



Microbial Agricultural Chemicals

Application information for registration under the Agricultural
Compounds and Veterinary Medicines Act 1997

11 August 2016

Title

Guidance Document: Microbial Agricultural Chemicals

About this document

This document explains the information that should accompany an application to register an agricultural chemical that contains a micro-organism under the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997.

Related requirements

ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand
Provisional Registration in New Zealand: ACVM Information Requirements

Document history

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1 Purpose

This document explains the information that should accompany an application to register an agricultural chemical that contains a micro-organism under the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997.

The information specified is in addition to the requirements in the following publications:

- ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand
- Provisional Registration in New Zealand: ACVM Information Requirements.

Therefore, these documents should be read in conjunction with each other.

2 Background

Before being imported, manufactured, sold, or used in New Zealand, agricultural compounds (including trade name products that contain a micro-organism) must be registered under the ACVM Act unless the trade name product is exempt under the ACVM (Exemptions and Prohibited Substances) Regulations 2011. Registration is required:

- to prevent or manage risks to trade in primary produce, public health, animal welfare, and agricultural security; and
- to make sure that the use of agricultural compounds does not result in breaches of domestic food residue standards; and
- to ensure the provision of sufficient consumer information.

Agricultural compound trade name products (TNPs) requiring registration are assessed following the risk assessment model under the ACVM Act. An application for registration must be in the form '[ACVM 1: Registration of an ACVM trade name product](#)' found on the ACVM website.

An application for registration of an agricultural compound TNP can be lodged provided the substance is not:

- a prohibited agricultural compound under the ACVM (Exemptions and Prohibited Substances) Regulations 2011; or
- exempt from registration under the ACVM (Exemptions and Prohibited Substances) Regulations 2011.

You are able to determine prohibition and exemption by using the [ACVM \(Exemptions and Prohibited Substances\) Regulations 2011](#) and the '[class determination](#)' information on the ACVM website. Alternatively, MPI offers a class determination service (fees apply).

2.1 What are 'microbial agricultural chemicals' (MACs)?

For the purposes of ACVM registration, microbial agricultural chemicals (MACs) are trade name products that contain micro-organisms in the product formulation and are used as agricultural chemicals. These micro-organisms are the active ingredient in the formulation and are here referred to as microbial active ingredients (MAIs).

MAI is defined as any organism classified as a micro-organism, including but not limited to bacteria, protozoa, fungi and viruses or the genetically modified or naturally occurring mutants of any of these micro-organisms, intended for sale to manage plants directly. MAIs include whole organisms (either viable or non-viable), organism organelles, metabolites produced by the organism, organism spores or

occlusion bodies used for the control or management of invertebrate pests, weeds or microbial pathogens of crops.

If the MAC trade name product is exempt from registration under Schedule 2 of the ACVM (Exemptions and Prohibited Substances) Regulations 2011, then the MAC trade name product does not require registration under the ACVM Act. However, exempt products must comply with the relevant conditions in the Regulations.

2.2 What are NOT microbial agricultural chemicals?

The following are not MACs:

- plant extracts, hormones, semiochemicals, natural plant growth regulators, insect growth regulators and other enzymes
- metabolites produced by a micro-organism that have been isolated as independent active ingredients in their own right
- gene vectors for the introduction of pesticide tolerance and pest resistance
- macro-organisms, which include insects, mites, nematodes, and any other organisms not considered to be micro-organisms.

Metabolites (e.g. toxins, venoms, enzymes or other biochemical substances) naturally produced by macro-organisms are not considered separate from the macro-organism unless the metabolite is isolated from the macro-organism and developed into an agricultural compound in its own right.

Micro-organisms that are part of a naturally occurring macro/micro-organism complex (e.g. entomopathogenic nematode associated with a symbiotic adventitious bacterium or fungus) are not considered separate from the complex; and the complex is considered to be a macro-organism. The complex is not an agricultural compound. However, if the micro-organism is separated from the macro-organism and developed as a MAC in its own right, then it would be an agricultural compound.

