control Act 1994*. Northern Territory classifies VEEV as a notifiable emergency disease under the *Livestock Act 2008*.

13. To avoid duplication of regulatory oversight, risks that have been considered by other regulatory agencies would not be re-assessed by the Regulator.

14. For the commercial supply of a GM veterinary vaccine, dealings regulated under the Act include the import, transport, storage and disposal of GMOs. The Regulator assesses risks to people as a consequence of conducting these activities and risks from persistence of the GMO in the environment.

Section 2 The proposed dealings

15. Feline leukemia virus (FeLV) is a retrovirus that infects domestic and wild cats. The virus is primarily spread through close contact between cats but can also occur through indirect contact or

through vertical transmission (Powers et al., 2018). Infection can have a variety of presentations, with progressive and regressive infection having the poorest clinical outcomes (Hartmann, 2012; Powers et al., 2018). There are currently 3 FeLV vaccines that are registered for use in Australia (APVMA PubCRIS database). These vaccines consist of inactivated FeLV or recombinant FeLV antigen based on the glycoprotein to induce immune responses.

16. Intervet Australia Pty Ltd (Intervet) is seeking authorisation for the commercial supply of vaccines containing attenuated core vaccine viruses or bacteria and genetically modified (GM) VEEV to prevent common infections in cats Australia-wide.

17. As part of the ongoing commercial supply of the vaccines containing a GMO, the dealings assessed by the Regulator are to:

(a) import the GMO;

(b) transport the GMO;

(c) dispose of the GMO;

and possession (including storage), supply or use of the GMO for the purposes of, or in the course of, any of the above.

2.1 Details of the proposed dealings

18. The vaccines, including the GMO, would be manufactured overseas in GMP licensed sites and imported into Australia under an import permit from DAFF. The products would need to be registered through the APVMA before commercial use. As mentioned in Section 1.1, the APVMA would also approve the labels for the vaccines, which would contain instructions for the handling and storage, and directions for supply to ensure safe use.

19. The vaccines would be transported to Schedule 4 licensed warehouses (prescription only medicines and prescription animal remedies, Therapeutic Goods (Poisons Standard—February 2026) Instrument 2026 - Federal Register of Legislation). The vaccines are supplied as freeze-dried material, in rubber stoppered vials with aluminium caps. Vials are contained within a product carton containing two vials; one containing the GMO formulation and one containing enough solvent to make up one dose. Cartons will be labelled with approved APVMA labels indicating the contents of the vials and an accompanying leaflet with instructions for use, storage and disposal. The label does not indicate that the vaccines contain a GMO but as part of the constituent statements, the labels indicate the combination for each dose of live attenuated strains (Feline herpesvirus type 1 strain G2620A, Feline calicivirus strain F9, Feline panleukopenia virus strain MW-1, *Chlamydophila felis* strain Baker) and the GMO labelled as FeLV RNA-particle (RP-FeLV).

20. The vaccines would be administered to cats according to the recommended vaccination schedules for cats, from 8 weeks of age. At this age, most young cats are still with a breeder and are kept isolated to limit exposure to diseases (Squires et al., 2024). Generally, owners are advised to keep cats indoors or allowed enclosed outdoor access only in order to limit exposure of vaccinated animals to pathogens in the environment before onset of immunity.

21. The vaccine would be used per an approved APVMA registration.

22. The vaccine will be administered by trained veterinarians, via subcutaneous injection into the scruff of the neck. The applicant proposes to register this method of administration with the APVMA.

23. All residual vaccine and waste which has come in to contact with the vaccine (such as syringes and vials) would be discarded in veterinary clinics in accordance with relevant State/Territory, local council and Environmental Protection Agency (EPA) requirements, and conditions imposed by the APVMA registration of the vaccine. These requirements all aim to limit the exposure of other people or animals to the waste.

Section 3 Parent organism

24. The vaccines contain combinations of live attenuated Feline herpesvirus type 1 strain G2620A, Feline calicivirus strain F9, Feline panleukopenia virus strain MW-1, *Chlamydophila felis* strain Baker, and GM VEEV (the GMO). The combinations include either all 4 attenuated strains and the GMO, or 3 attenuated strains (no *C. felis*) and the GMO. This assessment focuses on the GMO. The GMO is derived from an attenuated strain called VEEV TC-83 that has been used as a vaccine since 1961 (Alevizatos et al., 1967; Pittman and Plotkin, 2017). The characteristics of the parent organism provide a baseline for comparing the potential harm from dealings with vaccines containing the GMO. As such, the relevant properties of VEEV and VEEV TC-83 will be discussed here.

25. VEEV is a member of the *Togaviridae* family, *Alphavirus* genus (Luethy, 2023). VEEV comprises 7 species with 14 antigenic varieties that vary in virulence and in enzootic or epizootic[2] potential. Enzootic subtypes (ID, IE, IF and II-VI) are primarily maintained in reservoir hosts and are largely considered non-pathogenic (Sharma and Knollmann-Ritschel, 2019; Han et al., 2023). Epizootic subtypes (IA/B and IC) are associated with outbreaks in horses and humans, and have historically affected 75,000-200,000 people, largely in South America (Sharma and Knollmann-Ritschel, 2019; Han et al., 2023).

3.1 Pathology

26. VEEV infection causes symptomatic disease in equids and humans. The virus causes severe disease in equids including horses, mules, donkeys and zebras, ranging from general illness to progressive central nervous system disorders to sudden death (Sharma and Knollmann-Ritschel, 2019; Guzmán-Terán et al., 2020; Luethy, 2023). The virus can also infect humans, causing disease that ranges from mild flu-like symptoms to severe neurological illness that can be fatal (Sharma and Knollmann-Ritschel, 2019; Guzmán-Terán et al., 2020; Luethy, 2023). Initial symptoms in equids and humans include fever, chills, nausea and vomiting (Sharma and Knollmann-Ritschel, 2019; Guzmán-Terán et al., 2020). Clinical signs generally appear between 1-5 days following exposure in horses, or 1-2 weeks in humans after symptom onset in horses (Han et al., 2023).

27. In horses, the course of disease is variable depending on viremia, occurring either as a subclinical infection with low grade fever, or as a clinical infection with general febrile illness with or without encephalitis (Luethy, 2023). The encephalitis presentation presents between 7-14 days after infection and is often lethal 2-3 days after neurologic symptom onset (Luethy, 2023). The mortality rate in horses is estimated to range between 20-80% (Guzmán-Terán et al., 2020). Treatment of infected horses is primarily supportive care and medication to manage symptoms such as seizures and inflammation (Luethy, 2023).

28. In humans, VEEV most commonly causes flu-like symptoms, with neurological complications occurring in 4 to 14% of cases (Sharma and Knollmann-Ritschel, 2019). Neurological complications occur following viral invasion of the central nervous system, causing encephalitis with clinical symptoms including convulsions, seizures, behavioural changes, altered consciousness, coma or death (Sharma and Knollmann-Ritschel, 2019). Both clinical presentations typically resolve 4-7 days after disease onset. Cases progressing to encephalitis also result in brain lesions, with damage observed in the cerebral cortex, hippocampus and cerebellum that can have long-lasting neurological effects (Sharma and Knollmann-Ritschel, 2019; Han et al., 2023). The mortality rate of infections progressing to encephalitis is approximately 1% in adults and up to 20% in children (Sharma and Knollmann-Ritschel, 2019; Han et al., 2023).

[2] Enzootic refers to a disease that is persistently present in a particular animal population or geographic area, while epizootic refers to a disease outbreak with increased infections, affecting different animal populations, or spreading over larger geographic areas.

29. Inflammatory responses are a major contributor to VEEV pathology, correlated with viral titre and replication. Symptom severity can be reduced with anti-inflammatory medications (Sharma and Knollmann-Ritschel, 2019).

3.2 Structure and genomic organisation

30. VEEV has a single-stranded RNA genome approximately 11,500 base pairs (bp) in length (Figure 2). The genome contains two open reading frames (ORFs), the first encoding 4 non-structural proteins (nsP1 -4) and the second encoding 5 structural proteins (the capsid, a hydrophobic 6K protein, and three glycoproteins E1-E3) (Ma et al., 2021; Han et al., 2023) The non-structural proteins are required for viral replication, while the structural proteins are required for viral assembly. The E1 and E2 proteins make up 80 trimer spikes that are stabilised by E3 and form an outer glycoprotein shell, while the capsid protein forms a nucleocapsid shell made up of 240 copies (Figure 2) (Ma et al., 2021; Han et al., 2023).

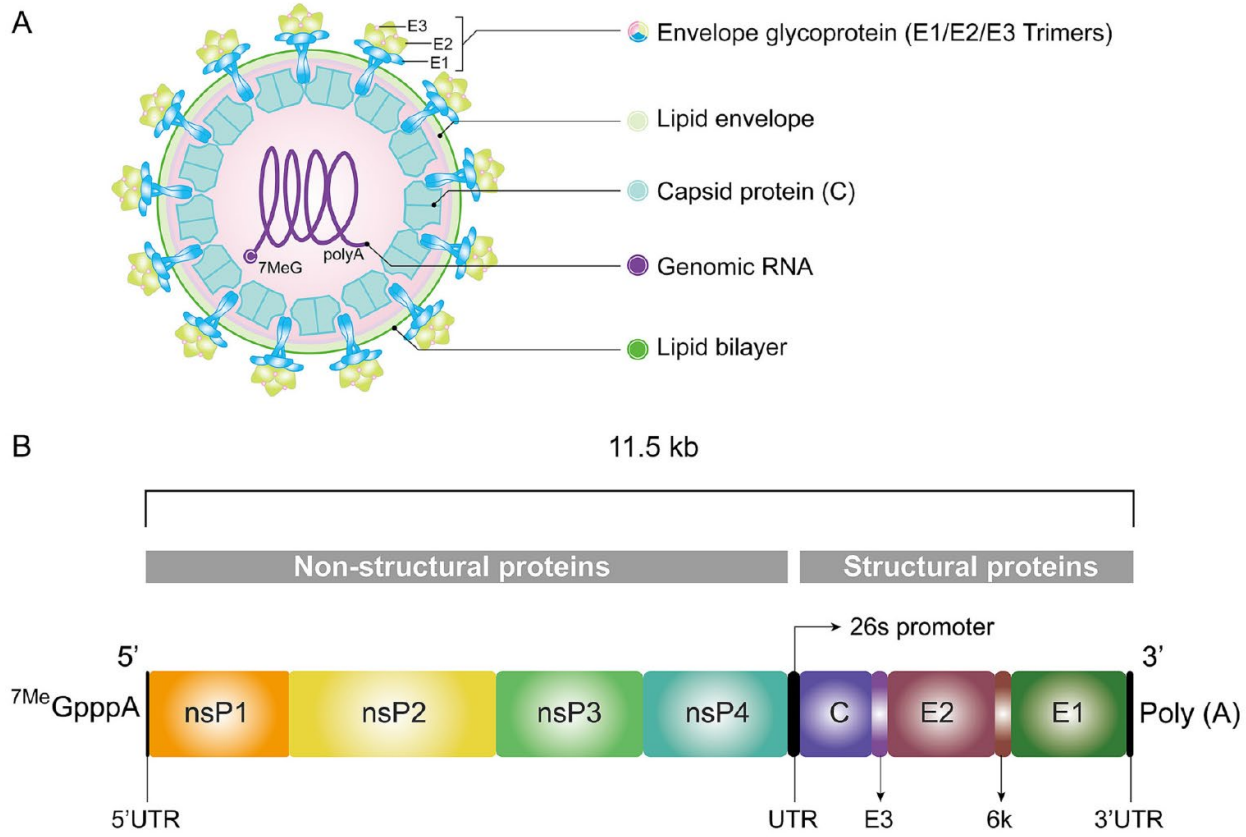

Figure 2. Structure and genome of VEEV. A. Virion structure, including surface glycoprotein trimers (E1, E2 and E3) and capsid proteins encasing genomic RNA. B. Organisation of the VEEV genome with 2 ORFs encoding non-structural proteins (nsP1, nsP2, nsP3 and nsP4) and structural proteins (E1, E2, E3, capsid and 6K protein) under control of a 26s promoter (Han et al., 2023).

