Medicines Control Authority of Zimbabwe

MCAZ/EVR/GL-08

GUIDELINES ON PHARMACOVIGILANCE OF VETERINARY MEDICINAL PRODUCTS (VMPs): MANAGEMENT OF ADVERSE EVENTS REPORTS (AERs) & MANAGEMENT OF PERIODIC SUMMARY REPORTS

EFFECTIVE DATE: 20/2/2024

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ABBREVIATIONS

VICH:	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products
VMP:	Veterinary Medicinal Product
GL:	Guidelines
RAs:	Regulatory Authorities
SADC:	Southern African Development Community
AE:	Adverse Event
AER:	Adverse Event Report
PSU:	Periodic Summary Update
MCAZ:	Medicines Control Authority of Zimbabwe
QPPV:	Qualified Person Responsible for Pharmacovigilance

1.0 APPLICATION

The scope of pharmacovigilance in this guidance document is defined as the management of the detection and investigation of the clinical effects of marketed VMPs mainly concerned with the safety and efficacy in animals and the safety in people exposed to these products. While pharmacovigilance in its broadest sense may entail a wide range of activities, this document only deals with the spontaneous reporting system and management of periodic summary update reports for the identification of possible adverse events following the use of marketed VMPs.

All stakeholders which include the animal health industry, veterinary surgeons, farmers and pet owners are encouraged to use this guidance for submitting reports to the Authority on adverse events.

2.0 PURPOSE

The objective of this document is to allow for ongoing monitoring of the safety and efficacy of VMPs and to assist in identifying any changes to the safety profile of VMPs after marketing authorization is granted.

3.0 BACKGROUND / INTRODUCTION

These guidelines were adapted from the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) guidelines GL 24 (management of adverse events), GL 29 (management of periodic summary update reports), GL 35 and GL 42 (data elements for submission of adverse reports) on veterinary pharmacovigilance.

Pharmacovigilance of veterinary medicinal products (VMPs) can be defined as the detection and investigation of the effects of the use of these products, mainly aimed at safety and efficacy in animals and safety in people exposed to the products. This document will only deal with the spontaneous reporting system and periodic summary update reports for identification of possible adverse events following the use of marketed VMPs.

Within all regions involved in the VICH process there are certain legal obligations for the pharmaceutical industry, the commercial party responsible for the products, with regard to adverse events reported to them. Those legal obligations relate to the acceptance of adverse event reports and the storage and submission of those reports to the regulatory authorities.

It is of importance for all parties, the principals of VMPs, the Regulatory Authorities (RAs) in the Southern African Development Community (SADC) and the users of VMPs to develop harmonized and common systems, common definitions and standardized terminology within pharmacovigilance. Harmonization of those elements between the regions facilitates the reporting responsibilities for the principals, many with worldwide activities. At the same time harmonization of systems and requirements facilitates the inter-regional comparison of data and exchange of information, thereby increasing the general knowledge of a product`s general performance and safety profile.

4.0 DEFINITIONS

The terms and definitions in this document are intended to harmonize other previously used terms referring to similar concepts. Within the scope of this document the following definitions of items or actions have been developed.

4.1 Adverse Event (AE)

An adverse event is any observation in animals, whether or not considered to be product-related, that is unfavorable and unintended and that occurs after any use of VMP (off-label and on-label uses). Included are events related to a suspected lack of expected efficacy according to approved labeling or noxious reactions in humans after being exposed to VMP(s).

An AE may at some point be concluded by a RA to be an adverse reaction when there is at least a reasonable possibility (i.e., relationship cannot be ruled out) that harmful and unintended observations were a response to a VMP administered at doses normally used in animals for prophylaxis, diagnosis or therapy of disease or for modification of physiological function.

4.2 Adverse Event Report (AER)

An adverse event report is a direct communication from an identifiable first-hand reporter (see 3.1.7) that includes at least the following information:

1. an identifiable reporter
2. an identifiable animal(s) or human(s)
3. an identifiable VMP
4. one or more adverse events

One animal or one human being, or a medically appropriate group exhibiting similar clinical signs should be included in a single report.

4.3 Periodic Summary Update (PSU)

The document submitted to the RA at set intervals to support the continued marketing and the adequacy of the approved labeling of the VMP and will include an analysis of all AERs received during the interval.

4.4 Principal

The principal is the commercial party who, according to the RA is responsible for the pharmacovigilance of the VMP.

4.5 Regulatory Authority (RA)

The Regulatory Authority is the national or regional authority which, according to the legislation, is responsible for the issuing, adaptation or withdrawal of marketing authorizations/licences of VMPs and for pharmacovigilance activities. With reference to this guidance document, RA refers to the Medicines Control Authority of Zimbabwe (MCAZ).

4.6 Serious Adverse Event

A serious adverse event is any adverse event which results in death, is life-threatening, results in persistent or significant disability/incapacity, or a congenital anomaly or birth defect. For animals managed and treated as a group, only an increased incidence of serious adverse events as defined above exceeding the rates normally expected in that particular group is considered a serious adverse event.

