Ministry for Primary Industries
Manatū Ahu Matua

Prudent Use of Antimicrobials on Animals and Plants

MPI Directive (December 2017)

IN THIS DOCUMENT

1 Introduction

The development of antimicrobials for preventing and curing diseases that were previously either untreatable, or difficult to treat, provided a significant advancement in both human and animal medicine. However, there are significant concerns in New Zealand and overseas regarding the increasing levels of antimicrobial resistance (AMR)[1] and the lack of new antibiotics being developed.

AMR in animals and plants will have significant adverse effects on productivity, animal welfare, and health and food safety.

In New Zealand, the Ministry for Primary Industries (MPI) and Ministry of Health (MoH) are working together and with stakeholders to manage AMR. MPI has produced an AMR Direction Statement, and MPI/MoH have jointly developed a National Action Plan that was presented at the World Health Assembly in May 2017.

In addition to the work by government agencies, a number of industry sectors and organisations have established guidance material on the prudent use of antimicrobials.

2 Purpose

This document is designed to provide direction on the prudent use of antimicrobials in relation to animals and plants, in accordance with Objective 4 of the New Zealand Action Plan on Antimicrobial Resistance. It will address MPI's expectations for prudent use on regulatory oversight, various industry sectors and end users of antimicrobials. It sets the overarching scene for more detailed and sector specific prudent use guidance.

[1] Antimicrobial resistance means microorganisms that cause infections or diseases in humans, animals and plants become resistant to antimicrobial agents that they were previously sensitive to, in such a way that infections or diseases are more difficult or impossible to treat. In this context, 'antimicrobial' is a general term for drugs, chemicals, or other substances that either kill or slow the growth of microbes. Substances considered antimicrobials include surface disinfectants, antibiotics, anti-fungal (or fungicides), bactericides, and anti-viral agents.

The intended outcome is to:

- ensure the appropriate level of regulatory oversight is maintained and enhanced
- ensure only appropriate persons have access to them and they are used appropriately
- ensure where possible antimicrobials are used only for disease management purposes
- encourage the use of alternative methods for management and/or control of disease, and
- promote a better understanding of AMR and the importance of using antimicrobials correctly.

This is a living document and as new information/science becomes available it will be updated accordingly.

3 Scope

This document focuses on antimicrobials regulated under the Agricultural Compounds and Veterinary Medicines 1997 (the Act). It covers importation, manufacture, distribution, retail, sale and use of antimicrobials. For veterinary medicines it aligns as much as possible with the relevant sections of the Veterinary Council of New Zealand (VCNZ) Code of Professional Conduct for veterinarians.

Out of scope of this document are:

- antimicrobials that are not considered of medical importance and for which AMR has not been identified as a significant risk, and
- residues of antimicrobials in food-producing animals/crops, and the compliance with maximum residue levels.

4 Regulatory framework

Antimicrobials used in the management of animals and plants are subject to the ACVM Act. The purpose of the Act is to:

- Prevent or manage risks associated with the use of agricultural compounds. These risks are:
    - risks to public health
    - risks to trade in primary produce
    - risks to animal welfare, and
    - risks to agricultural security.
- Ensure that the use of agricultural compounds does not result in breaches of domestic food residue standards.
- Ensure the provision of sufficient consumer information about agricultural compounds.

MPI has established thresholds for each of these areas.[2] AMR impacts in each of the above risk areas, particularly with respect to animal welfare and public health.

Before antimicrobials can be imported, manufactured, sold or used they require an authorisation under the Act. The two main types of authorisations are registration or compliance with the ACVM (Exemptions and Prohibited Substances) Regulations 2011 (the Regs). The latter exempts groups of products from

[2] The document outlining these thresholds can be found at http://www.mpi.govt.nz/dmsdocument/11833-risk-management-under-the-agricultural-compounds-and-veterinary-medicines-act-1997-overview

registration. Based on the risk thresholds and criteria, MPI has established that the majority of antimicrobials (including all antibiotics) require registration.

Registration of an antimicrobial requires the applicant to submit information in line with the requirements MPI has established to assess the risks and benefits of the antimicrobial. These requirements cover:

- identify and conformity (chemistry and manufacturing)
- efficacy
- safety
- their potential to select for resistant microorganisms (AMR potential), and
- residues (if applicable).

Additional requirements may be requested of the applicant.

The only risks and benefits relevant to a decision on whether or not to register an antimicrobial are outlined in the ACVM Act as follows:

- risks to public health
- risks to trade and market access for primary produce arising from the use of the trade name product
- risks to agricultural security
- risks to the welfare of animals which result from treatment with or exposure to any substance, mixture of substances, or biological compound that forms a part of the trade name product
- risks to domestic food residue standards, and
- the benefits of the trade name product and the likely consequences of the public not having access, or having restricted access, to the trade name product.

If a decision is made to register an antimicrobial, the Act provides for a range of tools to manage its risks at least cost to the public. The main regulatory tool is the application of conditions. These conditions cover a wide range of activities from importation, selling and who can use it through to labelling and advertising.

5 Prudent use expectations

The following outlines expectations placed on antimicrobials to ensure their authorisation, sale and use occurs in a prudent manner. While these expectations cover antimicrobials per se, there is particular emphasis on veterinary medicines.

General

Antimicrobials should be used only when alternative methods either have been ineffective or are not appropriate.

Regulatory oversight under the ACVM Act

The regulatory oversight of antimicrobials under the ACVM Act covers specifying requirements to support a registration application, assessment of the risks, setting appropriate controls and post-registration activities. Consequently, the following focuses on areas of relevance to the management of AMR for antimicrobials rather than covering all aspects of the regulatory system such as chemistry and manufacturing, good manufacturing practice (if applicable), residues, efficacy, target animal/plant safety, labelling, and conditions of registration.