3.3 Viral infection and replication

31. VEEV enters host cells by binding to low-density lipoprotein receptor class A domain-containing 3 (LDLRAD3) in mammalian cells (Ma et al., 2021). Alphaviruses can bind to a variety of LDLRs across a wide range of mammals and mosquitoes, as the main binding site is highly conserved, likely contributing to spillover events and infecting new hosts (Wang et al., 2024). Once inside the cell, the viral genome is released and translated by host cell machinery to produce non-structural and structural viral proteins, which remain localised in the cytoplasm and cannot enter the nucleus (Sharma and Knollmann-Ritschel, 2019; Han et al., 2023). Host cell translation of the viral genome produces the polyprotein p1234 which is then cleaved into nsP1, nsP2, nsP3 and nsP4. Once translated, the 4 nsPs form a viral replication complex to replicate the RNA genome, that is then packaged into the structural proteins to form new viral

particles (Han et al., 2023). New viral particles are then released from the host cell by budding or through cell lysis before spreading to new host cells.

32. VEEV entry into neural tissue is thought to occur via the olfactory system, following infection via aerosol transmission or mosquito transmitted infections that invade olfactory cells that can occur during systemic spread. Conflicting evidence in mice suggest that inflammatory responses against VEEV may facilitate blood-borne viral particles crossing the blood brain barrier, although the mechanism remains unclear (Sharma and Knollmann-Ritschel, 2019).

3.4 Potential for recombination

33. Recombination requires a cell to be simultaneously co-infected by 2 viruses, allowing exchange of genetic information. Alphaviruses have limited recombination potential due to a mechanism called superinfection exclusion, where the initial infecting virus impairs secondary infections by related viruses (Hick et al., 2024c). However, one documented occurrence of natural recombination resulted in three novel viruses, Western Equine Encephalitis Virus (WEEV), Highlands J Virus (HJV), and Fort Morgan Virus (FMV). Genomic studies of these chimeric alphaviruses suggests that it was a result of a historic recombination between Eastern Equine Encephalitis Virus (EEEV) and a Sindbis-like virus (Allison et al., 2015). The E1 and E2 glycoproteins of WEEV, HJV and FMV are more highly related to the Sindbis-like glycoprotein than the EEEV glycoprotein and neutralising antibodies are cross-reactive (Allison et al., 2015).

34. Superinfection exclusion in alphaviruses is thought to be mediated at the RNA replication level, where the primary infecting virus inhibits replication of the secondary infecting virus. This mechanism depends on nsP2 or nsP3 (Singer et al., 2021; Hick et al., 2024c). Studies in mammalian cell lines have shown that VEEV inhibits the replication of other alphaviruses as soon as 15 minutes after infection, with secondary viral replication strongly impaired within one hour of primary infection by VEEV (Hick et al., 2024c).

35. Experimental settings have demonstrated that replication competent alphaviruses can be produced via *in vivo* recombination of viral RNA (Petterson et al., 2016). Infectious and pathogenic salmonid alphavirus was recovered from Atlantic salmon injected with two cDNA plasmids. One plasmid contained the full-length viral genome without functional *6k* gene (essential for producing viral particles), and the other helper plasmid encoded only the 100 bases of nsp4 and all the structural genes including 6k, neither of which could produce infectious virus alone. Recovered infectious virus showed evidence of viral RNA recombination that could not be attributed to plasmid recombination (Petterson et al., 2016). It is important to note that in this study, the helper plasmid does not contain nsp2 or nsp3, which is shown to be important in the superinfection exclusion mechanism in alphaviruses. This could explain why the viral RNAs could be present in the same cell for RNA recombination to occur. Overall, this study shows that recombination could occur under specific laboratory conditions that are may not occur in nature.

36. Recombination between plasmids resulting in replication competent virus has been observed in the production of sa-mRNA vaccines (Hyvärinen et al., 2013; Hick et al., 2024b), primarily when single helper plasmids are used in manufacture. Recombination resulting in replication competent virus appears to require high sequence homology between plasmids, and no replication competent recombinants are derived when plasmids share no sequence homology (Hick et al., 2024b). Recombination events resulting in replication competent virus are greatly reduced by using split-helper plasmids to provide the structural proteins (Smerdou and Liljeström, 1999)

3.5 Epidemiology

3.5.1 Host range and transmissibility

37. VEEV is primarily transmitted by mosquitoes and infects many vertebrate species. Transmission via contagious aerosols has also been documented (Guzmán-Terán et al., 2020; Han et al., 2023). VEEV has a broad host range and replicates in vertebrate hosts.

38. VEEV is maintained in reservoir hosts such as rodents, birds and bats and transmitted by mosquitoes and ticks (Han et al., 2023). Mutations within the E2 protein play a significant role in the transmissibility of VEEV by affecting how effectively the virus binds to the midgut of most mosquitoes species, including those present in Australia (Smith et al., 2008; Stephenson et al., 2019; Wang et al., 2024). Smith et al. (2008) showed that mosquito midgut epithelial cells are more efficiently infected by epizootic VEEV strains than enzootic strains, depending on the mutations in E2. Attenuated strains of VEEV contain modifications that reduce midgut binding efficiency of E2 (Pittman and Plotkin, 2017; Han et al., 2023).

39. The infectious dose of VEEV in humans is low, estimated to be 10-100 plaque forming units for aerosol exposure (Burke et al., 2023). Studies in non-human primates have determined the aerosol infectious dose of different VEEV strains to be as low as 6.9 plaque forming units, based on detectable viremia 2 to 5 days after infection (Burke et al., 2023).

40. Horses can act as highly infectious amplifying hosts if infected with epidemic strains of VEEV as disease in horses is strongly correlated with high viremia, increasing the likelihood of mosquitoes becoming infected while feeding to transmit the disease (Quiroz et al., 2009). Humans could theoretically support epidemic human-mosquito-human transmission cycles of epidemic VEEV strains as viremia in humans is sufficient to infect susceptible mosquitoes, however the number of human infections in regions where VEEV is endemic remains low (Quiroz et al., 2009; Bonilla-Aldana et al., 2023).

41. Studies in mice have demonstrated that mosquitoes successfully transmit VEEV at doses as low as 8 plaque forming units and that overall pathogenesis is not dose dependent (Smith et al., 2006). Additionally, needles coated with similar dose ranges to those found in mosquito saliva (8-2,511 plaque forming units) transmitted VEEV to mice comparably to infected mosquitoes, resulting in similar pathogenesis and death rates over the course of infection (Smith et al., 2006).

3.5.2 Bio-distribution

42. In mouse models, VEEV is detected in lymph nodes 6 hours after infection, with full systemic viremia established in 12 hours and persisting for 4 to 5 days (Sharma and Knollmann-Ritschel, 2019). Virus is detected in brain tissue 36 hours after infection via aerosol inhalation, while subcutaneous infection requires viral replication within the olfactory neuroepithelium to invade the central nervous system (Sharma and Knollmann-Ritschel, 2019).

43. Systemic circulation of VEEV is demonstrated in macaques, along with tissue-specific transcriptional markers indicating localisation in the brain, lung and spleen (Koterski et al., 2007).

44. In humans, VEEV is detected in the bloodstream during febrile illness, indicative of systemic infection (Quiroz et al., 2009), while neurological clinical presentations are indicative of central nervous system involvement.

3.5.3 Prevalence

45. VEEV is not known to be present in Australia. The virus is endemic in South America.

3.5.4 Controls and vaccines currently available

46. There are currently no vaccines against VEEV that have been approved for general use in humans. There are several live-attenuated strains used to vaccinate equines and at-risk personnel in endemic

areas, including the live attenuated strain VEEV TC-83 (Sharma and Knollmann-Ritschel, 2019; Han et al., 2023).

3.5.5 Stability and decontamination methods

47. VEEV is primarily maintained in the environment within reservoir hosts. In the unlikely event that VEEV is outside a host, the virion half-life is 7 hours at 37°C and it is highly susceptible to UV, dry heat or drying (WOAH, 2021).

48. VEEV can be decontaminated using temperature or chemical methods. The virus is completely inactivated at temperatures of 65°C or more for at least 5 minutes, treatment with 500 mM of sodium hydroxide (NaOH) for 60 minutes, or treatment with TRIzol at a ratio of 3:1 (volume:volume; TRIzol:virus) for 15 minutes (Ibrahim et al., 2019).

3.5.6 VEEV strain TC-83

49. The parent strain (VEEV TC-83; subtype IAB) is a highly attenuated strain that has been used as a vaccine in horses and at risk personnel for decades (Pittman and Plotkin, 2017). The strain is derived from a field isolate and has been attenuated following consecutive passages in chicken embryo fibroblasts then guinea pig heart cells. The attenuation of the strain is attributed to 2 mutations within the E2 gene that render the strain more sensitive to host interferon responses and restrict cellular tropism (Pittman and Plotkin, 2017; Han et al., 2023). VEEV TC-83 is classified Category C according to Weight-of-evidence-based environmental hazard designations by the Centers for Disease Control (Rao et al., 2004). Category C is determined to pose *limited to negligible threat of dissemination and transmission in the environment and potential for limited adverse events.*

50. Mice injected with VEEV TC-83, either by subcutaneous or intramuscular administration, demonstrate infection in central nervous system tissue, indicative of systemic spread of replication competent VEEV TC-83 (Guerbois et al., 2013; Taylor et al., 2017).

51. Vaccination of people with VEEV TC-83 is largely well tolerated with the most commonly reported reactions including fever, malaise and headache that resolve without intervention within 4 days (Alevizatos et al., 1967; Pittman and Plotkin, 2017).

52. Infection of mosquitoes with 10^6-10^8 plaque forming units of TC-83 resulted in up to 4% of the mosquitoes becoming infected without any dissemination (Rao et al., 2004). This is much higher than the infectious dose described in Section 3.5.1 for wild type VEEV, supporting that TC-83 is less transmissable than WT VEEV. There are no documented cases of either mosquito-to-human or human-to-human transmission. No pathogenicity has been associated with the use of TC-83 as a vaccine other than mild symptoms that are typical of vaccination in general (Pittman and Plotkin, 2017).

53. Replication competent TC-83 has shown evidence of reversion to virulence following five passages in mice (Rao et al., 2004; Kenney et al., 2011).

54. VEEV is one of several alphaviruses used as a platform for self-amplifying mRNA (sa-mRNA) vaccines (Rodríguez-Gascón et al., 2014b). Several sa-mRNA vaccines are based on VEEV TC-83. These sa-mRNA vaccines retain non-structural genes, while the structural genes are replaced with an antigen, allowing for single round infection that produces large amounts of antigen mRNA to elicit an immune response, without producing more viral particles (Rodríguez-Gascón et al., 2014b).

Section 4 The GM vaccine - nature and effect of the genetic modification

4.1 The genetic modifications

55. Some information about the construction and testing of the GMO has been declared Confidential Commercial Information (CCI) under Section 185 of the Act. Under Section 187 of the Act, this information must not be disclosed except where it is made available to the Commonwealth or a

Commonwealth Authority, a State agency or the Gene Technology Technical Advisory Committee in the course of carrying our their duties or functions under the Act or under corresponding State law.

56. FeLV is retroviral pathogen that can cause immunodeficiency, cytopenia and anemia and can also persist in latent or progressive infection (Westman et al., 2016; Westman et al., 2019; Westman et al., 2025). The GMO is a sa-mRNA vaccine, comprising replication defective VEEV TC83 that produces the FeLV glycoprotein as an antigen, to induce an immune reponse against FeLV.

57. The FeLV glycoprotein is a trimeric protein complex made up of two subunit copies (gp70) and a transmembrane protein (p15E). The trimeric protein complex is collectively referred to as gp85. The subunits are involved in host cell receptor binding while the transmembrane protein plays a role in membrane fusion to allow cell entry (Ortiz et al., 2024). Antibodies against the FeLV glycoprotein typically compete with gp70 to prevent binding to host cell receptors, preventing cell entry (Ortiz et al., 2024).

58. The GMO was constructed in a multistep process to replace the gene encoding the structural proteins of TC-83 with codon-optimised glycoprotein gp85 gene from FeLV under control of a subgenomic promoter (Figure 3).

Figure 3. General scheme showing a sa-mRNA derived from an alphavirus in which structural genes have been replaced by a gene of interest (Rodríguez-Gascón et al., 2014a). The gene of interest in the GMO is the glycoprotein gene from FeLV type A.

59. The GMO contains the RNA genome contained in a virus-like particle that is produced during manufacturing. The structural genes that are involved with viral assembly (Section 29) are deleted from the RNA genome, rendering the GMO unable to produce new viral particles. The virus-like particle is made of VEEV TC-83 structural proteins, retaining the attenuating modifications in E2 provided by split helper plasmids to produce the assembled GMO. The helper plasmids are not present in the final GMO to be used in the vaccine.

