Environmental Protection Authority
Te Mana Rauhī Taiao

APPLICATION FORM
CONTAINMENT

Application Form: HS3 Import or Manufacture any Hazardous Substance in Containment

under section 31 of the Hazardous Substances and New Organisms Act 1996

To submit an application, please send by post to: Environmental Protection Authority, Private Bag 63002, Wellington 6140
OR email to: HSApplications@epa.govt.nz

Payment must accompany application: see our fees and charges schedule for details. Please allow 10 working days for processing.

Applicant:

Merial New Zealand Ltd

Name of substance:

MARDGC1- Experimental Veterinary Medicine Substances

APPLICANT CHECKLIST

Mandatory sections filled out	☐	**Appendices enclosed**	☐
Initial fees enclosed	☐	**Signed and dated**	☐
Electronic copy of application emailed to EPA	☐		

Office use only

Application code:

Date received:

EPA contact:

Initial fees paid: $

Application version no.:

Important

1. You can talk to an applications advisor at the EPA, who can help you scope and prepare your application. We need all relevant information early on in the application process. Quality information up front will speed up the process.
2. This application form may be used to seek approvals for more than one hazardous substance where the substances are related – for example, a concentrated compound (active ingredient) and its related formulations, or a range of substances for similar purposes to be tested in a field trial.
3. Any extra material that does not fit in the application form must be clearly labelled, cross-referenced, and included in an appendix to the application form.
4. Commercially sensitive information must be collated in a separate appendix.
5. Unless otherwise indicated, all sections of this form must be completed for the application to be progressed.
6. You can get more information at any time by contacting us. One of our staff members will be able to help you.

   Environmental Protection Authority
   Private Bag 63002
   Wellington
   New Zealand
   Telephone: 64 4 916 2426
   Facsimile: 64 4 914 0433
   Email: HSApplications@epa.govt.nz
   http://www.epa.govt.nz

Section 1 – Applicant details

1.1 Name and postal address in New Zealand of the organisation making the application:

Name: Merial New Zealand Ltd

Address: PO Box 76211, Manukau City 2241, New Zealand

Phone: 09 9801600

Fax: 09 9801601

1.2 The applicant's location address in New Zealand (if different from above):

Address: Level 3, 2 Osterley Way,

Manukau City, 2241

Auckland New Zealand

1.3 Name of the contact person for the application:

This person should have sufficient knowledge to respond to queries and either have the authority to make decisions that relate to processing the application on behalf of the applicant, or have the ability to go to the appropriate authority.

Name: Justin Hurst

Position: Regulatory Affairs and Technical Services Manager

Address: Level 3, 2 Osterley Way,

Phone: 09 980 1616

Fax: 09 980 1601

Email: justin.hurst@merial.com

Section 2 – Application type and related approvals required

This form is only for an application to import a hazardous substance into containment, or manufacture a hazardous substance in containment.

2.1 Is this application to manufacture or import a hazardous substance in containment for any of the following purposes?

Containment applications can only be made for a limited range of purposes. In particular, the substance must not be intended for commercial manufacture or sale.

Small amounts of any hazardous substance for use as an analytical standard, where approval to import or manufacture that substance has been declined?	☐ Yes	☒ No
Research on any hazardous substance to acquire information for use in assessing that substance for a HSNO approval?	☒ Yes	☐ No
Research and development on any hazardous substance?	☒ Yes	☐ No
Use in an emergency?	☐ Yes	☐ No
Formulating, relabelling, repackaging, or storing any hazardous substance for export to a destination outside New Zealand?	☐ Yes	☒ No
Other purposes?	☐ Yes	☒ No

2.2 If you answered 'yes' to one of the purposes listed above, please provide some supporting detail. If you answered 'yes' to 'other purpose', describe the purpose and explain why this purpose is appropriate to a containment application.

This is a generic application for approval to import or manufacture under containment conditions limited quantities of experimental veterinary medicine substances including active ingredients for the purpose of further characterisation for their use in treatment and control of animal health conditions (field trials) and to confirm product stability and to validate the production process. The veterinary medicine substances will be used in small scale containment trials to provide information for research and development of selected compounds. The substances will be trialled in New Zealand with the intention of gaining EPA approval and full ACVM registration. Agricultural compounds will required Research Approval or Provisional Registration under the ACVM Act before use. The types of substances and application methods that will be used (see confidential Appendix A) will be similar to those commonly used on farm or companion animals.

We propose to conduct a number of field trials over a period of up to five years.It is likely that the substances will be classified as hazardous. Actives imported under this approval will only be used in containment in order to formulate trial products and /or be uses in notified field trials.