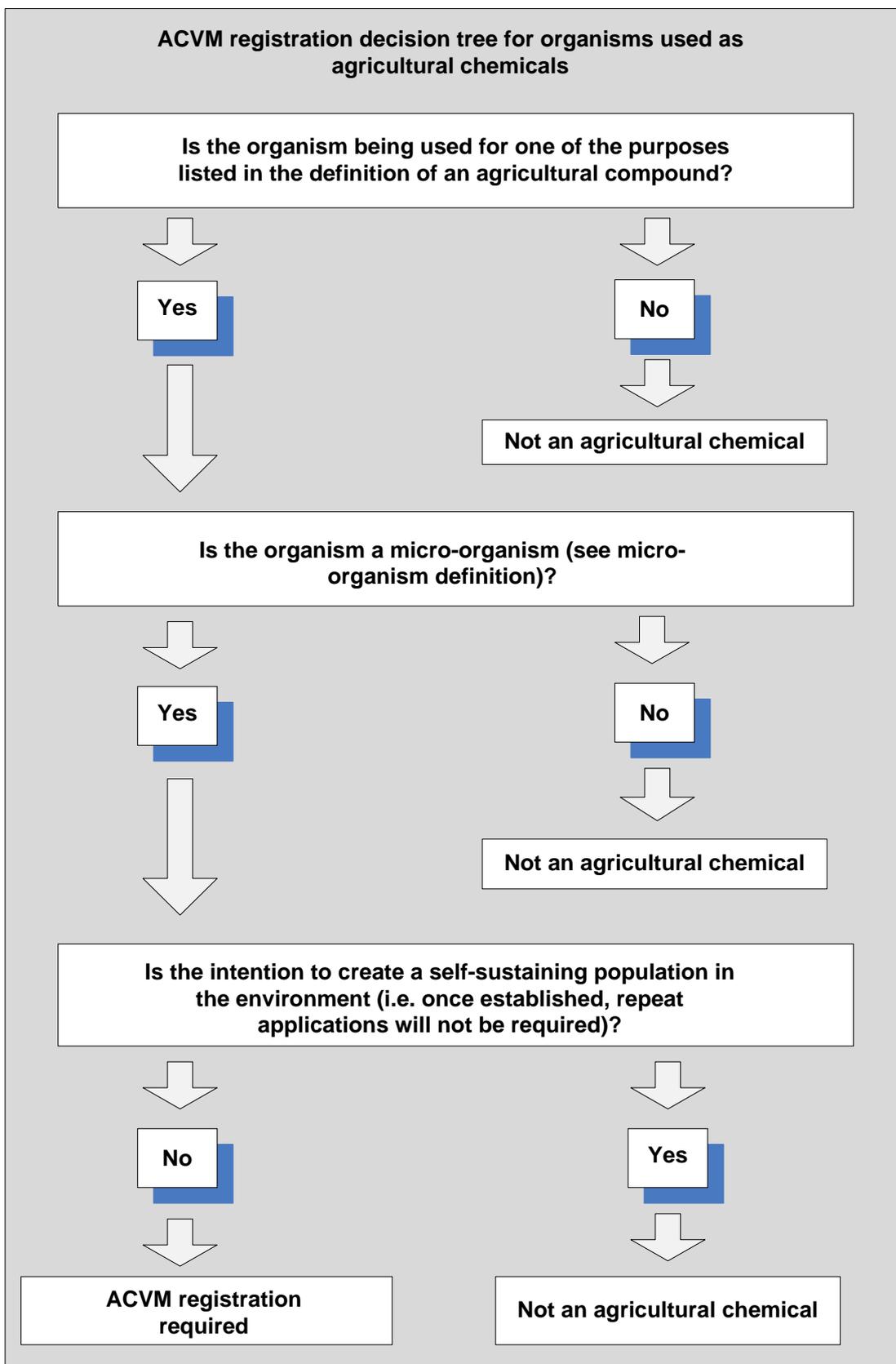
Macro-organisms that are artificially induced to be carriers or applicators of agricultural compounds (chemical or microbiological) are not agricultural compounds themselves. The chemical or microbiological entity effecting an agricultural benefit will be the agricultural compound.

- Under the scope of the ACVM Act, biological control agents (BCAs) are not MACs. BCAs are used with the intention of creating a sustainable, self-perpetuating population in the environment as part of a classical biological control programme. An initial release (or series of releases) of the BCA is required, but little or no intervention should be necessary after initial establishment of the BCA in the environment.