60. Following subcutaneous administration, the GMO is expected to enter cells via fusion of the VEEV TC-83 glycoprotein to cell surface receptors. Once taken up into cells, the GMO will be released and the 4 nsPs will be translated to assemble the viral replication complex, which remains localised to the cytoplasm and cannot enter the nucleus. The viral replication complex synthesises copies of the whole RNA genome and the sub-genome containing the FeLV glycoprotein. This results in large amounts of FeLV glyoprotein mRNA being generated and translated into protein by host cell machinery. The limited half-life of the mRNA and the viral replication complex results in transient expression between 3 and 15 days (Lundstrom, 2020; Kanechi et al., 2024). Due to the lack of structural proteins in the GMO, no additional viral particles are produced and the GMO is unlikely to be found in bodily fluids as it is cannot leave the cytoplasm of target cells, or transduce new cells once the virus-like particle has release the genome.

4.2 Characterisation of the GMO

4.2.1 Bio-distribution and shedding

61. Due to the instability of naked sa-mRNAs, resulting in ineffective vaccination or treatment, sa-mRNA formulations are contained within particles to facilitate delivery. These particles include lipid nanoparticles, liposomes, polymeric nanoparticles, or virus-like particles (Comes et al., 2023). These delivery particles protect the sa-mRNA and facilitate cell entry prior to their single-cycle replication of the target mRNA sequence (Comes et al., 2023; Casmil et al., 2025). The GMO is contained in a virus-like particle, consisting of the VEEV TC-83 structural proteins, for delivery. The biodistribution of the GMO is expected to be similar to TC-83 (Section 3.4.6).

62. The applicant provided shedding and biodistribution data for the GMO that has been declared CCI. The results show no systemic biodistribution, no evidence of shedding of the GMO and no transmission of the GMO between animals.

63. Field studies of the GMO or a similar GMO contained in a virus-like particle had no reports of accidental exposures or transmission to other animals (Carritt et al., 2025; Stachura et al., 2025).

64. Intramuscular or intravenous administration of a sa-mRNA contained in a TC-83 derived virus-like particle in mice showed limited biodistribution (Kowalski et al., 2007). RNA from the sa-mRNA was detected in blood and lymph nodes of some mice at 2 and 48 hours after intravenous administration, while RNA was only detected at the injection site of all mice 48 hours after intramuscular administration. No RNA was detected in other tissues at 2 or 48 hours after administration via either route, or 22 days after administration (Kowalski et al., 2007).

65. GMOs based on VEEV TC-83, but delivered using lipid nanoparticles, have been used in animal studies using antigens from SARS-CoV-2, rabies or influenza to assess bio-distribution, safety and efficacy. Bio-distribution studies in rats using a VEEV-based sa-mRNA vaccine against SARS-CoV-2 showed that vaccine RNA was detected 2 days after administration in muscle, lymph nodes, spleen, heart, liver, gonad and blood tissues (Maruggi et al., 2022). In blood, vaccine RNA levels were reduced 100-fold between 2 and 8 days post-administration and detected in low levels in 30% of rats 15 days after administration. RNA levels decreased in all tissues by 60 days post-administration. RNA was not detected in gonads beyond day 8 (Maruggi et al., 2022).

66. In mice, bio-distribution of sa-mRNAs is significantly affected by both the administration route and the composition of a delivery nanoparticle (Bathula et al., 2024). Differences in the surface charge of a lipid nanoparticle are thought to contribute to tissue localisation via a variety of administration methods. Bathula et al. (2024) demonstrated that particles contained in positively charged formulations accumulated in lungs, while negatively charged formulations localised to the spleen. This study also assessed transgene expression in tissues following intravenous (IV), subcutaneous (SC), intraperitoneal (IP), intranasal (IN), intramuscular (IM) or intradermal (ID) administration. Particles localised distinctly across the different administration methods, found in muscle tissue (IM), spleen (IP, IV, SC), kidney (IP), lung (IP, IN, IV), and the site of administration (IM, ID). This study also concludes that the transgenes expressed by sa-mRNA can persist in tissues beyond 30 days via all administration routes (Bathula et al., 2024).

67. There has been no reports of shedding in multiple pre-clinical and clinical studies with sa-mRNA vaccines or mRNA vaccines delivered with virus-like particles.

4.2.2 Phenotypic and genomic stability and recombination potential

68. As described in Section 3.4.6, replication competent VEEV TC-83 can revert to virulence following passages through mice. However, as the GMO is replication incompetent, reversion to virulence is not expected to occur.

69. The GMO retains the super-infection exclusion mechanism of the parent VEEV, mediated by nsp2, making recombination highly unlikely. Studies have demonstrated that sa-mRNAs still inhibit live wild type alphavirus replication in co-infected cells (Hick et al., 2024a)

70. Alphaviruses have a demonstrated capacity for recombination in laboratory settings, particularly during viral particle production for sa-mRNAs. Early sa-mRNA vaccine candidates using a single helper plasmid repeatedly had recombination events that produced replication competent virus (Hick et al., 2024a). The use of split helper plasmid systems, where packaging proteins are provided by two separate helper plasmids, increase the number of recombination events required to produce replication competent virus and reduce the overall likelihood of producing novel replication competent alphaviruses (Smerdou and Liljeström, 1999).

71. Co-infection of sa-mRNAs and wild type alphaviruses resulted in recoverable replication competent alphavirus recombination when grown in Vero cell cultures, under conditions optimised to promote recombination, such as using co-introduced viruses at titres higher than observed in pathogenic viremia and in highly permissive cells (Hick et al., 2024a). This recombination occurred between the sa-mRNA and Getah virus and not between other alphaviruses tested including Barmah Forest virus and Ross River virus. No recombination events could be replicated when Getah virus and the sa-mRNA were co-administered in three mice models (Hick et al., 2024a). The Getah virus/sa-mRNA chimera was unable to infect and replicate in *Culex* mosquito cell lines, the primary transmission vector for Getah virus (Hick et al., 2024a).

4.2.3 Efficacy and safety

72. Some information about the efficacy of the GMO has been declared Confidential Commercial Information (CCI) under Section 185 of the Act. Under Section 187 of the Act, this information must not be disclosed except where it is made available to the Commonwealth or a Commonwealth Authority, a State agency or the Gene Technology Technical Advisory Committee in the course of carrying our their duties or functions under the Act or under corresponding State law.

73. Field safety studies with the GMO resulted in adverse events in 2.71% of the 1,657 doses administered to cats above 8-weeks of age, with none considered serious. The most reported adverse events were injection site pain and lethargy (Carritt et al., 2025).

74. Field safety studies of a similar GMO against rabies, using the same backbone and virus-like particle, had adverse events occurring in 5.7% of vaccinated cats (665) and 6.8% of vaccinated dogs (622), with none considered serious (Stachura et al., 2025).

75. Several sa-mRNA vaccines, based on VEEV TC-83 delivered with lipid nanoparticles, have undergone extensive clinical trials in humans. The efficacy of these vaccines, primarily against SARS-CoV-2, demonstrated efficacy rates (based on seroconversion in trial participants) between 53.8-100%, depending on the vector and antigen design (Szubert et al., 2023; Aboshi et al., 2024; Casmil et al., 2025; Okada et al., 2025). The most commonly reported adverse reactions included injection site pain, fatigue, headache and fever that resolved without intervention (Szubert et al., 2023; Okada et al., 2025). More severe reactions were infrequently reported across 9 clinical trials with sa-mRNA vaccines, predominantly in high dose cohorts and presented as mild chest pain, severe fever or nausea, each resolving without intervention (Aboshi et al., 2024; Okada et al., 2025). No serious adverse events resulting in hospital administration (i.e. bacterial pneumonia, tonsilitis) were attributed to the study interventions (Szubert et al., 2023; Casmil et al., 2025; Okada et al., 2025).

76. A rabies sa-mRNA vaccine (RBI-4000), based on VEEV TC-83 and delivered with lipid nanoparticles, showed a favourable safety profile in both pre-clinical mouse studies and early Phase 1 human trials (Maine et al., 2025). No serious adverse events were reported, no dose limiting events were reported, and protective titres of antibodies were achieved at all dose levels tested (Maine et al., 2025).

77. Pre-clinical trials have been conducted in many animal species against a range of pathogens. Studies in chickens showed that a sa-mRNA vaccine against influenza, delivered with lipid nanoparticle, induced protective levels of antibodies either a single dose or two doses of the vaccine (Snoeck et al., 2026). Multi-valent sa-mRNA vaccines against *Toxoplasmosis gondii* demonstrated protective effects in mice (Wu et al., 2025).

4.2.4 Decontamination of the GMO

78. Methods to decontaminate VEEV, which have been described in Section 3.5.5, would also be effective against the GMO.

Section 5 The receiving environment

79. The receiving environment forms part of the context for assessing risks associated with dealings with the GMO (OGTR, 2013). It informs the consideration of potential exposure pathways, including the likelihood of the GMO spreading or persisting outside the site of release. Relevant information about the receiving environment includes state and local council requirements relevant to domestic cats; waste management practices; related viral species in the environment; and potential hosts in the environment.

5.1 Site of vaccination

80. The intended primary receiving environment for the GMO would be domestic cats, administered by qualified veterinarians within clinics or at cat breeding facilities Australia-wide. The mode of administration would be subcutaneous injection in the scruff of the neck. The applicant would also need to seek a registration from the APVMA to authorise this mode of administration or other modes of administration.

81. The principal route by which the GMO may enter the wider environment is via accidental spills of the vaccine, as the GMO is not expected to shed.

5.2 Cat breeders

82. Australian requirements for licensing of veterinary hospitals or other facilities offering cat breeding services are imposed by States and Territories, imposed by their respective legislation (Table 1). Vaccination is not required under any state or territory legislation but is recommended under standards and guidance for breeders Australia-wide. States and territories strongly recommend that kittens remain with the breeder until after 12 weeks of age.

Table 1 State and territory requirements for cat breeders in Australia.

State	Legislation	Additional requirements
Australian Capital Territory (ACT)	*Domestic Animals Act 2000* and *Animal Welfare Act 1992*	Mandatory licensing, offence to breed without a licence. No vaccination requirements. Cats must be permanently identified (microchipped) prior to transfer of ownership
New South Wales (NSW)	*Companion Animals Act 1998*	Mandatory licensing, offence to breed without a licence. Standards set out in *Animal Welfare Code of Practice Breeding Dogs and Cats*. Vaccinations required prior to sale or transfer of ownership under Code of Ethics (not legislatively required).
Northern Territory (NT)	*Animal Protection Act 2018*	Licensing encouraged. No vaccination requirements.
Queensland (QLD)	*Animal Management (Cats and Dogs) Act 2008*	Licensing not mandatory. Vaccination recommended.

South Australia (SA)	*Dog and Cat Management Act 1995*	Mandatory licensing, offence to breed without a licence. Welfare standards set out in *South Australian Standards and Guidelines for Breeding and Trading Companion Animals 2017*. Vaccination recommended.
Tasmania (TAS)	*Cat Management Act 2009* and *Cat Management Regulations 2022*	Mandatory licensing, offence to breed without a licence or permit. Breeders must comply with codes of practice. Vaccination with core vaccines is prescribed.
Victoria (VIC)	*Domestic Animal Act 1994* and *Domestic Animals Amendment (Rehoming Cats and Dogs and Other Matters) Bill 2025*	Mandatory licensing. Cats must be permanently identified (microchipped) prior to sale. Vaccination required prior to sale or transfer of ownership.
Western Australia (WA)	*Cat Act 2011*	Mandatory licensing as an approved cat breeder. Cats must be permanently identified prior to sale. Vaccination recommended.

5.3 Domestic cats

83. In 2025, it was estimated that 73% of Australian households have a pet and 34% have at least one cat, with 5.8 million domestic cats registered Australia-wide (Animal Medicines Australia, 2025).

84. Approximately 48% of Australian cat owners keep their cats indoors only, based on self-reporting. Of the cats kept outdoors, 74% are free to roam and the rest are confined to a lead or a cat run (Animal Medicines Australia, 2025).

85. Domestic cats must be registered or permanently identified with a unique microchip, except in NT, and this is enforced by states and territories under their respective legislation (Table 1).

5.4 Feline recommended vaccination schedule

86. Vaccines for cats in Australia follow the recommendations defined by the World Small Animal Veterinary Association (WSAVA) Vaccination Guidelines Group (VGG) (Squires et al., 2024), however overall vaccination coverage is not known. The VGG defines vaccines as core and non-core, with the recommendation that all cats should be vaccinated with core vaccines while non-core vaccines should only be used as necessary.