The maximum total quantity of each substance that may be imported is 200 litres or 200 kg. The maximum total quantity of each veterinary medicine that will be manufactured under this approval would be 2000 litres or 1000 kg

The maximum total quantity of each veterinary medicine that may be administered to animals under this approval is 100 litres or 150 kg per trial.

Sufficient information will be available to acknowledge the hazards and risks involved with the proposed use of these substances. At any time each veterinary medicine being transferred to a containment facility for trial work will be in the amounts of not more than 20L or 15kg solid per container.

The substances will be:

• imported into New Zealand as substances or completely finished product, or

• will be manufactured in exempt laboratory setting in New Zealand, for use by qualified personnel in trials.

It is proposed that the veterinary medicine substances would be used in containment trials in various regions of New Zealand and used in compliance with the controls assigned to this approval.

The veterinary medicine substances will be used in field and indoor trials on various animals. These will be applied to the animals at the trial sites by various administration methods (e.g. parenteral, oral, ruminal, topical, intramammary), the details being presented in the project plan (template provided in the Confidential section, Appendix 1) submitted confidentially to EPA. The location of the test sites will be provided to EPA and The Department of Labour, [Attn. HSNO Project Manager (Workplace Group) P O Box 3705, Wellington] as specified in the proposed controls.

Due to the nature of the veterinary medicines, it will exclude substances with application to water or by aerial application.

Product hazard classifications that the trial substances are likely to present are provided in the Confidential section, Appendix 1.

2.3 Is the information in this application relevant to import, manufacture or both?

Import the substance(s) only?	☐ Yes	☐ No
Manufacture the substance(s) only?	☐ Yes	☐ No
Import and manufacture the substance(s)?	☒ Yes	☐ No
If import only, indicate whether or not manufacture is likely in New Zealand:	☐ Yes	☐ No

.4 If the information in the application relates to manufacture of the substance(s) in New Zealand, provide information on the proposed manufacturing process and any alternatives.

Manufacturing processes will vary depending on the substance to be trialled. Please refer to the confidential section.

2.5 If this substance(s) needs an approval under any other legislation, has an application for this approval been made?
(Optional)

Name of approval	Application made
Agricultural Compounds and Veterinary Medicines Act 1997	☒ Yes ☐ No ☐ NA Application will be made as required
Food Act 1981	☐ Yes ☐ No ☒ NA
Medicines Act 1981	☐ Yes ☐ No ☒ NA
Chemical Weapons (Prohibition) Act 1996	☐ Yes ☐ No ☒ NA
Radiation Protection Act 1965	☐ Yes ☐ No ☒ NA
Biosecurity Act 1993	☐ Yes ☐ No ☒ NA
Resource Management Act 1991	☐ Yes ☐ No ☒ NA
Other (please specify):	
	☐ Yes ☐ No
	☐ Yes ☐ No
	☐ Yes ☐ No

Section 3 – Information on the substance(s)

Note that all information that is commercially sensitive must be attached as an appendix. The application form should be cross-referenced to the appendix but should be able to be read as a stand-alone document (which will be publicly available).

If approval is being sought for more than one hazardous substance, this section must be completed separately for each hazardous substance.

3.1 State the unequivocal identification of the substance(s).

This section should include all information necessary to unequivocally identify the substance(s) and may include:

- Chemical name (Chemical Abstracts Preferred Index name or IUPAC name)
- Common name
- Synonyms
- Trade names
- CAS Registry number
- Molecular formula
- Structural formula
- Impurities.

For mixtures, in addition to the above information being provided on the actual mixture, information is also required on the composition of the mixture – ie, the chemical name, CAS number, function (eg, active ingredient, emulsifier, surfactant, filler) and percentages of ALL components of the mixture (including non-hazardous components and impurities) should be provided. This information may be best expressed in tabular form. If the composition is variable, please ensure to state the limits.

If there are commercial reasons for not providing full information in the main part of the form, alternative approaches must be discussed with and agreed by the EPA. These must include the provision of a unique identifier of some kind.

The composition of each veterinary medicine substance to be evaluated will be provided confidentially to EPA prior to commencement of the trials.

3.2 Provide information on the chemical and physical properties of the substance(s).

Provide as much information as possible on the chemical and physical properties of the substance(s) [at 20°C and 1 atmosphere unless otherwise stated] – eg:

- Appearance (colour, odour, physical state or form)
- pH
- Density
- Vapour pressure
- Boiling/melting point
- Solubility in water
- Water/octanol partitioning co-efficient.