Metabolites (e.g. toxins, venoms, enzymes or other biochemical substances) naturally produced by a BCA are not considered separate from the BCA unless the metabolite is isolated from the BCA and developed into an agricultural compound in its own right.

If you are unable to determine whether the microbial organism fits the scope of MAC, contact Agricultural Compounds and Veterinary Medicines (approvals@mpi.govt.nz) prior to release of the product into the marketplace.

Decision tree for the purposes of registration of a microbial agricultural chemical under the ACVM Act.



3 Definitions and abbreviations

Act means the Agricultural Compounds and Veterinary Medicines Act 1997

expiry specifications means the specifications the product must comply with over the shelf life of the product

MAI means microbial active ingredient and refers to the technical grade active component used in the MAC trade name product

MAC means microbial agricultural chemical and refers to the trade name product

MRL Notice means the Food Notice: Maximum Residue Levels for Agricultural Compounds

release specifications means the specifications that must be tested for every batch (and complied with) prior to release of the product into the marketplace.

4 Information needed

The minimum information MPI considers necessary is numbered in each section, while any further guidelines are given (without numbers) at the end of a section under '**Additional guidance**'. Guidelines reflect principles commonly recognised by the scientific community as appropriate and necessary for collecting scientific data. MPI recognises that there are acceptable methods, other than those described in this guideline, that are capable of achieving the principles of this document.

Applicants are responsible for providing all information required by MPI to make a decision on the application. Applications that do not contain the required information will not be assessed. If further advice is required you are advised to contract the services of an appropriate consultant prior to submitting your application.

4.1 General data requirements

An application for registration of a MAC has to include technical data and/or scientifically sound arguments to support:

1. the quality, purity and stability of the product
2. the product's efficacy for all label claims
3. crop safety
4. in regard to maximum residue levels (MRLs):
 - the establishment of an MRL resulting from trial work that adheres to the residue guidelines (see 4.5 below), or
 - an argument or data to show that the MAI fits an existing exception in the MRL Notice (Schedule 2) or to promulgate a new exception
5. any possible impact on trade resulting from the use of the MAC in crops, and/or carry over residues as a result feed crops in food-producing animals, if applicable.

Additional guidance

The data requirements will vary depending on the nature of the MAI, its origin (local or imported), its host specificity, nature of dispersion and other factors.

For detailed information that has to be provided for full and provisional registrations, respectively, see:

- ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand
- Provisional Registration in New Zealand: ACVM Information Requirements.

The following explains what extra, or modified, information may be required for MACs.

4.2 Biological properties

In order to make a meaningful risk/benefit assessment of the proposed use of the MAC, MPI requires information on the biological properties and efficacy of the MAI. It is important to know which species are susceptible to the MAI and the degree of specificity for the target pest(s), if the MAI is naturally occurring in New Zealand and in what circumstances and, if appropriate, its geographical distribution. Information on the likely biological effects arising from use is required in order to assess possible long-term changes in the ecology of the crop and in the environment.

Provide the following information on the MAI:

1. brief description of the biology, including life cycle and growth stages (if applicable)
2. target pest(s) or disease(s)
3. history of the MAI and its use
4. natural occurrence and geographical distribution
5. site of colonisation, mode of action and of entry into host (if known)
6. effective dose level
7. description of proposed application method(s), and how product efficacy and stability may be affected by application method(s)
8. transmissibility and persistence of the MAI under likely environmental conditions (such as effects of temperature, moisture, exposure to air)
9. specificity, host range and effects on species other than the target pest (including species closely related to the target pest or disease) to obtain the taxonomic boundary of susceptibility:
 - studies should include colonisation capacity, pathogenicity and transmissibility, and
 - indicate whether the MAI is closely related to a crop pathogen or to a pathogen of vertebrate species or a non-target invertebrate species
10. if the MAI is closely related to a crop pathogen or to a pathogen of a vertebrate species, laboratory evidence of genetic stability, i.e. laboratory evidence of mutation rate using appropriate tests (consultation at an early stage with MPI is advisable)
11. if the MAI is genetically modified, a brief description of the method that was used, along with information on:
 - the donor organism, the vector and the recipient organism
 - genetic stability of MAI under environmental conditions of proposed use, and
12. any other likely biological effects arising from use.

