Ministry for Primary Industries
Manatū Ahu Matua

ACVM Requirement

Microbial Agricultural Chemicals

Information requirements for registration of a microbial organism used as an agricultural chemical

[Document Date]

Issued under the Agricultural Compounds and Veterinary Medicines Act 1997

New Zealand Government

TITLE

ACVM Requirement: Microbial Agricultural Chemicals

COMMENCEMENT

[This ACVM Requirement comes into force on [Effective Date]]

ISSUING AUTHORITY

[This ACVM Requirement is issued under section 10 of the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997]

Dated at Wellington this ... day of 2016

Allan Kinsella
Director, Systems Audit, Assurance and Monitoring
Ministry for Primary Industries
(acting under delegated authority of the Director General)

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Introduction

This introduction is not part of the ACVM Requirement, but is intended to indicate its general effect.

Purpose

This document specifies the information that must accompany an application to register a trade name product that contains a microbial agricultural chemical under the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997.

The requirements are in addition to the requirements for agricultural compounds in the following publications:

- ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand
- Provisional Registration in New Zealand: ACVM Information Requirements
- Chemistry and Manufacture of Agricultural Chemicals: ACVM Information Requirements.

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

Background

Before being imported, manufactured, sold or used in New Zealand, agricultural compounds (including microbial agricultural chemicals) must be registered under the ACVM Act, unless the product is exempt. Registration is required:

- to manage risks to trade in primary produce, public health, animal welfare, and agricultural security;
- 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.

Microbial agricultural chemicals requiring registration are assessed following the risk assessment model under the ACVM Act. Only trade name products can be registered. An application for registration must be in the form 'ACVM 1: Registration of an ACVM trade name product' found on the ACVM website at:
http://www.foodsafety.govt.nz/elibrary/industry/reg-pds-ac/index.htm

Anyone can lodge an application for registration of a microbial agricultural chemical as long as the substance is not:

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

You are able to determine prohibition and exemption by using the ACVM (Exemptions and Prohibited Substances) Regulations and the 'class determination' information on the ACVM website. Alternatively, MPI offers a 'class determination' service. For more information about 'class determination' go to:

http://foodsafety.govt.nz/elibrary/industry/class-determination-request-form/index.htm

Scope of 'Microbial Agricultural Chemicals'

For the purposes of ACVM registration, microbial agricultural chemicals are trade name products that contain microorganisms. Microorganisms are here defined as any classified as a microorganisms, including but not limited to bacteria, protozoa, Rickettsia, fungi and viruses or the genetically modified or naturally occurring

mutants of any of these microorganisms, intended for sale to manage plants directly. This includes control or management of invertebrate pests, weeds or microbial pathogens of crops.