For mixtures, information is required on the chemical and physical properties of the mixture itself. However, if this information is not available, you should provide information on the chemical and physical properties of EACH hazardous component of the mixture.

Details of the formulation and chemical/physical properties of each of the substances to be trialled will be submitted confidentially to EPA prior to the start of the trials.

3.3 Provide information on the hazardous properties of the substance(s).

Information should be provided on the hazardous properties of the substance(s) known to the applicant. You should consider each of the six hazardous properties below and provide information on those hazardous properties. This information is needed in order to assess risks and determine whether or not, and how, the substance can be adequately contained.

- Explosiveness
- Flammability
- Oxidising properties
- Corrosiveness
- Toxicity
- Ecotoxicity.

If your substance is a mixture and you cannot provide direct information on its hazardous properties, you can apply mixture rules to the hazardous components of the mixture. If you do this, then you will need to provide information on the hazardous properties of each hazardous component of the mixture, and show your workings.

Details of the hazardous properties of each of the substances to be trialled will be submitted confidentially to EPA prior to the start of the trials.

3.4 Provide information on what will happen to the substance throughout its whole life, from its introduction into New Zealand, its uses, through to disposal.

The information provided needs to reflect the containment character of the application. It will be used in the development of exposure scenarios and the assessment of risks, and hence the specification of the containment conditions.

The life cycle of the substance in New Zealand is as follows

1. Manufacture or importation of a investigational substance
2. Storage of the investigational substance samples
3. Dispensing of samples into trial quantities
4. Transportation of trial samples to trial sites
5. Preparation of treatment mixture
6. Application of mixture
7. Disposal of surplus mixture
8. Disposal of used containers
9. Disposal of treated produce
10. Disposal of surplus samples
11. Site close off

The controls and management processes for these stages are covered in this application. In particular each new substance will be imported and/or manufactured fully packaged, with the substances contained in hard plastic/glass/metal bottle or other suitable containers. In all cases these will be packed in UN approved packaging that is suitable for the shipment to and within New Zealand. Transport workers, wharf workers will only handle the fully packaged product, comprising the outer package (usually cardboard or reinforced cardboard), and the inner package containing the substance. Exposure during transport, storage and handling is only possible through the breach of this packaging. The other parts of the lifecycle are covered in the controls in the confidential Appendix 1.

3.5 Provide information on the quantity of the substance proposed to be imported or manufactured.

This information is used in the development of exposure scenarios and the assessment of risks.

Approval is sought to:

1) import the maximum total quantity of 200 litres or 200 kg for each veterinary medicine,
2) manufacture the maximum total quantity 2000 litres or 1000 kg. Manufacturing will be limited to the manufacturing site specified in the application (Appendix 1 - Confidential Section) or any alternative manufacturing site as notified under control 9.
3) administer to animals the maximum total quantity of each veterinary medicine of 100 litres or 100 kg.

The quantity of product imported or manufactured for each trial will vary between trials depending on use rates, numbers of animals treated and replicates. The entire quantity imported or manufactured shall be: a) tested/stored in a secure laboratory, b) only part of it will be used in containment and according to the proposed controls.

Section 4 – Information on the proposed containment system

4.1 Provide information on the proposed containment system.

It is essential that good information is provided on the containment system because the adequacy of containment, in conjunction with the hazardous properties of the substance, will have a major impact on whether or not approval is given.

You will need to provide a description of the containment proposed AND information on how you intend to address the following issues (proposed controls):

- Methods for preventing the escape of the contained hazardous substance and preventing the contamination of the facility
- Methods for excluding unwanted organisms from the facility or to control organisms within the facility
- Methods for excluding unauthorised people from the facility
- Methods for preventing unintended release of the substance by experimenters
- Methods for controlling the effects of any accidental release of the substance
- Inspection and monitoring requirements of the containment facility.

A management plan may be attached as an appendix. This plan should specify the procedures for implementing the above methods for containing the substance(s), and provide details of the qualifications of the person responsible for implementing those controls.

The proposed containment system for the trials using these veterinary medicine substances will be designed to provide appropriate safeguards commensurate with the hazardous properties of the substances. The proposed containment system is provided in the confidential section, Appendix 1.

1. To limit the likelihood of escape of any contained hazardous substance or contamination by hazardous substance
2. To exclude organisms or control organisms
3. To exclude unauthorised people
4. To prevent unintended release of the substance by experimenters working with the substance
5. To control the effects of any accidental release of the substance
6. Inspection and monitoring requirements
7. Qualifications required of the person responsible for implementing the controls

Section 5 – Identification and assessment of risks

In completing this section, it is important that you take account of the proposed containment system you described in Section 4. We are particularly interested in knowing about risks that may still remain with the containment system in place. You will need to consider the effects on the environment and public health, including any social effects. You should also take account of the quantity of material involved and the number of different locations that may be involved.