Additional guidance

Samples of the MAI should be deposited in one or more recognised reference collection. To deposit samples in a public or commercial recognised reference collection in New Zealand, contact Landcare Research at:

International Collection of Micro-organisms from Plants (ICMP)

Landcare Research

Tel: 64 9 574 4115

Email: icmp@LandcareResearch.co.nz

4.3 Chemistry and manufacturing

Provide the following information about the MAI used in the formulated product:

1. **Taxonomy**
Provide full taxonomic description of the MAI including serotype, strain or mutant, common name, and manufacturer's code number/synonym (if applicable).
2. **Identification**
State the appropriate tests, procedures and criteria used for identification of the MAI, such as morphology, primers, biochemistry and/or serology.
3. **Isolation process**
State the process by which the MAI is isolated, multiplied and stored.
4. **Seed line**
Provide details on the history of the original seed line. It has to be traceable to the current seed line or else independent verification of identity and absence of contamination of the current seed line has to be produced.
5. **Unformulated material**
Describe the unformulated material, such as the state and stage of the MAI (e.g. viable, non-viable, spores), colony forming units (cfu)/ml, nature and identity of any culture media, impurities, by-products, and content of extraneous organisms. State allowable levels of contamination.
6. **Batch analysis**
Provide batch analysis of the MAI, with purity and all relevant parameters measured (including showing absence of contamination if relevant).
7. **Batch analysis certificates**
All batch analysis certificates should clearly indicate name and address of the manufacturer(s) of the MAI, date of manufacture, batch size, batch identity, and site of manufacture.
8. **Quality control**
Provide details of the quality control process used to ensure that the composition of the technical grade MAI intended for integrated production processes is valid for each batch. Supply this for all MAI manufacturers.
9. **Concentration**
State the method for identifying the concentration of the MAI, either through direct techniques (e.g. counting) or through efficacy/pest mortality studies.
10. **Contamination or impurities**
State methods for identifying and quantifying contamination or impurities, including of any impurities that have been identified as being of toxicological significance (if any).

Additional guidance

It may be hard to delineate between "technical grade MAI manufacturing" and "formulated product manufacturing" (final product), especially if manufacturing is done as part of one process. However, for the purpose of specifications, batch analysis and impurities associated with the technical grade MAI, the MAI is considered to be at the point when the MAI is harvested, isolated and stored for future assimilation in the batch production of the final product.

Information on the taxonomy of the MAI is required for precise identification, establishing biological purity for registration purposes and, ultimately, for quality control of the commercial product. Consult MPI's ACVM Group and the EPA if difficulties exist in taxonomy so that the registrant can be sure of having cultures identified.

Any data generated should follow the requirements outlined in the ACVM Research Standard.

Formulated trade name product

Provide the following information on the MAC formulated trade name product:

1. **Trade name**
2. **Type of formulation**
3. **Composition of formulation**, including:
 - quantity
 - identity (including names and CAS numbers)
 - purpose of all active (technical grade MAI) and non-active ingredients such as diluents, ultra-violet protectors, water retaining agents.
4. **Formulation properties**

Describe any properties of the formulated product that differ from the MAI, including those that are designed to reduce hazards (such as encapsulation of spores, binding to substrates).
5. **Management of microbial contamination**

Describe microbiological purity, nature and identity of any culture media, impurities and content of extraneous organisms.
6. **Metabolites**

Describe relevant metabolites produced by the MAI: provide tests showing absence (or levels) of metabolites of toxicological relevance and describe methods of analysis.
7. **Manufacturer**

Provide name and physical address (include details for all manufacturers if more than one).
8. **Production process**

Provide summary in the form of a flow diagram of the manufacturing process identifying critical quality control points.
9. **Quality control**

State which parameters are measured at the points identified in the manufacturing flow diagram and at release, provide methods:

 - include methods for quantifying and identifying any contaminants
 - provide a full method description for in house methods
 - reference CIPAC methods.
10. **Analytical methods**

Used to determine the content of the technical grade MAI in the formulation (and its contaminants – either of chemical or microbiological nature) and methods to verify genetic stability (if a GMO)

 - reference CIPAC methods if appropriate, otherwise describe methods in full
 - demonstrate that all analytical methods used to determine the concentration(s) of the MAI in the formulated product are fit for purpose.
11. **Batch analysis (e.g. potency assay, number of live organisms/ml, mortality assay) of a commercial batch**

Provide results for all parameters specified in the release specifications, date of manufacture and batch number.