4.7 Unexpected Adverse Event

An unexpected adverse event is an adverse event of which the nature, severity or outcome is not consistent with approved labeling or approved documents describing expected adverse events for a VMP.

4.8 Veterinary Medicinal Product (VMP)

Any medicinal product with approved claim(s) to having a protective, therapeutic or diagnostic effect or to alter physiological functions when administered to or applied to an animal. The term applies to therapeutics, biologicals, diagnostics and modifiers of physiological function. The "same biological VMP" is defined as originating from the same principal being responsible for pharmacovigilance of this/these VMPs with same manufacturing specifications. The "same pharmaceutical VMP" is defined as originating from the same principal being responsible for pharmacovigilance of this/these VMPs with same formulations.

A "similar pharmaceutical VMP" is defined as:

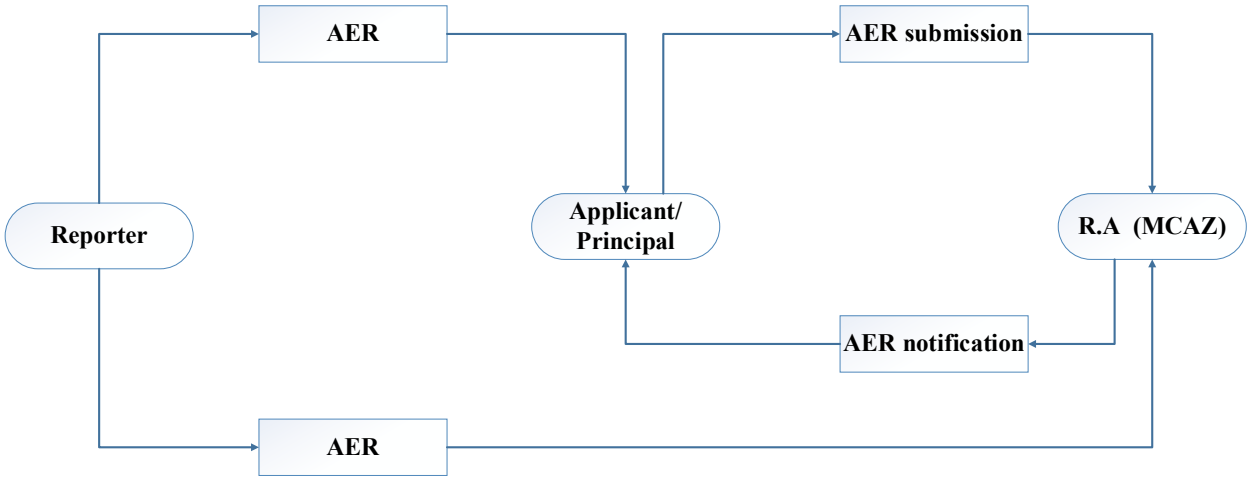
i. originating from the same principal being responsible for pharmacovigilance of this/these VMPs,
ii. the same active ingredients,
iii. major excipients with the same or similar pharmaceutical function,
iv. at least one common registered species.

5.0 GUIDELINES

5.1 Section A: Management of Adverse Events Reports (AERs)

5.1.1 The Pharmacovigilance Process

Information Flow in the Pharmacovigilance System.



Adapted from VICH GL24 guidelines.

5.1.2 Information Flow in the Pharmacovigilance System.

Data preferably flows as shown in the upper half of the figure, where the reporter communicates with the principal and the principal submits AERs it has received to the RA. An alternate path is shown in the lower half, where the reporter communicates with the RA and the RA notifies the principal of AERs it has received. When submitting AERs to either the MCAZ or the principal, reporters (*farmers, pet-owners, veterinarians*) are recommended to use the form attached to annex 1.

5.1.3 Informational Unit

The basic unit of information in the pharmacovigilance system covered by this document is the AER and PSU.

5.1.4 Recording AERs

The principal must record each AER received and store it in a manner which allows easy access to the data. The receipt, acknowledgement or recording of an AER by the principal or the RA does not necessarily have any implication regarding the veracity or authenticity of the AER nor implies any degree of causality.

5.1.5 Submitting AERs

The principal should submit an AER to the MCAZ as provided by the Medicines and Allied Substances Control (General) Regulations, S.I. 150 of 1991either as an expedited submission or as a periodic submission.

The submission of an AER does not necessarily imply an endorsement or agreement with its content, unless MCAZ regulations require differently.

5.1.6 Expedited AER Submissions

Expedited submission of certain AERs may be required, related to the seriousness or unexpectedness of the reported event or because of the urgency of its implications regarding the safety of animals or man.

Animal health industry and veterinarians should report all serious and unexpected adverse events occurring in Zimbabwe as soon as possible, but in no case later than 15 calendar days of initial receipt of the information. In case all the information needed is not available within 15 days, the Applicant should submit an initial report containing at least the minimum data elements required (i.e., patient details, suspected product details, reaction details and the reporter details) in order to meet the expedited reporting time frames. A follow-up report containing more detailed information should be submitted later as soon as this becomes available.