Complete this section as far as you can.

5.1 Identify all of the risks of the substance(s).

Include information on potentially significant, possible risks of the substance and whether or not these risks are *likely* to be significant. It is important to think about the source of the risk – ie, the way in which the risk is created (the exposure pathway) and then the consequences of exposure. Risks should be considered in relationship to:

- the sustainability of native and valued introduced flora and fauna
- the intrinsic value of ecosystems
- public health (including occupational exposure)
- the relationship of Māori and their culture and traditions with their ancestral lands, water, sites, waahi tapu, valued flora and fauna, and other taonga
- the economic and related benefits to be derived from the use of the hazardous substance
- New Zealand's international obligations.

The veterinary medicine substances covered by this application are experimental and limited information is available therefore suitable controls have been proposed. There are a number of activities that provide pathways for escape from containment. These activities are:

- **Importation and transport** Insecure packaging or an accident could result in spillage of the formulations either on arrival in New Zealand and unloading or during transport to the containment facilities. In the event of a transport accident between the airport and the containment facilities the environment could be exposed to the substance. The substance will be transported in liquid or solid form and therefore the environment could come into contact with it if the packaging split and a member of the public (or the driver) attempted to clean it up. If water is used to wash the product away it could reach stormwater systems or waterways and result in adverse effects on terrestrial ecosystems.
- **Storage** Inadequate containment during storage of the substance, prior to use, could lead to effects to the ecosystems through direct contact or spillage.
- **Dispensing and Mixing** Similarly dispensing and mixing may pose risks to ecosystems if the product is spilt.
- **Use i.e. various administration methods** There is a risk of adverse environmental effects on ecosystems and species, during application, although in most cases the substance will be administered by a closed system of non-leakage equipment.
- **Disposal of surplus mix, surplus concentrate, treated produce.** Disposal risks relate to excess product remaining after the trial has been completed (at the storage facility), excess product taken to the trial sites and not used, and excess mixed product at the trial site. Excess product poses potential risks to ecosystems. Removal by contamination of unauthorised visitors/ animals accessing the site, or from product being moved from the site by water, air, or carried on workers clothing, may also lead to risks to the environment.
- **Accidents, natural hazards and sabotage** Risks may arise from accidents, natural hazards such as earthquakes, and through sabotage or deliberate misuse of the substance

The main benefit of the approval of this application is that Merial Ltd will be able to maximise the number of development candidates evaluated and thus provide new solutions for veterinary medicines, with the potential to provide farmers and growers in New Zealand new tools to manage animal health conditions in a safe and effective manner with minimal environmental impact.

5.2 Provide an assessment of the potential risks identified in Section 5.1.

An explicit risk assessment only needs to be provided for those risks which might be significant. The assessment should consider whether the identified risks can be adequately managed by the proposed containment system, and the substance(s) itself adequately contained.

The assessment should include the nature, probability of occurrence, and magnitude of each adverse effect. The uncertainty bounds of the information contained in the assessment should also be discussed.

(Optional)

	Hazard Low/Medium or High	Risk Low/Medium or High	Managed	Controls used in management
Importation and transport	Very Low	Low	Yes	Small amounts of product, suitable packaging, MSDS's
Storage	Very Low	Low	Yes	Suitable storage facilities
Dispensing and Mixing	Very Low	Low	Yes	Trained personnel
Application/Use of sample	Very Low	Low	Yes	Trained personnel Appropriate equipment
Disposal of surplus mix, surplus concentrate.	Very Low	Low	Yes	Trained personnel, procedure to return surplus concentrate to MERIAL.
Disposal of treated animals.	Very Low	Low	Yes	Trained personnel Project plan including ACVM approval requirements
Site Contamination	Low	Low	Yes	Trained personnel Small doses used
Accidents, natural hazards and sabotage	Very Low	Low	Yes	Suitable storage facilities and packaging, trained personnel

All risks can be adequately managed by the proposed containment system and the containment of the substance itself. The relatively small amounts of veterinary medicine substance being imported and/or manufactured at any one-time means that the risk involved is very low and the magnitude of any effect is low.