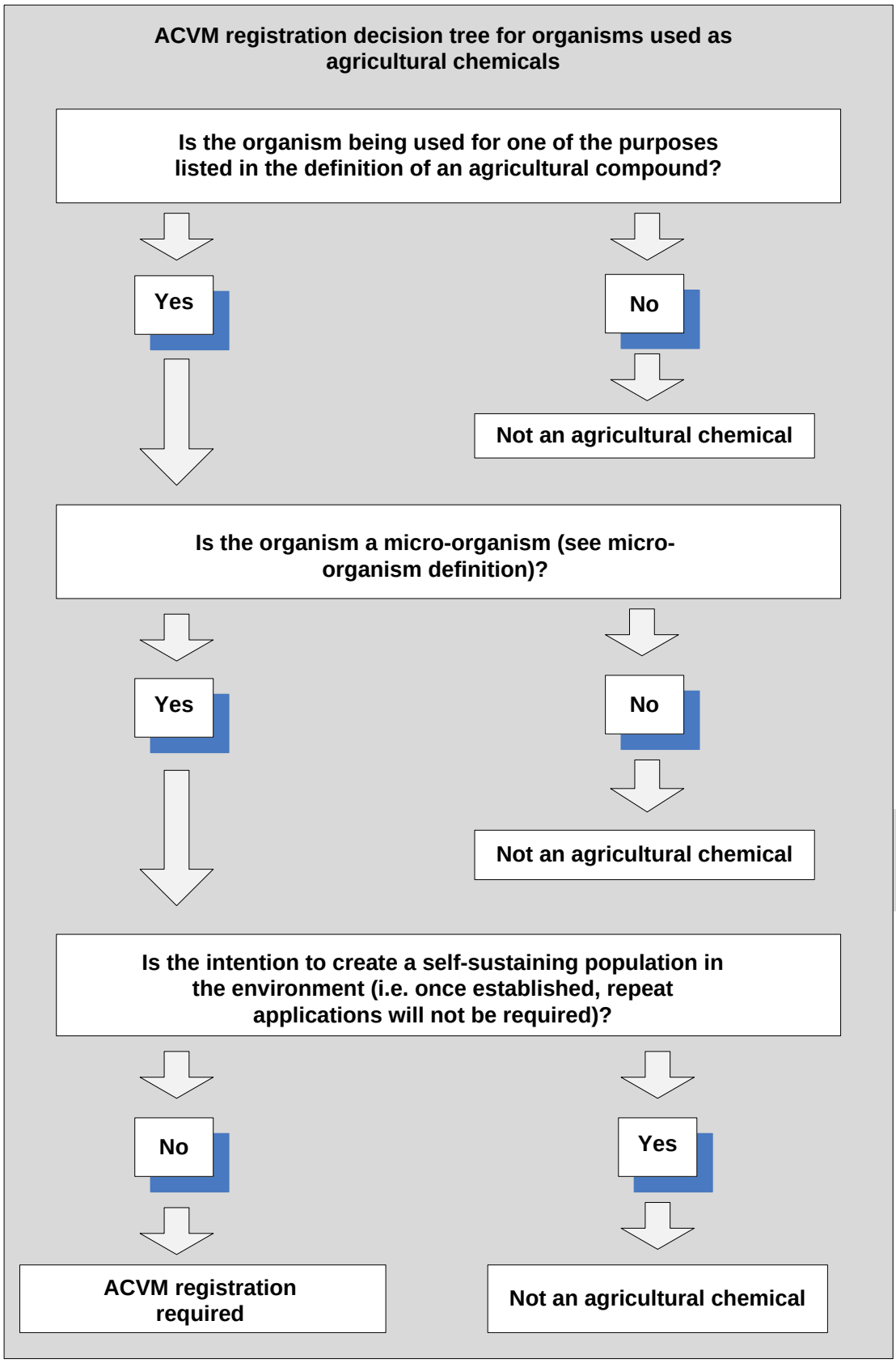
Microbial agricultural chemicals that increase beneficial microbial activity are considered to be fertiliser additives and are exempted from the requirement for ACVM registration. To be exempt from registration, the product must comply with the relevant conditions in the ACVM (Exemptions and Prohibited Substances) Regulations 2011.

Out of scope

- plant extracts, hormones, semiochemicals, natural plant growth regulators, insect growth regulators and other enzymes
- gene vectors for the introduction of pesticide tolerance and pest resistance
- Macro-organisms are not microbial agricultural chemicals. Macro-organisms include insects, mites, nematodes, and any other organisms that as a rule are not defined as a microbial agricultural compound.
  - 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 an agricultural compound in its own right, then it would be an agricultural compound if the organism fits the definition of microbial agricultural compounds.
  - 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.

- Biological control agents are not microbial agricultural chemicals. Biological control agents are used with the intention of creating a sustainable, self-perpetuating population in the environment. An initial release (or series of releases) is required, but little or no intervention should be necessary after initial establishment of the biological agent in the environment.
  - Metabolites of biological control agents can be agricultural chemical in their own right if they are isolated from the biological control agent and developed into an agricultural chemical in their own right. Conversely, if the biological control agent is the agent effecting an agricultural benefit via a naturally produced metabolite, then the metabolite itself will not be considered separate from the biological control agent.