All batch analyses of the formulated product must clearly indicate:

 - date of manufacture
 - batch size and identity
 - site(s) of manufacture.
12. **Release and expiry specifications of the trade name product**

If an overage is used for the MAI, state and provide rationale for the amount of overage used.

Provide an explanation to support the release and expiry specifications.

13. Stability

Provide results from stability trial of formulated product:

- show effects of temperature change, retention of biological activity in storage, any increase in contamination or by-products and all parameters given in the expiry specifications
- supply details of the trial, packaging material, method of packing and storage, temperature, duration and size of sample used in trial
- state the recommended shelf-life and methods of analysis.

Real time stability data is required rather than accelerated (high temperature) stability trials.

- if specific storage conditions are required (such as refrigeration or freezing), detail these
- conduct storage stability testing according to the type of formulation and in accordance with the recommended storage conditions.

14. Packaging type(s)

Include size, material, any features specific to the MAC. Packaging must be designed to adequately contain the MAC over the product shelf life.

Additional guidance

Recommended physicochemical parameters based on formulation type to be used for quality control, batch analysis and release/expiry specifications are listed in the Annex 1 of the Chemistry and Manufacture of Agricultural Chemicals. Tested parameters must be representative and ensure that the wider product properties are consistent throughout the product shelf life. Applicants are required to provide a rationale supporting any deviations from general limits of these physical parameters.

Relevant metabolites produced by the MAI are metabolites likely to have an adverse effect on food or feed crops in a way that could adversely impact animal or human health.

MPI's Biosecurity team and the EPA will also require additional information on any contaminating organisms deemed 'New Organisms' and whether they are of pathogenic, infective or toxicological concern (or would need to be assessed to cover these points).

Any data generated should follow the requirements outlined in the ACVM Research Standard.

4.4 Efficacy and plant safety data

1. Provide data to show that the MAC trade name product, when used according to directions, is effective and safe for the purposes claimed in New Zealand under local conditions.
2. The total number of field trials will be dependent upon the robustness of the supporting information, but also how consistent the results are for all trials (e.g. in all conditions and on representative varieties over multiples seasons and during the critical periods). Field trials should:
 - be performed on relevant crop varieties and account for varieties more susceptible to the pest/disease/weed
 - include varieties typically sensitive to phytotoxicity
 - cover critical use periods for efficacy and phytotoxicity within the use window, and
 - be conducted in the main growing areas or at least conditions representative of these.
3. The data should clearly support the claims and directions that will be proposed on the product label.
4. Overseas data may be used to support and/or replace local field trials for the purposes of registration if the data provided is shown to be relevant to the application. If you are providing overseas data to support the registration of a trade name product, the supporting information should meet the following criteria:

- the formulation of the product must be the same used in New Zealand
- target pest/disease/weed and its life cycle must be the same as in New Zealand
- field trials must be performed in similar growing/environmental conditions as in New Zealand, and
- use patterns, including application rates and timing, must be the same as those proposed in New Zealand.

Additional guidance

Any data generated should follow the requirements outlined in the ACVM Research Standard.

4.5 Residue data

1. If the MAI, or its metabolites, have been demonstrated to affect food or feed crops in a way that could adversely impact animal or human health and is applied on food-producing crops or crops used for animal feed, provide the following information:
 - identification of viable and non-viable residues on treated crops at harvest or in grazing animals, the viable residues by culture or bioassay and non-viable by appropriate techniques
 - likelihood of multiplication in or on animals, crops or food, and its effect on food quality and safety
 - extent of indirect contamination of adjacent non-target crops, other plants, soil and water that may get into the food chain, and
 - presence of metabolites of toxicological relevance after the application of the product and at harvest or grazing.
2. Information specified above is in addition to the requirements in Residue Data for Agricultural Chemical Registration.

Additional guidance

It may be necessary to identify and measure residues remaining on an edible crop at harvest or in grazing animals following the use of MACs. This information is of particular importance when toxicological data suggests there may be a hazard to grazing animals and consumers. Although no known human pathogens are involved, there may be objections to or reasons for determining the presence of biologically active or inactive material on food. If the MAI remains active for a significant period the question of further multiplication should be considered, as should contamination of non-target crops, water and the environment generally. While NZ EPA will consider the effect of any contamination of toxicological concern on the environment, MPI will still require further information in this area if it is suspected that the contamination may end up in the food chain.