Risk to Māori:

Assessment of the known and possible adverse effects throughout the life cycle of the substance group on the relationship of Maori and their culture, traditions, ancestral lands, water, sites, waahi tapu, valued floras and fauna and other taonga including Taha wairua, Taha whanaunga, Taha hinengaro, Taha tinana, Economic Development Outcomes and Tirito O Waitangi Outomes has been conducted in accordance with the Table 1 assessment framework contained in the EPA New Zealand User Guide "Working with Maori under the *HSNO Act 1996*".

It is concluded that there will be minimal or no significant cultural effects likely from the import or manufacture of up to 200L (kg) of each of these substances into a laboratory**,** manufacture of up to 2000L (liquids) or 1000 kg (solids) of each of the new formulations in containment for use in animal studies located on selected sites that will comply with the proposed EPA controls.

The contained use of these substances (veterinary medicine) at only a few locations, away from public access and with no application to crops producing food for consumption, means there will be no involuntary community exposure and there will not be any significant exposure to the environment.

Section 6 – International considerations

6.1 The EPA is interested in whether this substance (or any of its components) has been considered by any other regulatory authority in New Zealand, or by any other country. If you are aware of this, please provide details of the results of such consideration.

(Optional)

It is likely that the same or similar substance(s) or one or more of the component active pharmaceutical ingredients will have been approved by the ACVM Group and the EPA. Additionally, most if not all of the non-active excipients will also have been approved by the EPA. EPA will be advised of the registration status of substances in any other country prior to the start of the trials.

Section 7 – Miscellaneous

7.1 Provide a glossary of scientific and technical terms used in the application.

The following is a glossary of scientific and technical terms used in this application.

Active ingredient	The component in the substance that is active as a veterinary medicine.
Substance	The final form in which the veterinary medicine is used in the trial.
Project	A series of individual trials to characterise chemical compounds and are conducted over one or more seasons.
Trial site	An area, being a group of separate but contiguous plots (either treated and/or untreated), with a specifically delineated and defined boundary.

7.2 Provide here any other information you consider relevant to this application that is not already included.

Not applicable.

Section 8 – Summary of public information

The information provided in this section may be used in the EPA's public register of substances, required under Section 20 of the HSNO Act.

This summary information will be used to provide information for the people and agencies (eg, Ministry for the Environment, Department of Conservation, Regional Councils etc) that will be notified of the application, and for potential submitters who request information. This information will also be used to prepare the public notice of the application.

For these reasons, applicants should ensure that this summary information does not contain any commercially sensitive material.

8.1 Name of the substance(s) for the public register:
Please use a maximum of 80 characters.

MARDGC1- Experimental Veterinary Medicine Substances

8.2 Purpose of the application for the public register:

This should include an abstract (in a maximum of 255 characters) giving information on the intended use of the substance and why an application is needed, based on its hazardous properties.

Approval to import or manufacture under containment conditions limited quantities of experimental veterinary medicine substances for their use in treatment and control of animal health conditions (field trials) and to confirm product stability and to validate the production process.

8.3 Use categories of the substance(s):

The EPA has adopted the system of use categories developed by the European Union, which identify various functional uses of substances. This information is pertinent to the assessment of exposure scenarios and the determination of risk, and is also useful for building up a profile of the substance. There are three sets of use categories. Within each of these, applicants should state which use categories are relevant to all intended uses of the substance(s).

1. Main category: There are four main categories.
2. Industry category: There are 16 industry categories.
3. Function/Use category: There are 55 function/use categories.

(Optional)

Main category: 3 – Non-dispersive use
Industry category 1 – Agricultural industry
Function/Use category: 41 – Pharmaceuticals-veterinary medicine

8.4 Executive summary:

In this section, the applicant should provide a summary of information contained in this application, including:

- the identification of the substance, its hazardous properties, intended uses and disposal
- an assessment of the adverse effects of the substance
- information on the proposed containment.

This is a generic application for approval to import or manufacture under containment conditions limited quantities of experimental veterinary medicine substances which may contain toxic and/or ecotoxic active and inactive ingredient(s) for the purpose of further characterisation for their use in treatment and control of animal health conditions (field trial) and to confirm product stability and to validate the production process. The intention is to conduct small-scale contained field trials to provide information relevant for the further development of these substances.

The containment practices proposed with this application are designed to contain the substances and manage any hazards and risk.

The test formulations do not present an additional risk to human or environmental safety, and are comparable with the hazard profile of other marketed veterinary medicines.

All clinical trials will be conducted in accordance with NZ and international regulatory guidelines, by suitably qualified personnel. Due to the small volumes of test substances being used and the proposed controls, the risk to human and environmental health is minimal.

16 SEPT 2013

Signature **Date**

Appendix 1 – Commercially sensitive information