87. All vaccines must be administered by a qualified veterinarian, who are trained to administer vaccines via multiple routes, including subcutaneously using sharps.

88. Vaccination protocols and labels typically recommend only vaccinating healthy animals and avoiding live vaccines in immunocompromised animals (Squires et al., 2024).

89. The core vaccines always include Feline panleukopenia virus (live or inactivated), Feline herpesvirus-1 (live or inactivated) and Feline calicivirus (live or inactivated). Rabies is included as a core vaccine in areas where the disease in endemic. The most recent update to the WSAVA Guidelines includes FeLV (inactivated) as core in cats under 1 year of age who are confirmed to be seronegative for FeLV (Squires et al., 2024).

90. Non-core vaccines include Feline immunodeficiency virus, *Chlamydia felis*, and *Bordatella bronchiseptica*. Non-core vaccines are indicated in cats who are expected to be at sustained risk of exposure (Squires et al., 2024).

91. Vaccines against these pathogens are commonly administered together and there is no evidence to date of recombination or complementation between species resulting in novel viral or bacterial strains.

92. Vaccines are not mandatory in any state or territory, however veterinary associations, veterinary clinics, national breeder associations and state and territory departments responsible for biosecurity strongly advocate vaccination in accordance with international WSAVA Guidelines (Squires et al., 2024). These bodies further recommend that kittens have limited environmental exposure until 2 weeks after the completion of their vaccination schedule and that all cats who may spend time outside should be vaccinated against FeLV (Day et al., 2016; Squires et al., 2024).

93. While not mandatory, standard practices for animal shelters and animal care facilities (animal daycare and long stay services) require all animals to be vaccinated to limit disease spread. Shelters and care facilities should be designed for effective cleaning and disinfection which should be carried out at least daily using disinfectants that are effective against feline pathogens.

5.5 Biosecurity

94. Each state and territory has its own biosecurity regulations and legislation. The following departments are responsible for the biosecurity:

- Environment, Planning and Sustainable Development Directorate – Environment (ACT);
- Department of Primary Industries (NSW);
- Northern Territory government (NT);
- Department of Agriculture and Fisheries (QLD);
- Department of Primary Industries and Regions (SA);
- Department of Natural Resources and Environment Tasmania (Tas);
- Agriculture Victoria (Vic); and
- Department of Primary Industries and Regional Development (WA).

95. Biosecurity considerations include the following: import of animals for domestic or commercial purposes, management of animal diseases (including vaccination and risk of transmission), and animal welfare. Australia also has a national *Biosecurity Act 2015* and a website for managing and reporting national pest and disease outbreaks, which is managed by DAFF.

5.6 Presence of related viral species in the receiving environment

96. The presence of related viruses may offer an opportunity for introduced genetic material to transfer between the GMO and other organisms or for genetic recombination in the receiving environment.

97. Australia has an estimated 75 species of endemic arboviruses that include alphaviruses Barmah Forest virus, Sindbis virus and Ross River virus (Yuen et al., 2022). Ross River virus is primarily transmitted by *Aedes* mosquito species, while Barmah Forest virus is primarily transmitted by *Culex* mosquito

species, however several other mosquito species are competent for transmission (Pyke et al., 2024). Ross River virus currently represents the greatest disease burden with an estimated 5,000 cases in humans reported annually (Ong et al., 2021; Pyke et al., 2024). Ross River virus is largely maintained in reservoir hosts such as kangaroos, possums, flying foxes, birds and horses, while Barmah Forest Virus is thought to be maintained in avian species (Pyke et al., 2024). Sindbis virus is not a notifiable disease as it is significantly less pathogenic than other endemic alphaviruses, therefore the prevalence of Sindbis virus in Australia is not well documented (Yuen et al., 2022).

98. Both Ross River virus and Barmah Forest virus circulate in the same geographic areas of Australia and there is no evidence of recombination between them to date.

5.7 Presence of similar genetic material in the environment

99. The balance of an ecosystem could be disrupted by the introduction of new genetic material through horizontal gene transfer or through release of GMO into the environment. However, the effect of disruption would be relatively small if the genetic material was already present in the system and did not confer any selective advantage to an organism that gained this genetic material.

100. The GMO encodes the glycoprotein from FeLV. The FeLV infection rate in Australian domestic cats is estimated to be between 2%-11%, and is likely under-reported due to the different disease presentations (Westman et al., 2016; Westman et al., 2025). The genes for the encoded glycoprotein are expected to be present in the environment.

5.8 Potential hosts in the environment

101. There are several potential hosts for the GMO present in Australia, including mosquitoes and horses. Cats could also potentially be an unintended host as they may encounter vaccinated cats.

102. Horses, both feral and domestic, are widely distributed across Australia with total population estimates ranging between 1.5-2 million (DSEWPC, 2011; IER, 2025). Studies utilising government datasets in combination with field surveys estimate that domestic horses are predominantly distributed across both agricultural and urban land in Queensland, NSW and Victoria (IER, 2025; Linnegar et al., 2026). Feral horses are predominantly in the Northern Territory and Queensland, with scattered populations also found in Western Australia, South Australia, NSW and Victoria and estimated at around 400,000 nationwide in invasive species reports (DSEWPC, 2011; Scasta et al., 2022). Several arboviruses, including alphaviruses, are known to circulate in horse populations in Australia (Ong et al., 2021; Pyke et al., 2024).

103. Australia has many species of mosquitos and many of these can transmit alphaviruses. Ecological studies of mosquito feeding behaviour suggest that there is variation between generalist and specialist feeders, even when occupying the same niche. There is evidence that *Culex* species have a larger host feeding range (between 100-170, primarily bird species) than *Aedes* species (7-29, predominantly mammalian species) (Lee et al., 2025), both of which can transmit alphaviruses.

104. Feral cats are present Australia-wide at an estimated density between 0.27-0.858 cats per kilometre (McHugh et al., 2025). A subset of domestic cats spend some or all of their time outdoors and are the most at risk of infection from all sources.

Section 6 Previous authorisations

105. This GM vaccine has not been previously authorised for commercial supply in Australia.

106. This GM vaccine has been authorised for use in by the United States Department of Agriculture since 2024 and is under assessment by the European Medicines Agency.

Chapter 2 Risk assessment

Section 1 Introduction

107. The risk assessment identifies and characterises risks to the health and safety of people or to the environment from dealings with GMOs, posed by or as the result of gene technology (Figure 4). Risks are identified within the established risk assessment context (Chapter 1), taking into account current scientific and technical knowledge. A consideration of uncertainty, in particular knowledge gaps, occurs throughout the risk assessment process.

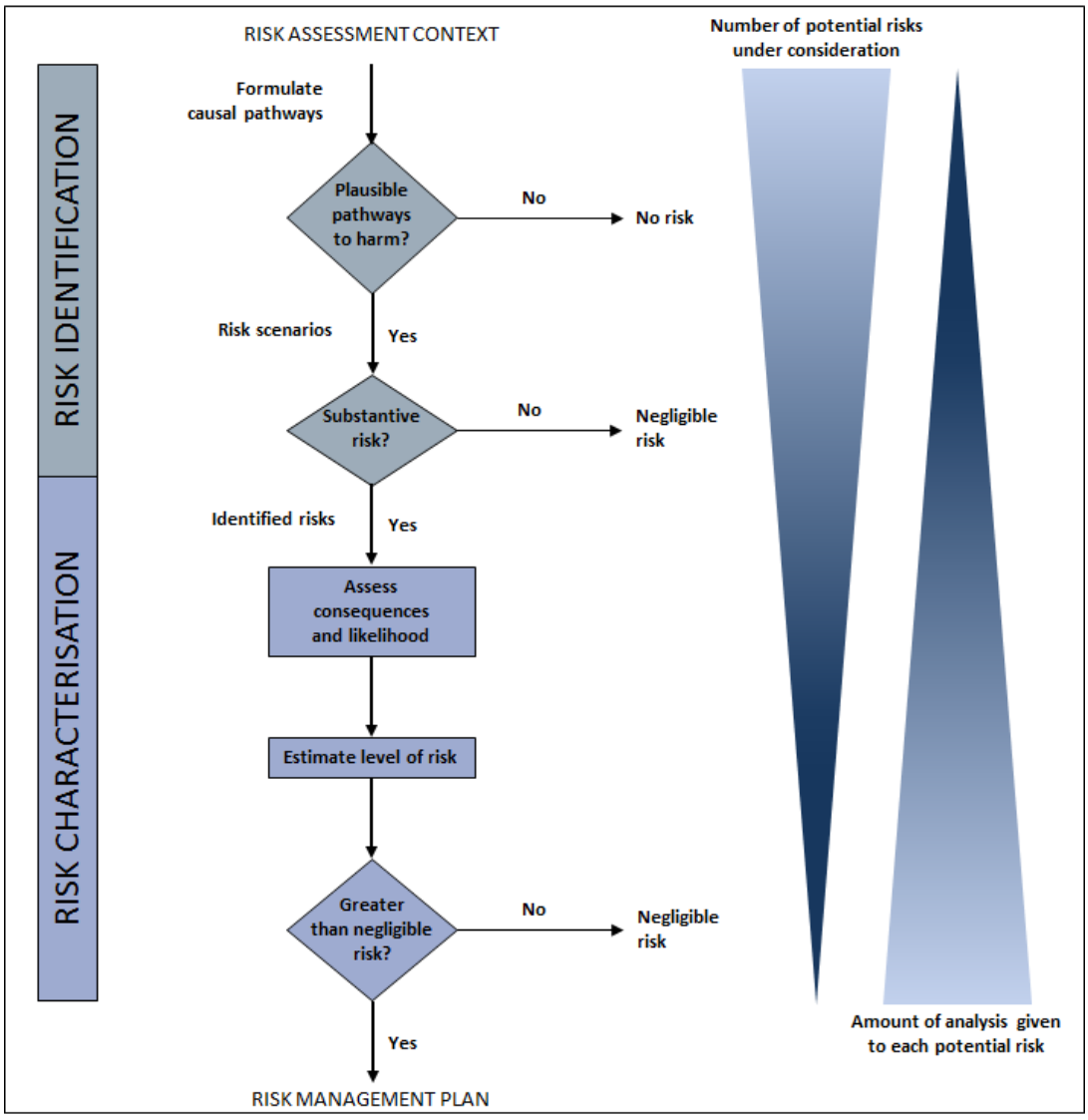

Figure 4: The risk assessment process

108. The Regulator uses a number of techniques to identify risks, including checklists, brainstorming, previous agency experience, reported international experience and consultation (OGTR, 2013).

109. Risk identification first considers a wide range of circumstances in which the GMO, or the introduced genetic material, could come into contact with people or the environment. This leads to postulating causal pathways that may give rise to harm for people or the environment from dealings with a GMO. These are called risk scenarios.

110. Risk scenarios are screened to identify substantive risks, which are risk scenarios that are considered to have some reasonable chance of causing harm. Risk scenarios that could not plausibly occur, or do not lead to harm in the short and long term, do not advance in the risk assessment process (Figure 4), i.e. the risk is considered no greater than negligible.

111. Risk scenarios identified as substantive risks are further characterised in terms of the potential seriousness of harm (Consequence assessment) and the likelihood of harm (Likelihood assessment). The consequence and likelihood assessments are combined to estimate the level of risk and determine whether risk treatment measures are required. The potential for interactions between risks is also considered.

Section 2 Risk identification

112. Postulated risk scenarios are comprised of three components (Figure 5):

i. The source of potential harm (risk source)

ii. A plausible causal linkage to potential harm (causal pathway), and

iii. Potential harm to people or the environment.

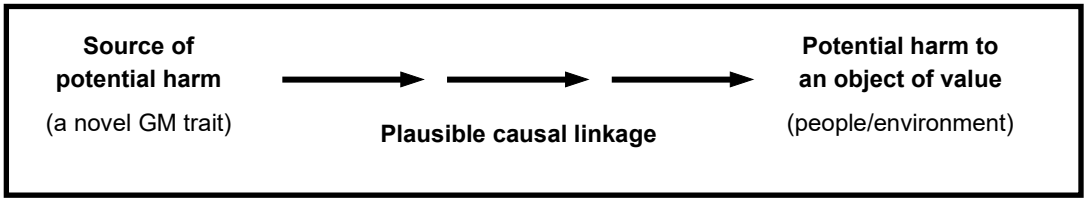

Figure 5: Components of a risk scenario

113. When postulating relevant risk scenarios, the risk context is taken into account, including the following factors detailed in Chapter 1:

- the proposed dealings
- the proposed limits including the extent and scale of the proposed dealings
- the proposed controls to limit the spread and persistence of the GMO and
- the characteristics of the parent organism(s).