Decision tree for the purposes of registration of a microbial agricultural chemical



Who should read this ACVM Requirement?

This requirement applies to:

- all persons applying to register a trade name product containing a microbe as the active ingredient in New Zealand; and
- all persons acting as consultants for registering microbial agricultural chemical trade name products containing a microbe as the active ingredient in New Zealand.

Why is this important?

If you fail to comply with these requirements, your application for product registration will be declined.

Document history

These requirements are being issued for the first time. They do not supersede or replace any other versions.

Other information

Legislative requirements

Before a microbial agricultural chemical is imported into New Zealand, MPI must approve it. The Environmental Protection Authority (EPA New Zealand) also has specific requirements for new or genetically modified organisms (GMOs).

For new organisms (including GMOs), contact:

EPA New Zealand
PO Box 131
Wellington
Tel: 64 4 916 2426
Fax: 64 4 914 0433
E-mail: NewOrganisms@epa.govt.nz

Additional requirements
MPI will not approve applications (either provisional or full registrations) for microbial agricultural chemicals unless the application is accompanied by the appropriate biosecurity permit. This permit will either be:

- an approval to introduce the microbe into New Zealand; or
- a statement from the agency holding the appropriate collection 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
Contact: Animal Imports/Exports Biosecurity New Zealand Ministry for Primary Industries PO Box 2526 Wellington	**Contact:** Plant Imports Team Biosecurity New Zealand Ministry for Primary Industries PO Box 2526 Wellington

Tel: 64 4 894 0100 Fax: 64 4 894 0733 Email: animalimports@mpi.govt.nz	Tel: 64 4 894 0862 Fax: 64 4 894 0662 Email: plantimports@mpi.govt.nz

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.

Part 1: Requirements

1.1 General data requirements

(1) Applications for registration of a microbial agricultural chemical must include technical data and/or scientific sound arguments to support:

a) the quality, purity and stability of the product; and
b) the product's efficacy for all label claims; and
c) crop safety; and
d) the establishment of a maximum residue limit (MRL) (or argument/data to gain an exemption) resulting from trial work that adheres to the residue guidelines (see ACVM website); and
e) any possible impact on trade resulting from the use of the microbial agricultural chemical in crops, and/or carry over residues as a result feed crops in food-producing animals; and
f) compliance with the domestic food residues.

(2) Applications for ACVM registration of a microbial agricultural chemical must follow the requirements outlined in this document.

Guidance

- The data requirements will vary depending on the nature of the microbe, its origin (local or imported), its host specificity, nature of dispersion and other factors.
- Refer to the publications:
  - ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand
  - Provisional Registration in New Zealand: ACVM Information Requirements.
- The documents listed above detail information that must be provided for full and provisional registrations, respectively. The following explains what extra, or modified, information may be required for biological agricultural chemicals.

1.2 Biological properties

Guidance

- In order to make a meaningful risk/benefit assessment of the proposed use of the microbial agricultural chemical, MPI will require information on the biological properties and efficacy of the microbe. It is important to know which species are susceptible to the microbe and the degree of specificity for the target pest(s), if the microbe 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.

(1) You must provide the following information on the microbe:

a) brief description of the biology of the microbe, including life cycle and growth stages (if applicable); and
b) target pest(s) or disease(s) affected by the microbe; and
c) history of the microbe and its use; and
d) natural occurrence and geographical distribution; and
e) site of infection, mode of action and of entry into host; and
f) infective dose level and indication of numbers of organisms to be used or released; and
g) description of proposed application method(s), and how infectivity and product stability may be affected by application method(s); and

h) transmissibility and persistence of the microbe under likely environmental conditions (such as effects of temperature, moisture, exposure to air); and
i) 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 infectivity, pathogenicity and transmissibility. Indicate whether organism is closely related to a crop pathogen or to a pathogen of vertebrate species or a non-target invertebrate species; and
j) if the microbe 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 should be produced (consultation at an early stage with the registration authorities is advisable); and
k) if the product is genetically modified, brief description of the method that was used, along with information on the donor organism, the vector and the recipient organism. Genetic stability of microbe under environmental conditions of proposed use; and
l) any other likely biological effects arising from use.