Registration and related matters

Regulatory requirements for registration

These requirements must be sufficient to ensure the applicant supplies the appropriate information to allow the regulator to quantify the AMR potential of the antimicrobial.

Risk assessment

The risk assessment of the antimicrobial should consider:

- the potential for the antimicrobial to cause resistance
- the importance of the antimicrobial for humans
- the importance of the antimicrobial for disease treatment in animals, and
- whether restrictions on who can sell, authorise and use the antimicrobial are required.

This assessment should be based on the information supplied by the applicant, along with consideration of domestic and international policies and standards.

Labelling

The label must have sufficient and clear information to minimise the potential for AMR when using the antimicrobial. This includes detailed information on use patterns and indications.

Sale

Persons who sell antimicrobials must be limited to those who have the appropriate expertise and knowledge on storage of products, record keeping, security and legal requirements.

Authorisation (veterinary medicines)

The authorisation to allow purchase and use of antimicrobials must only be by persons (i.e. the authoriser) who have the knowledge and expertise to determine whether, how and who should use the antimicrobial. The authoriser must comply with relevant obligations under legislation. Should the authoriser decide a person other than themselves can administer the antimicrobial, the authoriser must ensure the person is competent and capable to do so.

The length of period that a user can hold the authorised antimicrobial must only be sufficient to achieve the purpose. This must be done only within the confines of the authoriser having sufficient confidence in maintaining the appropriate level of oversight of the end user.

Use

If the person using the antimicrobial is not the authoriser, the use of antimicrobials in animals must be in accordance with the authoriser's instructions, including medical reason for use, dose rates, intervals, duration of treatment, and withholding periods, if applicable.

For antimicrobials used on plants, the use must be in accordance with the specified application rate and use instructions including withholding periods.

Advertising

The advertising of antimicrobials must be limited to those persons who have the knowledge and expertise to make an informed choice on the appropriate antimicrobial to use in any situation.

Surveillance and monitoring

Programmes must be in place to inform on compliance with the regulatory oversight and this Directive of antimicrobials. Such programmes must be consistent with international best practices.

Compliance and enforcement
All parties must comply with their legal obligations. If non compliances with the regulatory controls including this Directive on antimicrobials are identified, they are investigated and, if confirmed, the most appropriate sanction must be applied.

Compounded veterinary preparations and human antimicrobials for use on animals
The compounding of a substance to be used as an antimicrobial, or access to a human antimicrobial, must be limited to those persons who have the expertise and knowledge to assess that a compounded preparation or human antimicrobial is appropriate to use instead of a registered antimicrobial.
The person must not promote or advertise the compounded or human antimicrobial. In addition, the person must not sell a compounded or human antimicrobial to any person for use on that person's animal if the authoriser is not directly managing that animal's care.

Registrants
The registrants of antimicrobials must:

- when applying for registration (or variation) of an antimicrobial, supply information as outlined in guidance documents along with any other information relevant to the product to the regulator to ensure a full and appropriate assessment can be undertaken
- have technical information on the antimicrobial readily available for the authoriser and/or user to assist them in the authorisation and use of the antimicrobial
- ensure advertising and promotion of the antimicrobial is consistent with its registration and the conditions placed on it, and
- monitor the performance of the antimicrobial particularly in regard to product failure and comply with the legal requirements for the reporting of Adverse Events (AER).

Resellers
The reseller (who could also be the authoriser) must:

- ensure the antimicrobial is stored appropriately to maintain its integrity
- verify that the authorisation supplied to them is valid, and
- comply with the authorisation supplied to them.

Authorisers (veterinary medicines)
The authoriser must be familiar with the history of the herd, flock, or animal(s) being treated.

They must take the following into consideration when determining the choice of antimicrobial (whether registered, compounded veterinary preparations and human antimicrobials for use on animals) they will authorise:

- If there is a condition (or an imminent condition) that clearly indicates use of an antimicrobial is the appropriate treatment.
- A veterinary consultation must be undertaken (in line with guidance/requirements MPI and VCNZ have issued on this).
- If there is a need to undertake culture and sensitivity testing to confirm the pathogen and appropriate treatment.
- If there are any restrictions or contraindications for use of the antimicrobial in the treatment of the animal(s) that must be considered.
- The shelf-life of the product must align within the period of the authorisation to ensure the product is not used outside of its shelf life.
- If any legal obligations associated with the use of the chosen treatment must be complied with.

Financial incentives and/or convenience must not influence the choice of antimicrobial. The choice of antimicrobial must be consistent with the cascade principles under the Veterinary Council of New Zealand's Code of Professional Conduct.

Users (other than the Authoriser)

The user must:

- follow best practices to manage plant and animal health, which must include prudent use of antimicrobials
- for treatment of animals:
    - rely on the advice of the authoriser on appropriate use of the antimicrobial, and
    - follow the instructions of the authorisation for the antimicrobial.
- for application to crops:
    - follow the label directions on the antimicrobials, and
    - comply with industry best practice guidance, if applicable.

Producer sectors

The following is relevant to those sectors producing food/feed from animals and plants.

The producer must:

- have established best practices to manage plant and animal health, which should include minimising the use of antimicrobials via prudent use guidelines, and
- promote the above best practices/guidelines to their members and ensure compliance.

Communication

The following messages must be used by all stakeholders when communicating about AMR:

- Antimicrobials are important tools in the management of plant and animal health and animal welfare.
- Inappropriate use of antimicrobials can lead to diseases becoming resistant in both animals and plants and potentially in humans via contact with animals or food.
- Industry bodies with prudent use guidance material must ensure this information is available to their stakeholders.