2.1 Risk source

114. The parent organism of the GMO is VEEV TC-83. Details of the pathogenicity and transmissibility of VEEV, and specific consideration of VEEV TC-83, are discussed in Chapter 1. Infection is the result of direct contact with cats administered the vaccine or indirectly via the transmission by mosquitoes.

115. The sources of potential harms can be intended novel GM traits associated with the genetic modification, or unintended effects arising from the use of gene technology.

116. The GMO, as a sa-mRNA, is localised to the cell cytoplasm and does not have a mechanism to integrate with the genome of host cells. For integration to occur, RNA must first be transcribed into DNA, which is unlikely to occur as mammalian cells do not have the machinery for reverse transcription. Therefore, the possibility of integration will not be considered.

117. The risk of recombination between the GMO and circulating strains for FeLV will not be considered further in the risk scenarios, as any resulting recombinant FeLV would retain wild type characteristics and will not produce more virulent strains.

118. Other sa-mRNA vaccines have shown reversion to virulence and recombination occurring during manufacturing steps (Chapter 1, Section 3). All manufacturing will occur overseas and only the

final GMO product, tested to confirm that no replication competent virus is present, will be imported and used in Australia. Therefore, reversion to virulence and recombination with the parent VEEV TC-83 during the manufacturing process will not be considered further.

119. As discussed in Chapter 1, Section 5.6, there are other alphaviruses present in the Australian environment. Hence, there is a potential for the GMO to recombine or be complemented by the structural genes from other alphaviruses. Therefore, the potential for recombination or complementation with other alphaviruses is considered further.

120. The vaccine containing the GMO also contains live attenuated strains of other viral pathogens, and the vaccine may also be administered with other viral vaccines. However, alphaviruses are not known to undergo recombination with other viruses that are not alphaviruses. Therefore, this pathway is not discussed further.

121. The current assessment focuses on risks posed to people and to the environment, including long term persistence of the GMO, which may arise from the transport, storage or disposal of the GMO.

2.2 Causal pathway

122. The following factors are taken into account when postulating plausible causal pathways to potential harm:

- the proposed dealings, which are transport or disposal of the GMO and possession (including storage) in the course of any of these dealings,
- regulations in placed for the transport or disposal of the GMO by other regulatory agencies, the States and Territories,
- characteristics of the parent organism,
- routes of exposure to the GMOs,
- potential for transmission,
- potential effects of the genetic modification on the properties of the organism,
- potential exposure of other organisms to the GMOs in the environment,
- the release environment,
- spread and persistence of the GMOs (e.g. dispersal pathways and establishment potential),
- environmental stability of the organism (e.g. tolerance to temperature, UV irradiation and humidity),
- potential risk of revertant/novel strains due to HGT,
- practices before and after administration of the GMO including veterinary practices.

123. Although these factors are taken into account, some are not included in the risk scenarios because they are regulated by other agencies, have been considered in previous RARMPs or are not expected to give rise to substantive risks (see Sections Chapter 11.1.1 to 2.4.3 below).

124. The APVMA regulates the quality, safety and efficacy, and trade risks associated with the GM vaccine under the AgVet Code, as mentioned in Chapter 1, Section 1.1. This includes safety and efficacy of the vaccine; environmental risks; and recommended practices for the use, transport, storage and disposal of the GM vaccine. Therefore, risk scenarios in the current assessment focus primarily on risks posed to people and to the environment from the GMO, and not the intended vaccine recipients (cats).

125. The Act provides for substantial penalties for unauthorised dealings with GMOs or non-compliance with licence conditions and also requires the Regulator to have regard to the suitability of an applicant to hold a licence prior to the issuing of the licence. These legislative provisions are

considered sufficient to minimise risks from unauthorised activities. Therefore, unauthorised activities will not be considered further.

2.3 Potential harms

126. Potential harms from the GMO include:

- harm to the health of people or desirable organisms, including disease in humans, cats, horses and other vertebrates or adverse immune responses to the GMO
- the potential for establishment of a novel virus that could cause harm to people or the environment.

2.4 Postulated risk scenarios

127. Four risk scenarios were postulated and screened to identify substantive risks. These hypothetical scenarios are summarised in Table 2.

128. In the context of the activities proposed by the applicant and considering both the short and long term, none of the 4 risk scenarios give rise to any substantive risks that could be greater than negligible (discussed in depth in sections 2.4.0-2.4.4; this chapter).

Table 2 Summary of hypothetical risk scenarios from dealings with GM vaccine

Risk scenario	Risk source	Possible causal pathway	Potential harm	Substantive risk	Reason
1	GMO	Exposure of people to the GMO during preparation and administration via: - Needlestick/sharps injury; - Inhalation of aerosolised GMO; or - Contact with the GMO ⬇ Transduction of cells ⬇ Localised expression of transgenes	Adverse immune response	No	• Transfer of GMOs from the vial to the syringe does not involve any open transfer of solutions outside of the syringe or vaccine vial; therefore, reducing the likelihood of aerosols being released. • Vaccination would be conducted by registered veterinarians who are trained in the appropriate use of sharps, reducing the risk of exposure by sharps injury. • Contact with broken skin or mucous membranes is unlikely due to the GMO being fully contained within vials during preparation. The GMO may come into contact with broken skin or mucous membranes in the event of accidental spills. In the event of exposure: • The amount of GMO a person would be exposed to during preparation and administration would be very small, representing a fraction of the original dose, and therefore it is highly unlikely that exposure to the GMO would result in ill health. • Any potential adverse immune response or inflammatory reaction is expected to be minor and self-limiting. • The parent VEEV TC-83 and sa-mRNAs are not known to be transmitted by aerosol inhalation. • Other sa-mRNA vaccines have a history of safe use with no reported adverse effects in people from direct exposure.

Risk scenario	Risk source	Possible causal pathway	Potential harm	Substantive risk	Reason
					• Transgene expression is expected to decline over time.
2	GMO	Exposure of people and animals to the GMO during import, transport, storage or disposal ⬇ Transduction of cells ⬇ Localised expression of transgenes	Adverse immune response	No	• Import will follow IATA requirements. • The GMO will be stored in licensed Schedule 4 warehouses and only handled by delegated personnel. • Procedures for transport and disposal are in line with the Regulator's TSDs. • Disposal of the GMO and materials that come into contact with the GMO will follow standard veterinary clinical practises, which are designed to manage risks from infectious agents. In the event of exposure: • Animals exposed to the GMO are not expected to develop disease. • Additional reasons as listed in Risk Scenario 1.
3	GMO	Exposure of people and animals to the GMO via transmission from vaccinated cats or shedding of the GMO into the environment ⬇ Transduction of cells ⬇ Localised expression of transgene	Adverse immune response	No	• Pre-clinical studies indicate that the GMO localises to the site of injection. • The GMO is replication incompetent and cannot produce viral particles to escape transduced cells. • Exposure to other animals is minimised due to recommended vaccination protocols. • Transmission via mosquitoes is highly unlikely as the GMO cannot replicate, is expected to have limited

Risk scenario	Risk source	Possible causal pathway	Potential harm	Substantive risk	Reason
					circulation in blood, and does not bind efficiently to mosquito midguts. • Most kittens receive their first vaccines while in the care of a breeder, limiting their exposure to other susceptible cats, horses, and the environment. • The applicant provided data demonstrating that the GMO does not shed. • Multiple clinical trials, pre-clinical studies and studies in many animal hosts support that sa-mRNA vaccines are highly unlikely to shed. In the event of exposure: • GMO is unlikely to cause disease in susceptible animals housed with the vaccinated cat due to attenuation of the virus. • As in Risk Scenario 1 and 2.
4	GMO	Vaccination of cats with the GMO Or People or animals exposed as described in Risk Scenario 1-3 ⬇ Cells transduced by GMO ⬇ Transduced cells co-infected with wild type alphavirus ⬇	Adverse immune response, disease from GM VEEV with altered virulence	No	• Exposure of people or animals is unlikely for the reasons discussed in Risk Scenarios 1-3. • Alphavirus epidemics infecting people or animals are sporadic in Australia. • Co-infection of a cell containing the GMO with another alphavirus is highly unlikely as alphaviruses have superinfection exclusion mechanisms that inhibit infection of the same cell by a closely related virus after primary infection. The GMO retains this mechanism.

Risk scenario	Risk source	Possible causal pathway	Potential harm	Substantive risk	Reason
		Complementation of deleted viral proteins leading to formation of transducing viral particles Or Viral recombination leading to replication competent VEEV ⬇ GMO or recombinant VEEV transduces other cells ⬇ Systemic infection and expression of the transgene or infection with replication competent VEEV			• Sequence analyses of many alphaviruses suggests that recombination events resulting in novel alphaviruses is extremely rare. • Compatible live alphavirus vaccines are not available in Australia and therefore recombination is highly unlikely. • In the event of complementation of the deleted structural proteins, the resulting viral particle would still be replication defective and would only result in one round of replication. Cells transfected with the GMO would be rapidly cleared as the antigens still present in the GMO would trigger an immune response.

2.4.1 Risk scenario 1

Risk source	GMO
Causal pathway	Exposure of people the GMO during preparation and administration via: - Needlestick/sharps injury; - Inhalation of aerosolised GMO; or - Contact with the GMO ⬇ Transductions of cells ⬇ Localised expression of transgenes
Potential harm	Adverse immune response

Risk source

129. The source of potential harm for this postulated risk scenario is the GMO.

Causal Pathway

130. People could be exposed to the GMO during preparation and administration. The GMO could be transmitted by a needlestick or sharps injury, inhalation of aerosolised GMO from small spills, or by direct contact with the GMO to mucous membranes or open wounds. These exposures could potentially result in the GMO transducing cells and the expression of the FeLV antigen, which could cause an adverse immune response.

Exposure via needlestick/sharps injury

131. As discussed in Chapter 1, Section 2.1, the GMO would be supplied as a freeze-dried vaccine in sealed vials, which would need to be reconstituted prior to use. There is the potential for exposure to the GMO via needle stick injury during the preparation of the vaccine or during administration to a cat.

132. The GMO would be prepared and administered by a qualified veterinarian who is trained in the use of sharps and vaccine administration. According to self-reported data, 58.9-75.3% of veterinarians suffer at least one needlestick injury per year, across all vaccine and drug administrations to all animals (Leggat et al., 2009). Therefore, a needle stick injury could occur, depending on how many doses of the GMO are administered per year.

Exposure through inhalation of aerosolised GMO

133. As mentioned in Chapter 1, Section 3.1, VEEV can be transmitted by aerosols. The GMO could be aerosolised during spills or during administration to uncooperative cats and inhaled by people within the immediate area.

134. Preparation of the GMO does not involve open transfer of solutions, reducing the likelihood of producing aerosols during preparation.

135. To date, there have been no reports of nor demonstrated evidence of aerosol transmission of VEEV TC-83 or sa-mRNAs. Further, the GMO cannot produce new viral particles, reducing the possibility of further transmission from people exposed.

Exposure via contact with broken skin or mucous membranes

136. If the GMO was unintentionally/accidentally spilled people could be exposed via contact with mucous membranes or broken skin.

137. As described in Chapter 1, Section 2.1, the GMO would be supplied as lyophilised and packaged in sealed vials. The applicant proposes that the vaccine should be administered within half an hour of resuspension. Therefore, spills of prepared GMO are likely to be limited to a small number of doses at any given time.

138. VEEV, VEEV TC-83 or sa-mRNAs are not known to be transmitted via this route.

Controls in place to minimise exposure

139. Veterinary clinics have strict cleaning procedures using appropriate disinfectant for veterinary pathogens, including aerosol particle settling periods prior to cleaning. These procedures would minimise the likelihood of exposure to the GMO

140. Based on other registered vaccines, the APVMA registration of veterinary vaccines would include a label indicating the dosage; method of administration; precautions; personal protective equipment (PPE) requirements; and instructions relating to first aid, storage, and disposal of the GMO. Compliance with these behavioural practices by veterinarians would reduce the likelihood of unintended exposure of people to the GMO.

141. The existing requirements mentioned above would minimise the potential exposure of people to the GMOs due to aerosol inhalation, needlestick/sharps injury, or direct contact during preparation and administration of the vaccine.