Guidance

- We recommended that a sample of the microbe be deposited in one or more recognised reference laboratories.

1.3 Chemistry and manufacturing

(1) You must provide information that identifies the microbe, including:

a) a full taxonomic description of the microbe including serotype, strain or mutant, common name, and manufacturer's code number/synonym (if applicable); and
b) the appropriate tests, procedures and criteria used for identification of the microbe, such as morphology, primers, biochemistry and/or serology; and
c) the process by which the microbe is isolated, multiplied and stored; and
d) details on the history of the original seed line and it must be able to be traced to the current seed line, or else independent verification of identity and absence of contamination of the current seed line must be produced; and
e) description of the unformulated material, state and stage of the organism (such as spores), microbiological purity (such as colony forming units (cfu)/ml; give number of live organisms, although weight or volume can be used as well, nature and identity of any culture media, impurities, by-products, and content of extraneous organisms. State allowable limits of contamination; and
f) batch analysis of the microbe, with purity and all relevant parameters measured (including showing absence of contamination if relevant); and
g) details of the quality control process used to ensure that the composition of the inoculum is valid for each batch. This must be supplied for all microbe manufacturers; and
h) the method for identifying the concentration of the microbe, either through direct counting techniques or through efficacy/pest mortality studies; and
i) methods for identifying and quantifying contamination or impurities, especially of any that have been identified as being of toxicological significance.

Guidance

- It may be hard to delineate between 'active manufacturing' and 'formulated product manufacturing', especially if manufacturing is done as part of one process. However, for the purpose of specifications,

batch analysis and impurities associated with the microbe, the microbe is considered to be at the point where the primary culture is prepared and used as an inoculum for batch production.

- Information on the taxonomy of the microbe 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 if difficulties exist in taxonomy so that the registrant can be sure of having cultures identified.
- Please note that all batch analyses must clearly indicate name and address of the manufacturer(s) of the microbe, date of manufacture, batch size, batch identity, and site of manufacture.
- Data generated must follow the requirements outlined in the ACVM Research Standard.

(2) You must provide the following information on the formulated product:

a) trade name; and
b) type of formulation; and
c) composition of formulation, which must include quantity, identity (including names and CAS numbers) and purpose of all active and non-active ingredients such as diluents, ultra-violet protectors, water retaining agents; and
d) description of any properties of the formulated product that differ from the microbe, including those that are designed to reduce hazards (such as encapsulation of spores, binding to substrates); and
e) management of microbial contamination (describe microbiological purity, nature and identity of any culture media, impurities and content of extraneous organisms); and
f) description of metabolites produced by the microbe. Tests showing absence (or limits) of metabolites of toxicological relevance should be provided, and methods of analysis described;
g) manufacturer's name and physical address (include details for all manufacturers if more than one); and
h) summary of production process in the form of a flow diagram of the manufacturing process identifying critical quality control points; and
i) 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. A full method description should be provided for in house methods or the appropriate CIPAC method referenced; and
j) analytical methods used to determine the concentration(s) of the microbe in the formulation (and its contaminants - either of chemical or microbiological nature) and methods to verify genetic integrity (if a GMO). CIPAC methods should be referenced if appropriate, otherwise methods should be described in full. It must be demonstrated that all analytical methods used to determine the concentration(s) of the active ingredient(s) is specific to the active ingredient and have acceptable specificity, accuracy and precision; and
k) 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; and
l) release and expiry specifications of the trade name product. If an overage is used for the active ingredient, please state and provide rationale for the amount of overage used. Provide an explanation to support the release and expiry specifications; and
m) results from stability trial of formulated product, showing 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 microbial formulation and in accordance with the recommended storage conditions; and

n) packaging type(s), including size, material, any features specific to the microbe. Packaging must be designed to adequately contain the microbial formulation over the product shelf-life.

