Adverse Event and ACVM Risk Area Management Reporting Programme for Veterinary Medicines

ACVM guideline for veterinarians and animal owners (July 2022)

1. Introduction

The adverse event reporting programme is a quality assurance programme developed by New Zealand Food Safety, which is part of the Ministry for Primary Industries (MPI). It aims to ensure that all veterinary medicines in the marketplace are safe, efficacious, of acceptable quality, used appropriately, and that product labels provide sufficient consumer information for correct use.

2. Risks posed by veterinary medicines

The Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997 legislates the importation, manufacture, sale and use of veterinary medicines. (*Veterinary medicine* means any substance, mixture of substances, or biological compound used or intended for use in the direct management of an animal.)

The purpose of the ACVM Act is to prevent or manage the following risks associated with the use of veterinary medicines:

- risks to trade in primary produce
- risks to public health
- risks to animal welfare
- risks to agricultural security.

In addition, the Act is to ensure that there are no breaches in domestic food residue standards and that there is provision of sufficient consumer information about the veterinary medicine.

In New Zealand, veterinary medicines are reviewed and appraised by MPI. Some veterinary medicines pose minimal risks, such as oral nutritional compounds (animal feeds, pet foods and animal supplements), and may qualify for exemption from registration. All other veterinary medicines must be registered and undergo a review and appraisal of their safety, quality, residue profile and efficacy as appropriate.

However, this process will not always detect unexpected events following the use of a veterinary medicine because of:

- the relatively small number of animals used in registration trials compared to the wider animal population
- the wide range of environmental conditions encountered under practical farming conditions
- the fact that it is impossible to include in registration trials all breeds, age groups, classes of animals, and all disease states or pests that may be exposed to the product, and
- all possible drug combinations and/or uses once a product is in the marketplace.

Therefore, even after a thorough review and appraisal prior to registration, it is possible that unforeseen problems that may affect the treated animals or trade can arise. It is critical that adverse events (see definition below) are brought to the attention of the person responsible for the product (that is, the registrant or distributor) and to MPI's attention so that that all unintended effects can be characterised under field conditions and necessary action can be taken.

It is also important that where it is identified that products have been used in contravention of a condition of registration that these are reported to MPI to maintain the integrity of the New Zealand regulatory system (e.g., the use of phenylbutazone in a food producing animal or failure to adhere to a label direction where there is no obvious justification for doing so).

DEFINITION OF AN *'ADVERSE EVENT'*

MPI defines a veterinary medicine 'adverse event' as any observation in animals that is unfavourable and unintended, that occurs after the use of a veterinary medicine. This may include side effects, target animal safety issues, residue issues, lack of efficacy, human safety issues, or alleged interactions with other products or compounds.

Note that all of these issues that are suspected to be related to product use, and that may or may not be identified on the product label, are classified as adverse events. The likelihood that the product caused or contributed to the event is assessed when the adverse event is reported to the registrant and MPI. If a link is suspected, then the event will be ruled to be a possible or probable adverse product reaction.

Events that do not create an obvious adverse outcome, but could pose a threat to animal welfare, trade in primary produce, public health, agricultural security or cause unacceptable residues in produce from treated animals without proactive management, should also be reported. Such events could be caused by:

- Administering the product via the incorrect route.
- Inadvertent access by another animal.
- Inadvertent over-dosing.
- Use in an on-label prohibited species or class of animal

3. The Adverse Event Reporting Programme

OBJECTIVES

Specifically, objectives of the programme are to:

- ensure risks under the ACVM Act are appropriately managed
- maintain public confidence in the registration process.

SCOPE

The programme covers adverse event reports involving:

- animal health and welfare issues
- inefficacy, if applicable, and
- residue issues.

It includes:

- adverse event reports (AERs) recorded in products that are registered or exempt from registration under the ACVM Regulations 2011, such as animal feeds and shampoos
- off-label use of products (with or without expert advice)
- use of human drugs in animals.
- human adverse symptoms following exposure to a veterinary medicine

SOURCE OF REPORTS

There are two complementary components of the Adverse Event Reporting Programme: registrants and others.

Registrants

The registrant component is a legal requirement under condition of registration and is mandatory. Registrants of veterinary medicines must report the full details of any adverse events that they become aware of for their products to MPI.

Others

The voluntary component encourages veterinarians and the general public (including animal owners, farmers and other users) to report any adverse events to MPI and the product registrant. (**Veterinarians:** The *Code of Professional Conduct for Veterinarians* states that you are expected to report adverse events.)