Potential harm

142. If people are exposed to the GMO an adverse immune response could occur. Adverse responses could be against the viral particles containing the GMO or against the FeLV transgene expressed in transduced cells. FeLV is most similar to human endogenous retrovirus, which is thought to contribute 8% of the human genome and the glycoprotein is expressed in several cancers and other autoimmune diseases (Shek et al., 2025).

143. Veterinarians have a long history of working with FeLV infected cats and have not demonstrated any infection by, or adverse response to wild type FeLV. Therefore, adverse immune reactions against the FeLV antigen are not expected to be more severe than exposures to wild type FeLV.

144. VEEV TC-83 is known to elicit immune responses in persons receiving it as a vaccine (Chapter 1, Section 3.4.6), predominantly fever and malaise, that resolve without intervention. Any exposures arising from this pathway would be to amounts much smaller than a full dose. As the GMO is replication incompetent and cannot produce new viral particles, any adverse immune response is likely be less severe than exposure to VEEV TC-83.

145. VEEV is not known to cause disease in animals other than horses and humans. The GMO is further attenuated and cannot produce viral particles. Multiple pre-clinical trials with sa-mRNAs have not demonstrated any pathogenicity or serious adverse events in multiple vertebrate species. Therefore, any potential adverse immune response in humans is considered unlikely and is expected to be transient and self-limiting.

Conclusion

146. The exposure of people to the GMO resulting in adverse immune responses is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further detailed assessment.

2.4.2 Risk scenario 2

Risk source	GMO
Causal pathway	Exposure of people and animals to the GMO during import, transport, storage or disposal ⬇ Transductions of cells ⬇ Localised expression of transgenes
Potential harm	Adverse immune response

Risk source

147. The source of potential harm for this postulated risk scenario is the GMO.

Causal Pathway

148. People and animals could be exposed to the GMO though the inhalation or direct contact during import, transport, storage or disposal of the GMO. This could occur during spills or incorrect disposal of the GMO. Potential persistence of the GMO in the environment is discussed in Chapter 1, Section 3.5.5. This exposure could potentially result in the GMO transducing cells and the expression of the FeLV antigen, which could cause an adverse immune response.

149. As described in Chapter 1, Section 2.1, the GMO would be packaged in sealed vials and subsequently packaged into a cardboard box prior to import and transport. This would lower the likelihood of unintended dispersal of the GMOs.

150. The GMO will be imported into Australia in accordance with IATA requirements for veterinary products. IATA prescribes Packing Instructions (PIs) depending on the type of substance. The GMO and the overall vaccine meet the standard of Category A Infectious Substances UN2900 (affecting animals) and PI620. PI620 requires accredited training for persons handling the product, packaging limits up to 50 mL per package, triple packaging, labelling, and documentation for the product. These import requirements would reduce the likelihood and scale of spills during import of the GMO.

151. The GMO will be transported for storage at Schedule 4 licensed distribution centres prior to transportation to veterinarian clinics. APVMA registered vaccines include storage instructions on labels.

152. The transport and storage procedures discussed above would meet the containment requirements of the Regulator's *Guidelines for the Transport, Storage and Disposal of GMOs*, which ensures that the GMO would be properly contained for transport and storage. This would mitigate exposure due to spills of the GMO during these dealings.

153. The applicant has stated that all residual vaccine and associated waste (such as syringes and vials) would be discarded in waste disposal streams at veterinary clinics. Veterinary clinics have strict cleaning protocols using appropriate disinfectants for veterinary pathogens. APVMA vaccines can include disposal instructions on their labels to discard the vial/container in designated biological containers, as determined during product assessment.

154. The disposal and decontamination procedures discussed would minimise the likelihood of exposure of people that could be associated with conducting these dealings with the GMOs.

Potential harm

155. People or animals could be exposed to the GMO from spills during import, transport, storage or disposal. People or animals exposed to the GMO this way may be exposed to higher amounts of the GMO than from a single dose. The GMO may cause an adverse immune response following transduction in cells due to the expression of the transgene. However, the immune response is still expected to be self-limited and unlikely to require intervention.

156. Animals exposed to the GMO are not expected to develop disease. VEEV is not known to cause disease in animals other than horses and humans. The GMO is further attenuated and cannot produce viral particles.

157. The harms to people arising from this causal pathway are the same as those discussed in risk scenario 1.

Conclusion

158. The exposure of people or animals to the GMO via import, transport, storage or disposal resulting in an adverse immune response is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further detailed assessment.

2.4.3 Risk scenario 3

Risk source	GMO
Causal pathway	Exposure of people and animals to the GMO via transmission from vaccinated cats or shedding of the GMO into the environment ⬇ Transduction of cells ⬇ Localised expression of transgene
Potential harm	Adverse immune response

Risk Source

159. The source of potential harm for this postulated risk scenario is the GMO.

Causal Pathway

160. People or animals (e.g. wild, feral, pest, native or pet/household animals) may be exposed to the GMO via transmission by mosquitoes feeding on vaccinated cats or via direct contact with the GMO via shedding in faeces, urine or saliva.

Transmission via direct contact with the GMO shed from vaccinated cats

161. People, cats and other animals may be exposed to the GMO while co-localised with vaccinated cats. As discussed in Chapter 1, the GMO and other VEEV-based GMOs do not demonstrate any capacity for shedding, nor is any seroconversion against vaccine antigens or VEEV antigens observed in co-housed naïve animals.

162. Animals outside the home, including other cats, feral cats, horses, and other vertebrate species, are unlikely to come into direct contact with recently vaccinated cats if vaccination protocols are adhered to. Vaccination protocols recommend that animals vaccinated for the first time are not taken out into the environment to limit their exposure to disease until the vaccine has taken effect,

typically two weeks. Catteries and cat shelters also restrict the housing of animals to those that have completed their vaccination schedule. Many pet owners are conscious of the health of their animals and are likely to adhere to the recommendations.

163. Some States and Territories have mandated regions where domestic cats are not allowed to roam freely outdoors, with penalties including fines. Therefore, the likelihood of the potential exposure to the GMO in the environment is reduced.

164. As the GMO is considered highly unlikely to shed, direct transmission from vaccinated cats is considered highly unlikely to occur.

Transmission via mosquitoes feeding on vaccinated cats

165. The natural transmission route for VEEV is primarily through mosquitoes. Mosquitoes feeding on vaccinated cats could transmit the GMO to people or other vertebrates.

166. Studies on similar GMOs have shown that sa-mRNAs or recombinant sa-mRNAs do not replicate in mosquito cell cultures, or infect mosquitoes, irrespective of how it is delivered (Hick et al., 2024a).

167. The GMO is expected to be primarily localise to the injection site and is unlikely to circulate in blood, similar to other sa-mRNA vaccines. Therefore, mosquitoes would need to feed on vaccinated cats at the injection site to potentially take up the GMO. GMO taken up in this way is expected to be a small amount.

168. The GMO is within a virus-like particle that contains the capsid and glycoprotein of VEEV TC-83 and could bind to the midgut of mosquitoes. As discussed in Chapter 1, replication competent VEEV TC-83 does not bind efficiently to mosquito midguts and is not transmitted effectively by mosquitoes. As the GMO cannot produce additional viral particles, transmission efficiency is expected to be further reduced and would be substantially smaller than a full dose of the GMO or VEEV TC-83. Therefore, transmission of the GMO from vaccinated cats via mosquitoes is considered highly unlikely.

Potential harm

169. If susceptible animals are exposed to the GMO, they could have an adverse immune response through production of the antigen in transduced cells. However, any exposure resulting from this causal pathway is likely to be to smaller amounts of the GMO than a full dose and are likely to be self-limiting and transient.

170. In addition, studies provided by the applicant show that the GMO administered as a full dose does not cause disease or adverse reactions in cats or horses, nor does it transmit between co-located animals.

Conclusion

171. The potential of direct or indirect exposure of people or animals to the GMO via transmission from vaccinated cats or from shedding of the GMO into the environment is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further assessment.

2.4.4 Risk scenario 4

Risk source	GMO
Causal pathway	Vaccination of cats with the GMO OR People or animals exposed as described in Risk Scenarios 1-3 ⬇ Cells transduced by GMO ⬇ Transduced cells co-infected with wild type alphavirus ⬇ Complementation of deleted viral proteins leading to formation of transducing viral particles OR Viral recombination leading to replication competent VEEV ⬇ GMO or recombinant VEEV transduces other cells ⬇ Systemic infection and expression of the transgene or infection with replication competent VEEV
Potential harm	Adverse immune response, disease from GM VEEV with altered virulence

Risk source

172. The source of potential harm for this postulated risk scenario is the GMO.

Causal Pathway

173. People or animals could be exposed to the GMO via the pathways described in the previous risk scenarios. Exposure could potentially result in the GMO transducing cells. If people or animals are co-infected with another alphavirus, the GMO could undergo complementation or recombination and generate a novel alphavirus or replication competent VEEV. A novel alphavirus could have altered pathogenicity relative to other alphaviruses present in Australia or introduce a VEEV-like alphavirus into the Australian environment, where it is not currently present.

174. Complementation requires the presence of different viral products capable of functionally rescuing a phenotype by providing different proteins. For the GMO, this would require the provision of structural proteins by another virus. Recombination is the exchange of genetic material between similar viruses, resulting in replication competent virus or genetically novel strains with potentially altered virulence or host ranges.

175. Complementation and recombination both require the GMO and another alphavirus strain to be present in the same cell as the same time. This could occur if:

a. The vaccinated cat is exposed to another alphavirus immediately prior to or after vaccination; or

b. A susceptible animal or person is infected with an alphavirus then exposed to the GMO as described in risk scenarios 1-3; or

c. The vaccinated cat is given two alphavirus-based vaccines at the same time; or

d. The GMO is mistakenly administered or is used off-label in a non-feline species infected with an alphavirus.

Potential for co-infection of cells by the GMO and another alphavirus

176. The likelihood of viruses co-infecting cells is dependent on co-circulation of different viruses in the same geographical area, genetic similarity between the viruses, rate of co-infection of a host with both viruses and viral population size within the infected host cell.

177. Cats may be exposed to alphaviruses immediately prior to or after vaccination with the GMO. This could occur if cats are housed near animals that are known alphavirus reservoirs or near horses where an alphavirus outbreak is occurring, and mosquitos are prevalent. Cats are susceptible to mosquito bites whether they are kept indoors or outdoors, however cats kept outdoors are more exposed.

178. Cats are highly unlikely to be given two alphavirus-based vaccines at the same time, as alphavirus based or live attenuated alphavirus vaccines are not currently used in Australia, according to the APVMA's PubCris database.

179. Susceptible people or animals infected with an alphavirus are unlikely to be infected with the GMO transmitted from a vaccinated cat as the GMO is not expected to shed and is not expected to be transmitted by mosquitoes.

180. Animals receiving the vaccine accidentally or through off-label use could be infected with an alphavirus. As horses are the main vertebrates that exhibit a severe disease pathology from alphavirus infection, and the administration of any vaccine is only recommended for healthy animals, horses are highly unlikely to receive the vaccine via this route. Other animals that could be infected with an alphavirus asymptomatically are more at risk of receiving the GMO accidentally or through off label use.

181. The GMO, being replication incompetent, is expected be limited in the overall number of cells transduced in a vaccinated cat and likely significantly fewer cells in the event of exposures to lower doses. This reduces the overall likelihood of the GMO and an alphavirus both being present in the same cell.

182. Alphaviruses are thought to be infectious for approximately 7 days (Hick et al., 2024a), however viral RNA can be detected for much longer. This is likely to limit the temporal window in which the GMO and an alphavirus could potentially enter the same host cell.

183. Alphaviruses contain superinfection exclusion mechanisms that inhibit the replication of a secondary infecting alphavirus in the same cell. In VEEV, this is mediated by the nsPs which are still present in the GMO. There is evidence that this mechanism effectively inhibits secondary infecting viral replication within an hour, further reducing the temporal window available for two alphaviruses to infect the same cell.

Complementation of the GMO with a wild type alphavirus

184. Complementation would have two primary outcomes; the GMO complements another alphavirus with nsp1-4 derived from VEEV TC-83, or another alphavirus complements the GMO with structural proteins enabling the GMO to form new viral particles.