If the MAI (and its metabolites of toxicological concern) is likely to be present on food-producing crops or crops used for animal feed, an MRL or an exception from an MRL will be required under the MRL Notice.

MPI will assess the information provided to determine if the microbe fits under any existing MRL exceptions, for example the exception for MAIs, or whether an application for an MRL or MRL exception is required. Existing MRLs and exceptions can be found in the latest MRL Notice.

In many cases, setting an MRL under the MRL Notice is not appropriate. For example:

- the MAI is viable at harvest and may still reproduce after harvest, so while the level at harvest may be measurable it is not relevant
- the residue levels at harvest cannot be measured due to confounding factors in the environment (such as natural presence of a similar organism).

4.6 Toxicological and pathogenicity data

1. If the MAI(s), or its metabolites, have been demonstrated to affect food or feed crops in a way that could adversely impact animal or human health, provide MPI with information on pathogenicity and toxicological data in respect to mammals for the organism and any metabolites or contaminants produced.

Additional guidance

The information must cover the colonisation capacity of the living MAI and reproduction potential. Some assessment of acute toxicity and pathogenicity will normally be required. More prolonged studies with the MAI and/or any relevant metabolites or contaminants will be required if effects are seen. Carcinogenicity, genotoxicity and teratogenicity studies may be appropriate for those MAIs that are either known or may be shown to produce toxic substances.

Much of the above is likely to be assessed by EPA. However, if there may be a concern regarding animal or human health on food or feed crops, additional information for the MAI and any metabolites or contaminants will be required.

4.7 Off-target effects

1. If the MAI(s), or its metabolites, have been demonstrated to affect food or feed crops in a way that could adversely impact animal or human health, provide a dossier accounting for what is already known of the biological 'side effects' on the environment of the use or natural occurrence of the MAI. This includes any information relevant to likely off-target exposure of food or feed crops (such as ingestion by mammals).

Additional guidance

Consideration should be given to off-target animal welfare and human dietary intake risks.

A MAI may harm non-target species in and beyond a treated crop if it causes diseases that are likely to spread.

5 Non-ACVM requirements

EPA approval

The Environmental Protection Authority (EPA New Zealand) also has specific requirements for hazardous substances, for organisms that are new to New Zealand, and for genetically modified organisms (GMOs).

MPI will not approve applications (either provisional or full registration) for any formulations containing micro-organisms until an appropriate EPA approval is obtained (both from a new organism perspective, if applicable, as well as a component of a potential hazardous substance).

For new organisms (including GMOs), contact EPA New Zealand at:

EPA New Zealand
PO Box 131
Wellington
Tel: 64 4 916 2426
E-mail: NewOrganisms@epa.govt.nz

For hazardous substances, contact EPA New Zealand at:

EPA New Zealand
PO Box 131
Wellington
Tel: 64 4 916 2426
E-mail: hazardous.substances@epa.govt.nz

Biosecurity clearance

MPI will not approve applications (either provisional or full registrations) for any formulations containing a MAI unless the application is accompanied by the appropriate biosecurity clearance. These permits will either be:

- an approval to introduce the microbe into New Zealand, or
- a statement from MPI's Biosecurity saying that the microbe in the trade name product is already present in New Zealand and is not an unwanted organism.

For material of animal origin	For material of plant origin
Application to Import Biological Products, Micro-organisms and Cell Cultures	Application for Permit to Import Micro-organisms or Biological Products
<p>Contact: Animal Imports/Exports Ministry for Primary Industries P O Box 2526 Wellington Tel: 64 4 894 0100 Fax: 64 4 894 0733 Email: animalimports@mpi.govt.nz</p>	<p>Contact: Plant Imports Team Ministry for Primary Industries P O Box 2526 Wellington Tel: 64 4 894 0862 Fax: 64 4 894 0662 Email: plantimports@mpi.govt.nz</p>

Live organisms

There is a further requirement for the importation of live organisms into New Zealand. The importer must meet the requirements of the relevant Import Health Standard for each importation of the trade name product. This standard ensures that the imported product is not accompanied by any other organism and may require an import health permit prior to importation.