Some adverse product reactions are already managed by registration or label information. However, to monitor the ongoing acceptability of these controls adverse events should be reported where they occur and especially when they:

- are observed at an increased frequency
- are not consistent with the expected outcome described on the label, or
- are considered severe.

Where there is a limited body of knowledge surrounding a recently registered veterinary medicine, reporting of adverse events is a critical tool in confirming the safety and efficacy of the product.

4. What to do if an adverse event occurs

Animal owners: If your animal has been adversely affected after the use of a veterinary medicine, you should seek veterinary advice from your usual veterinarian. Your veterinarian can assess the situation and determine the appropriate treatment. The issue should then be reported as an adverse event to the registrant of the product (refer to the contact details on the product label). As mentioned above, the registrant must report the matter to MPI but you may also provide a report directly to MPI using this AER form:
Adverse event report: veterinary medicines

For adverse events that result in a residue issue with risk to food safety, it is important to notify MPI as soon possible. This includes violative residue detections, and any overdose/inappropriate dosing event that is likely

to result in a residue violation when sending the stock to slaughter. These notifications will help ensure that the label information and controls are adequate to manage the associated risk and prevent future issues.

If the event involves the treatment of animals with doses of product other than what is approved on-label it is important to remember that the specified withholding period may not be adequate to manage resulting residue risks. Animal owners should obtain advice from a veterinarian or MPI with respect to the appropriate residue management steps to take.

INFORMATION REQUIRED

The AER form provides a guide to what information should be submitted. Please take the time to complete the form as thoroughly as possible because this allows a more robust investigation. MPI assesses AER forms on receipt and may have to return them to the reporter for more information if insufficient data is provided.

Veterinarians: When describing the adverse event, please describe the clinical signs observed in addition to the end diagnosis, for example:

- clinical signs: urticaria, oedema of head and hyperaemia
- diagnosis: hypersensitivity reaction.

This allows more accurate comparison to other reports. Include case notes, laboratory tests and post-mortem reports if appropriate.

CONFIDENTIALITY, RIGHTS AND RESPONSIBILITIES

All information provided on suspected adverse events is treated as confidential. However, all information MPI holds is subject to the provisions in the Official Information Act 1982 and the Privacy Act 2020. Any request for information will be considered on case-by-case basis under these Acts. The consideration will take into account whether the request for information relates to information that could be considered to be commercially sensitive under section 12 or Part 6 of the ACVM Act.

The Adverse Event Reporting Programme is not intended to replace a person's right or responsibility to contact the registrant or distributor about an adverse event with a veterinary medicine.

5. What happens once an adverse event report is received

Reports made directly to MPI are copied to the product registrant or distributor for immediate investigation. The registrant may then contact the reporter and discuss the matter to determine if any follow up laboratory, pathology or other veterinary work is required.

The product registrant will subsequently provide MPI with an investigation report into the incident and a classification of the report. MPI will assess this information and determine whether any further investigative work is required. In some cases, additional expert opinion may be sought. MPI also consider scientific information publicly available either on the Internet or from other international regulatory agencies (such as in Australia, UK, Canada or USA).

A standard method of assessment is used to determine whether the adverse event may have been related to the use of a veterinary medicine (that is, the *'causality assessment'*). MPI also consider whether the product was used according to the label directions.

The person making the report of an adverse event will be advised of the outcome of the investigations. This will include an explanation of whether the observed adverse effects were considered likely to be related to the use of or exposure to the product. MPI will explain what these conclusions are and what corrective action, if any, will be taken in response to the information.

Note that if a causal link is not established between the adverse event and the use of or exposure to the product, or if there is insufficient information to make a definite conclusion, then no action may be taken.

If an adverse event is reported directly to the product registrant, they will investigate the matter and provide a report to MPI. MPI will then assess this information and determine whether any further investigative or regulatory work is required, and if any corrective actions should be taken.

6. Possible regulatory outcomes

Based on evaluation of the investigation information, the causality assessment and whether there have been any other similar reports for the product, MPI will determine if any regulatory action is required. If considered necessary, this may take the form of:

- additional label warning statements
- product recalls
- suspension of product registration
- cancellation of product registration
- formulation or manufacturing process changes, or
- education of product users through the media or other appropriate forums.

FURTHER INFORMATION

For further information about the Adverse Event Reporting Programme please send an email to the dedicated adverse event address:

ACVM-AdverseEvents.mpi.govt.nz