185. A broad range of alphaviruses have a demonstrated capacity for complementation of the non-structural replicases across different species in laboratory settings (Wang et al., 2025). The GMO complementing an alphavirus would provide VEEV TC-83 replication machinery that could replicate the wild type alphavirus genome until lysis of the host cell. This would be highly unlikely to alter the virulence of the other alphavirus.

186. Complementation of the GMO with structural proteins (capsid or glycoprotein) from another alphavirus would result in additional viral particles containing the GMO being produced, that could then transduce other cells. However, as complementation could not restore replication competence to the GMO, the most likely outcome would be one additional cycle of replication and potentially longer persistence of the GMO in a person or animal. There is no experimental evidence that demonstrates complementation of the capsid or glycoprotein across alphavirus species, which are the proteins required to produce new particles for the GMO. Therefore, any complementation occurring between alphaviruses and the GMO is highly unlikely to result in novel viral particles.

Recombination of the GMO with a wild type alphavirus

187. Recombination of the GMO with another alphavirus could potentially occur in certain circumstances. For example, recombination between sa-mRNAs in laboratory conditions requires directly introducing two viruses into the same cell at the same time, using high titres of each virus, in cell lines that are highly permissive to replication (Hick et al., 2024a). These conditions are highly unlikely to occur under field conditions, supported by the lack of overall recombination events reported between alphavirus species, and no recombination events reported for any pre-clinical or clinical trial using sa-mRNAs.

188. The recombinant sa-mRNA and alphavirus produced in the Hick et al. (2024) study only occurred between the sa-mRNA and Getah virus, which is not present in Australia, with no recombination events observed with Barmah Forest Virus, Ross River Virus, or the other alphaviruses tested. Further, the recombinant virus produced was unable to replicate in mosquito cells or infect mosquitoes through blood meals (Hick et al., 2024a).

189. Recombination between the GMO and another alphavirus could result in either a wild type alphavirus gaining VEEV nsp1-4 or FeLV glycoprotein from the GMO, or the GMO gaining the structural proteins from an alphavirus and is able to regain the ability to produce viral particles.

190. The majority of alphavirus cell tropism and transmissibility is dependent on the structural proteins, therefore a wild type alphavirus with VEEV nsp1-4 from the GMO would not be expected to have an altered cell tropism or transmission compared to the WT alphavirus resulting from this recombination.

191. A wild type alphavirus receiving the FeLV glycoprotein from the GMO through homologous recombination would lose its ability to form structural proteins that are important to generate viral particles. Therefore, this recombinant virus would not be expected to persist.

192. Recombination could result in the GMO regaining the structural proteins and lose the FeLV glycoprotein. This would make the GMO replication competent. However, this recombinant virus would have the structural proteins of an alphavirus already present in Australia, likely retaining the cell tropism and transmission characteristics of the wild type alphavirus.

193. The overall potential for the GMO and another alphavirus to produce a novel virus that could become establish in the environment would require multiple highly unlikely steps to occur:

a. The GMO is likely to have limited distribution beyond the initial administration site, reducing the likelihood of the same cells being infected as a mosquito acquired infection;

b. The GMO and another alphavirus would need to be in the same cell at the same time, within a temporal window that precedes the super-infection exclusion mechanism, which is likely to be approximately 1 hour;

c. Recombination between the GMO and the alphavirus would need to result in restored replication competence, which is rarely observed even under optimised laboratory conditions;

d. The recombinant virus would need to be capable of infecting and replicating in mosquitoes, which is not observed even under optimised laboratory conditions.

Potential harm

In the event of complementation

194. This could lead to a higher level of the transgene and viral particles present, however the GMO, even with an additional round of replication, is still likely to be cleared and any adverse response would be self-limiting and transient.

In the event of recombination

195. Recombinant viruses could lead to clinical disease, due to the presence of a wild type alphavirus glycoprotein. However, this is not expected to be more severe than an infection with a wild type alphavirus.

Conclusion

196. The potential for the GMO and other alphaviruses to produce novel replication competent virus or novel viral particles due to complementation or recombination is not identified as a risk that could be greater than negligible. Therefore, it does not warrant further detailed assessment.

Section 3 Uncertainty

197. Uncertainty is an intrinsic property of risk analysis and is present in all aspects of risk analysis. This is discussed in detail in the Regulator's Risk Analysis Framework document.

198. Uncertainty is addressed by approaches such as balance of evidence, conservative assumptions, and applying risk management measures that reduce the potential for risk scenarios involving uncertainty to lead to harm. If there is residual uncertainty that is important to estimate the level of risk, the Regulator will take this uncertainty into account when making decisions.

199. Uncertainty can arise from a lack of experience with the GMO. There is uncertainty regarding the potential for recombination of the GMO with circulating alphaviruses in the Australian environment. The GMO has been approved for use in the USA since 2024, where wild type VEEV may be present, and there have been no recorded recombination events to date. Additional information regarding the potential for recombination between sa-mRNA vaccines and any alphavirus is considered in Chapter 1, and the overall risk has been assessed as posing negligible risk..

200. Post release review (PRR) will also be used to address uncertainty regarding future changes to knowledge about the GMO or the receiving environment. PRR is typically required for commercial GMO releases, which generally do not have limited durations.

Section 4 Risk evaluation

201. Risk is evaluated against the objective of protecting the health and safety of people and the environment to determine the level of concern and, subsequently, the need for controls to mitigate or reduce risk. Risk evaluation may also aid consideration of whether the proposed dealings should be authorised, need further assessment, or require collection of additional information.

202. Factors used to determine which risks need treatment may include:

- risk criteria,
- level of risk,

- uncertainty associated with risk characterisation, and
- interactions between substantive risks.

203. Four risk scenarios were identified whereby the proposed dealings might give rise to harm to people or the environment. The level of risk for each risk scenario was considered negligible, considering both the short and long term. The principal reasons for these conclusions are summarised in Table 2.

204. Therefore, risks to the health and safety of people, or the environment, from the proposed release of the GMO into the environment are considered to be negligible. The *Risk Analysis Framework* (OGTR, 2013), which guides the risk assessment and risk management process, defines negligible risks as risks of no discernible concern with no present need to invoke actions for mitigation[3].

205. While no specific risk management measures are required, control measures are likely to be imposed by the APVMA during the registration process to manage any risks associated with the vaccine. Control measures for administration of other live attenuated vaccines are currently imposed under other APVMA registrations. These control measures are considered important for maintaining the risk context and discussed further in Chapter 3

[3] As none of the proposed dealings are considered to pose a significant risk to people or the environment, section 52(2)(d)(ii) of the Act mandates a minimum period of 30 days for consultation on the RARMP. However, the Regulator has allowed up to eight weeks for the receipt of submissions from prescribed experts, agencies and authorities and the public.

Chapter 3 Risk management plan

Section 1 Background

206. 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 addresses risks evaluated as requiring treatment and considers limits and controls proposed by the applicant, as well as general risk management measures. The risk management plan informs the Regulator's decision-making process and is given effect through proposed licence conditions.

207. Under section 56 of the Act, the Regulator must not issue a licence unless satisfied that any risks posed by the dealings proposed to be authorised by the licence are able to be managed in a way that protects the health and safety of people and the environment.

208. All licences are subject to three conditions prescribed in the Act. Section 63 of the Act requires that each licence holder inform relevant people of their obligations under the licence. The other statutory conditions allow the Regulator to maintain oversight of licensed dealings: Section 64 requires the licence holder to provide access to premises to OGTR inspectors and Section 65 requires the licence holder to report any information about risks or unintended effects of the dealing to the Regulator on becoming aware of them. Matters related to the ongoing suitability of the licence holder are also required to be reported to the Regulator.

209. The licence is also subject to any conditions imposed by the Regulator. Examples of the matters to which conditions may relate are listed in Section 62 of the Act. Licence conditions can be imposed to limit and control the scope of the dealings. In addition, the Regulator has extensive powers to monitor compliance with licence conditions under Section 152 of the Act.

Section 2 Risk treatment measures for substantive risks

210. The risk assessment of risk scenarios listed in Chapter 2 concluded that there are negligible risks to people and the environment from the proposed commercial release of the GMO. These risk scenarios were considered in the context of the scale of the proposed release and the receiving environment, considering both the short and long term. The risk evaluation concluded that no specific risk treatment measures are required to treat these negligible risks.

211. As there were no substantive risks identified, no specific conditions were included to require that only healthy cats are vaccinated. However, it is noted that the commercial supply of the product containing the GMO will also require the registration of the product with the APVMA, which is likely to contain restrictions of only vaccinating healthy cats.

Section 3 General risk management

212. All DIR licences issued by the Regulator contain conditions that relate to general risk management. These include conditions relating to:

- applicant suitability
- testing methodology
- identification of the persons or classes of persons covered by the licence
- reporting structures
- access for the purpose of monitoring for compliance
- other modes of administration.

3.1 Applicant suitability

213. In making a decision whether or not to issue a licence, the Regulator must have regard to the suitability of the applicant to hold a licence. Under Section 58 of the Act, matters that the Regulator must take into account include:

- any relevant convictions of the applicant
- any revocation or suspension of a relevant licence or permit held by the applicant under a law of the Commonwealth, a State or a foreign country
- the capacity of the applicant to meet the conditions of the licence.

214. If a licence were issued, the conditions would include a requirement for the licence holder to inform the Regulator of any circumstances that would affect their suitability.

3.2 Testing methodology

215. If a licence were issued, Intervet Australia Pty Ltd would be required to provide a method to the Regulator for the reliable detection of the GMO, and the presence of the introduced genetic materials in a recipient organism. As part of the application, the applicant supplied appropriate detection methods to detect the RNA sequences of the GMO. Therefore, a requirement to provide detection methods is not included in the draft licence.

3.3 Identification of the persons or classes of persons covered by the licence

216. If a licence were issued, any person, including the licence holder, could conduct any permitted dealing with the GMO.

3.4 Modes of administration

217. The applicant has proposed one mode of administration (subcutaneous injection). The risks associated with this method of administration has been included in the risk assessment for DIR 220.

3.5 Reporting requirements

218. If issued, the licence would oblige the licence holder to immediately report any of the following to the Regulator:

- any additional information regarding risks to the health and safety of people or the environment associated with the dealings;
- any contraventions of the licence by persons covered by the licence;
- any unintended effects of the release.

219. The licence holder is also obliged to submit an Annual Report containing any information required by the licence.

220. There are also provisions that enable the Regulator to obtain information from the licence holder relating to the progress of the commercial release (see Section 4, below).

221. If issued, the licence would also require the licence holder to notify the Regulator of the following authorisations by the APVMA:

- inclusion on the Public Chemicals Registration Information System (PubCRIS); and
- any amendments to the registration.

3.6 Monitoring for compliance

222. The Act stipulates, as a condition of every licence, that a person who is authorised by the licence to deal with a GMO, and who is required to comply with a condition of the licence, must

allow the Regulator, inspectors or other person authorised by the Regulator, to enter premises where a dealing is being undertaken for the purpose of monitoring or auditing the dealing.

223. In cases of non-compliance with licence conditions, the Regulator may instigate an investigation to determine the nature and extent of non-compliance. The Act provides for criminal sanctions of large fines and/or imprisonment for failing to abide by the legislation, conditions of the licence or directions from the Regulator, especially where significant damage to the health and safety of people or the environment could result.

Section 4 Post release review

224. Regulation 10 requires the Regulator to consider the short and the long term when assessing risks. The Regulator takes account of the likelihood and impact of an adverse outcome over the foreseeable future and does not disregard a risk on the basis that an adverse outcome might only occur in the longer term. However, as with any predictive process, accuracy is often greater in the shorter rather than longer term.

225. For the current application for a DIR licence, the Regulator is including conditions that require ongoing oversight to provide feedback on the findings of the RARMP and ensure the outcomes remain valid for future findings or changes in circumstances. If a licence was issued, this ongoing oversight would be achieved through PRR activities. The three components of PRR are:

- adverse effects reporting system (Section 4.1)
- requirement to monitor specific indicators of harm (Section 4.2)
- review of the RARMP (Section 4.3).

The outcomes of these PRR activities may result in no change to the licence or could result in the variation, cancellation or suspension of the licence.

4.1 Adverse effects reporting system

226. Any member of the public can report adverse experiences/effects resulting from an intentional release of a GMO to the OGTR through the Free-call number (1800 181 030), mail (MDP 54 – GPO Box 9848, Canberra ACT 2601) or via email to the OGTR inbox (ogtr@health.gov.au). Reports can be made at any time on any DIR licence. Credible information would form the basis of further investigation and may be used to inform a review of a RARMP (see Section 4.3 below) as well as the risk assessment of future applications involving similar GMOs.