Guidance

- Recommended 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. Some physical properties may differ between chemical and microbial formulations. In such situations, applicants are required to provide a rationale supporting any deviations from general limits of these physical parameters.
- Name and address of the manufacturer(s) of the formulated trade name product must be supplied and all batch analyses of the formulated product must clearly indicate: date of manufacture, batch size and identity, and site(s) of manufacture.
- Data generated should follow the requirements outlined in the ACVM Research Standard.

1.4 Toxicological data

(1) If the microbe(s), or its metabolites, could have or is likely to have an adverse effect on food or feed crops in a way that could adversely impact animal or human health, you must provide the following information to MPI's ACVM group for the organism and any metabolites or contaminants produced:

a) pathogenicity to mammals; and
b) likelihood of causing hypersensitivity reactions to humans.

Guidance

- This information will differ in several respects from that required for chemical pesticides. It must cover the infectivity of the living microbe, reproduction potential, and (especially when airborne fungal spores may be involved) its allergenic potential. Some assessment of acute toxicity will normally be required while more prolonged studies, including carcinogenicity and teratogenicity may be appropriate for those microbes that are either known or may be shown to produce toxic substances.
- Much of the above is likely to be assessed by EPA NZ. However, in cases where there may be a concern regarding animal or human health on food or feed crops, additional information for the organism and any metabolites or contaminants will be required.

1.5 Residue data

(1) If the microbe(s) is used on food-producing crops or crops used for animal feed, you must provide the following information:

a) identification of viable and non-viable residues in grazing animals or on treated crops at harvest, the viable residues by culture or bioassay and non-viable by appropriate techniques; and
b) likelihood of multiplication in or on animals, crops or food, and its effect on food quality; and
c) extent of indirect contamination of adjacent non-target crops, other plants, soil and water that may get into the food chain; and

d) presence of metabolites of toxicological relevance after the application of the product and at harvest.

(2) These requirements are in addition to the requirements for agricultural compounds in *Residue Data for Agricultural Chemical Registration*.

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 microbes. This 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 microbe remains active for a significant period the question of further multiplication must be considered, as must 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.

Guidance

- If the microbe (and its metabolites of toxicological concern) is likely to be present on food producing crops or crops used for animals feed, an MRL (maximum residue limit) or an exemption from an MRL will be required under the New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards 2015.
- MPI will assess the information provided to determine if the microbe fits under any existing MRL exemptions, for example the exemption for microbial pesticide organisms, or whether an application for an MRL or MRL exemption is required. Existing MRLs and exemptions can be found in the latest New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards.
- In many cases, setting an MRL under the MRL Standard is not appropriate. For example:
  -
  - the microbe 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 at harvest cannot be measured due to confounding factors in the environment (such as natural presence of a similar organism).

1.6 Efficacy and plant safety data

(1) You must provide data to show that the trade name product, when used according to directions, is effective and safe for the purposes claimed in New Zealand under local conditions.

Guidance

- Data generated should follow the requirements outlined in the ACVM Research Standard for agricultural chemicals.
- Refer to ACVM Registration Information Requirements for Agricultural Chemicals in New Zealand.

1.7 Off-target effects

(1) Supply MPI's ACVM Group with a dossier accounting for what is already known of the biological 'side effects' on the environment of the use or natural occurrence of the microbe. This includes any information relevant to likely off-target exposure of food or feed crops (such as ingestion by mammals).

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

Guidance

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

Schedule 1 – Definitions

(1) In this notice, unless the context otherwise requires:

ACVM Act means the Agricultural Compounds and Veterinary Medicines Act 1997.

ACVM (E&PS) Regulations means the Agricultural Compounds and Veterinary Medicines (Exemptions and Prohibited Substances) Regulations 2011.

MRL Standard means the New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards and amendments.

(2) Unless the context otherwise requires, terms used in this notice that are defined in the Act or the Regulations have those meanings.