4.2 Requirement to collect additional specific information

227. Collection of additional specific information on an intentional release provides a mechanism for ‘closing the loop’ in the risk analysis process and for verifying findings of the RARMP.

228. This may involve monitoring specific indicators of harm that have been identified in the risk assessment. The term ‘specific indicators of harm’ does not mean that it is expected that harm would necessarily occur if a licence was issued. Instead, it refers to measurement endpoints which are expected to change should the authorised dealings result in harm. Should a licence be issued, the licence holder would be required to monitor these specific indicators of harm as mandated by the licence.

229. The triggers for this component of PRR may include risk estimates greater than negligible or significant uncertainty in the risk assessment.

230. The characterisation of the risk scenarios discussed in Chapter 2 did not identify risks greater than negligible. Therefore, they were not considered substantive risks that warranted further detailed assessment. No specific indicators of harm have been identified in this RARMP for application DIR-220. However, specific indicators of harm may also be identified during later stages,

e.g. following the consideration of comments received on the consultation version of the RARMP, or if a licence were issued, through either of the other components of PRR.

231. Conditions have been included in the licence to allow the Regulator to request further information from the licence holder about any matter to do with the release, including research to verify predictions of the risk assessment.

4.3 Review of the RARMP

232. The third component of PRR is the review of RARMPs after a commercial/general release licence is issued. Such a review would take into account any relevant new information, including any changes in the context of the release, to determine if the findings of the RARMP remained current. The timing of the review would be determined on a case-by-case basis and may be triggered by findings from either of the other components of PRR, or by relevant new scientific information, or be undertaken after the authorised dealings have been conducted for some time. If the review findings justified either an increase or decrease in the initial risk estimate(s) or identified new risks to people or to the environment that require management, this could lead to changes to the risk management plan and licence conditions. In the case of a veterinary vaccine where the APVMA is the primary regulatory body overseeing the vaccine, any review of the RARMP or licence would likely only be initiated in consultation with APVMA.

Section 5 Conclusions of the consultation RARMP

233. The risk assessment concludes that the proposed commercial release of the vaccines containing a GMO poses negligible risks to the health and safety of people and a negligible risk to the environment as a result of gene technology.

234. The risk management plan concludes that these negligible risks do not require specific risk treatment measures. However, if a licence were to be issued, general conditions are proposed to ensure that there is ongoing oversight of the release.

Chapter 4 Draft licence conditions

Section 1 Interpretations and Definitions

1. In this licence:

    (a) unless defined otherwise, words and phrases used in this licence have the same meaning as they do in the Act and the Regulations;

    (b) words importing a gender include every other gender;

    (c) words in the singular number include the plural and words in the plural number include the singular;

    (d) expressions used to denote persons generally (such as “person”, “party”, “someone”, “anyone”, “no-one”, “one”, “another” and “whoever”), include a body politic or corporate as well as an individual;

    (e) references to any statute or other legislation (whether primary or subordinate) are a reference to a statute or other legislation of the Commonwealth of Australia as amended or replaced from time to time and equivalent provisions, if any, in corresponding State law, unless the contrary intention appears;

    (f) where a word or phrase is given a particular meaning, other grammatical forms of that word or phrase have corresponding meanings;

    (g) specific conditions prevail over general conditions to the extent of any inconsistency.

2. In this licence:

‘**Act**’ means the *Gene Technology Act 2000* (Cth) or the corresponding State legislation under which this licence is issued.

‘**Annual Report**’ means a written report provided to the Regulator by the end of September each year containing all the information required by this licence to be provided in the Annual Report.

‘**GM**’ means genetically modified.

‘**GMO**’ means the genetically modified organism that is the subject of the dealings authorised by this licence.

‘**OGTR**’ means the Office of the Gene Technology Regulator.

‘Regulations’ means the Gene Technology Regulations 2001 (Commonwealth) or the corresponding State law under which this licence is issued.

‘**Regulator**’ means the Gene Technology Regulator.

Section 2 General conditions and obligations

3. This licence remains in force until it is suspended, cancelled or surrendered. No dealings with the GMO are authorised during any period of suspension.

4. The licence holder is Intervet Australia Pty Ltd.

5. Any person, including the licence holder, may conduct any authorised dealing(s) with the GMO.

6. The dealings authorised by this licence are:

    (a) import of the GMO;

    (b) transport of the GMO;

(c) disposal of the GMO;

and the possession (including storage) and supply of the GMO for the purposes of, or in the course, of any of these dealings.

Note: Use of the GMO for veterinary purposes is not covered by the Gene Technology Act 2000 and therefore this licence is not required to authorise such use. The GMOs are also subject to regulation by other federal and state departments and agencies, including the Australian Pesticides and Veterinary Medicines Authority and the Department of Agriculture, Fisheries and Forestry. These other departments and agencies may impose further requirements for, or limitations on, the use of the GMO or these dealings.

7. Dealings with the GMO may be conducted in all areas of Australia.

8. Dealings described in Condition 6 must not occur unless authorised by registration with the APVMA.

9. The licence authorises dealings with the GMO described in **Attachment A**.

2.1 Obligations of the Licence Holder

10. The licence holder must immediately notify the Regulator if any of its contact details change.

Note: Please address correspondence to OGTR.Applications@health.gov.au

Prior to issuing a licence, the Regulator considers suitability of the applicant to hold a licence. The following conditions address ongoing suitability of the licence holder.

11. The licence holder must:

(a) inform the Regulator immediately in writing, of:

i. any relevant conviction of the licence holder; and

ii. any revocation or suspension of a licence or permit held by the licence holder under a law of the Australian Government, a State or a foreign country, being a law relating to the health and safety of people or the environment; and

iii. any event or circumstances that would affect the capacity of the holder of this licence to meet the conditions in it; and

(b) provide any information related to the licence holder's ongoing suitability to hold a licence, if requested, within the timeframe stipulated by the Regulator.

12. The licence holder must inform any person covered by this licence, to whom a particular condition of the licence applies, of the following:

(a) the particular condition, including any variations of it; and

(b) the cancellation or suspension of the licence; and

(c) the surrender of the licence.

2.2 Provision of new information to the Regulator

Licence conditions are based on the risk assessment and risk management plan developed in relation to the application using information available at the time of assessment. The following condition requires that any new information that may affect the risk assessment is communicated to the Regulator.

13. The licence holder must inform the Regulator if the licence holder becomes aware of:

(a) additional information as to any risks to the health and safety of people, or to the environment, associated with the dealings authorised by the licence; or

(b) any contraventions of the licence by a person covered by the licence; or

(c) any unintended effects of the dealings authorised by the licence.

Note: The Act requires, for the purposes of the above condition, that:

(a) the licence holder will be taken to have become aware of additional information of a kind mentioned in condition 13 if he or she was reckless as to whether such information existed; and

(b) the licence holder will be taken to have become aware of contraventions, or unintended effects, of a kind mentioned in condition 13, if he or she was reckless as to whether such contraventions had occurred, or such unintended effects existed.

Note: Contraventions of the licence may occur through the action or inaction of a person.

14. If the licence holder is required to inform the Regulator under condition 13, the Regulator must be informed without delay.

Note: An example of informing without delay is contact made at the time of the incident via the OGTR free call phone number 1800 181 030 or email to OGTR.M&C@health.gov.au.

15. If at any time the Regulator requests the licence holder to collect and provide information about any matter to do with the progress of the dealings authorised by this licence, including but not confined to:

(a) additional information as to any risks to the health and safety of people, or to the environment, associated with the dealings authorised by the licence, whether or not the licence holder has provided information to the Regulator under condition 13(a);

(b) any contraventions of the licence by a person covered by the licence, whether or not the licence holder has provided information to the Regulator under condition 13(b);

(c) any unintended effects of the dealings authorised by the licence, whether or not the licence holder has provided information to the Regulator under condition 13(c);

(d) research, including by way of survey, to verify predictions of the risk assessment, or for any purpose related to risks to the health and safety of people, or to the environment;

(e) scientific literature and reports in respect of the GMO authorised by this licence, for a nominated period;

(f) details of any refusals of applications for licences or permits (however described) to deal with the GMO made pursuant to the regulatory laws of a foreign country;

and the request is reasonable, having regard to consistency with the Act and relevance to its purpose, then the licence holder must collect the information and provide it to the Regulator at a time and in the manner requested by the Regulator.

Note: The Regulator may invite the licence holder to make a submission on the reasonability of a request by the Regulator to collect and provide information relevant to the progress of the dealings with the GMO.

2.3 Obligations of persons covered by the licence

16. If a person is authorised by this licence to deal with the GMOs and a particular condition of this licence applies to the dealing by that person, the person must allow the Regulator, or a person authorised by the Regulator, to enter premises where the dealing is being undertaken, for the purposes of auditing or monitoring the dealing.

Section 3 Reporting and Documentation

3.1 Notification of authorisations by the Australian Pesticides and Veterinary Medicines Authority

17. If the GMOs are included on the Public Chemical Registration Information System (PubCRIS), the licence holder must notify the Regulator in writing within 14 days of registration.

18. The licence holder must notify the Regulator in writing of any subsequent amendments to the conditions of the PubCRIS registration involving the pattern of usage, handling, storage, transport or disposal of the GMOs, within 14 days of the change occurring.

3.2 Annual Report

19. The licence holder must provide an Annual Report to the Regulator by the end of September each year covering the previous financial year. An Annual Report must include:

(a) information about any adverse impacts, unintended effects, or new information relating to risks, to human health and safety or the environment caused by the GMOs or material from the GMOs;

(b) information about the numbers of vaccine doses distributed to each State and Territory.

Note: Please address correspondence to OGTR.M&C@health.gov.au

ATTACHMENT A

DIR No: 220

Full Title: Commercial supply of multivalent cat vaccines containing a genetically modified component for the prevention of feline leukemia virus infection

Licence Holder Intervet Australia Pty Ltd

GMO Description

GMO covered by this licence

The GMO has viral structural genes deleted from the Venezuelan Equine Encephalitis Virus vaccine strain TC-83 to render the GMO unable to produce new viral particles and the codon-optimised glycoprotein gp85 gene from Feline Leukemia Virus (FeLV) under the control of a subgenomic promoter inserted to trigger an immune response against FeLV and protect against later infection.

Parent Organism

Common Name: Venezuelan Equine Encephalitis Virus vaccine strain TC-83

Scientific Name: Venezuelan Equine Encephalitis Virus

Modified traits

Category: Vaccine – attenuated

Description: The GMO has been genetically modified to be replication incompetent, to be attenuated and induce an immune response against circulating FeLV, to be used as a vaccine.

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Appendix A: Summary of submissions

The Regulator received several submissions from prescribed experts, agencies and authorities[4] on matters relevant to preparation of the RARMP. All issues raised in submissions relating to risks to the health and safety of people and the environment were considered. These issues, and where they are addressed in the consultation RARMP, are summarised below.

Submission	Summary of issues raised	Comment
1	Has no advice or comments on the risk management plan for DIR-220.	Noted.
2	Agrees that the following should be included in the RARMP. The potential for: • accidental exposure of humans and animals to the GMO leading to harm; • complementation and recombination of the GMO with other alphaviruses; the GMO to be harmful to the environment.	Noted.
3	Has no specific advice at this stage on the development of the RARMP for DIR-220. Noted that there will be an opportunity to comment on the draft RARMP.	Noted.
4	Advised that the supply of the multivalent cat vaccine does not have an impact on the LGA. Recommends that the following be considered in the preparation of the RARMP: - The WHO-compliance of the trial information about the product; - Storage requirements of the GMO throughout import, transport and storage; - Import of final, unaltered, ready-to-use GMO only; - Restrict the handling of the GMO to qualified veterinary professionals; - Detailed spill management and biosafety protocols to be used in dealings with the GMO; - The genetic stability of the GMO and unintended host interactions that may occur as a result of the GMO; and - Clinical safety data demonstrating low incidence of adverse reactions.	Noted. These considerations are taken into account in Chapter 1 and Chapter 2 of the draft consultation RARMP. Clinical safety considerations and WHO-compliance of trial information is outside the scope of assessments conducted by the OGTR and will be considered by the APVMA.
5	Has no comments at this time on application DIR-220.	Noted.

[4] Prescribed expects, agencies and authorities include GTTAC, State and Territory Governments, Australian government agencies and the Minister for the Environment.

Submission	Summary of issues raised	Comment
	Noted that there will be an opportunity to comment on the draft RARMP.	