Cases of non-serious adverse events, whether expected or not, are also to be reported to the MCAZ as soon as possible, within a period of 28 calendar days of initial receipt of the information.

5.1.7 Periodic AER Submissions

At regular intervals, the principal should submit all AERs not previously submitted. Principals should submit AER to the MCAZ annually.

5.1.8 Reporting Source

Although reporting via the attending veterinarian is encouraged, an AER may be initiated by anyone directly involved with the purported adverse event. Preferably, an AER is communicated by the reporter directly to the principal, but the AER may also have been routed through an agent or the RA. A communication through an intermediate agent is considered an AER only if the agent has been authorized by the reporter and provides sufficient information to allow direct contact between the reporter and the principal.

5.2 Section B: Management of Periodic Summary Reports

5.2.1 Timing of Reporting

PSUs shall be submitted when this is given as a condition of registration of the product or at any point post marketing authorization when requested by MCAZ based on safety concerns or when MCAZ deems it necessary.

When given as a condition of registration, PSUs should be submitted every 6 months for the first two years, yearly for the following 4 years, and at 3-year intervals thereafter.

When requested by MCAZ, PSUs should be submitted within 30 calendar days of the request.

Other details will be communicated by MCAZ on a case-by case basis. The MCAZ will provide feedback on any PSU submission within sixty (60) working days.

5.2.2 Contents

When submitting PSUs to the MCAZ, principals or applicants on behalf of principals are recommended to use the following guide:

5.2.2.1 Name and address of the principal responsible for the VMP detailed in the PSU.

5.2.2.2 The PSU will clearly identify the VMP(s).

5.2.2.3 Time period covered by the PSU (start date and end date).

5.2.2.4 The PSU will contain AERs for the VMP(s) identified in the PSU and AERs for same and similar pharmaceutical VMP(s) or same biological VMP(s).

5.2.2.5 All data elements for the AERs submitted in the PSU are described in GL 42. Until electronic submission (GL 35) has been implemented by the RA, a subset of GL 42 may be submitted as a line listing of AERs.

5.2.2.6 A bibliographic listing of scientific articles that address AEs found in a widely accepted search engine published during the time period of the PSU that pertains to the VMP(s) identified in the PSU, and a brief statement assessing the relevance of these articles to the VMP(s). Additionally, a bibliographic listing of the studies that address AEs and the principal has sponsored for the VMP(s) identified in PSU should be included.

5.2.2.7 The PSU must address the relationship of sales volume of the VMP(s) identified in the PSU to the number of AERs. Sales volume by country should be provided.

5.2.2.8 For the same and similar VMP(s), an update should be presented if there are RA-mandated or principal-initiated regulatory actions (e.g., changes to the VMP(s), changes to labelling, and market suspensions) that have been taken, or are pending for safety and effectiveness reasons during the reporting period. The format should be a brief narrative stating the reasons for the action(s), with documentation appended when appropriate.

5.2.2.9 The PSU should include a concise critical analysis and opinion on the risk/benefit profile of the VMP(s) identified in the PSU. Comment on important developments for the following:

i. Evidence of previously unidentified concerns
ii. Changes in frequency of AEs
iii. Drug interactions
iv. Human AEs

The evaluation should indicate whether the data remain in line with the cumulative experiences to date and the approved labels, including proposed actions.

5.3 Section C: Qualified Person Responsible for Pharmacovigilance

The applicant or manufacturer shall put in place pharmacovigilance measures to actively monitor the safety of their VMPs in practice for a length of time determined by the Authority. The applicant or manufacturer must always have a properly Qualified Person Responsible for Pharmacovigilance (QPPV) or Responsible Personnel for Pharmacovigilance on hand.

5.3.1 Responsible person for PV or QPPV

Every applicant or manufacturer who has registered a VMP in Zimbabwe shall designate a responsible person for PV or QPPV to oversee the pharmacovigilance system. The individual shall be responsible for the safety of VMPs marketed by an applicant or manufacturer in Zimbabwe. However, the applicant retains the overall responsibility for their VMPs and is answerable to any issues regarding the products. All feedback/responses will be addressed to the applicant in line with our legislation. The responsible person for PV or the QPPV may be resident in Zimbabwe or be an external party. For administrative purposes the applicant should notify the MCAZ in writing who their responsible person for Pharmacovigilance or the QPPV is, their curriculum vitae, contact details and their responsibilities. The responsible person should be adequately qualified to execute her or his duties. The QPPV should have received a formal training in pharmacovigilance recognized by the Authority and should have knowledge of the Zimbabwe pharmacovigilance legislation and guidelines and other international standards for Pharmacovigilance.

The applicant should:

5.3.1.1 Provide comprehensive training in Pharmacovigilance to the QPPV

5.3.1.2 Ensure that the QPPV has sufficient authority to implement pharmacovigilance activities, provide input into Risk Management Plan when necessary, provide input into the preparation of regulatory documents to emerging safety concerns (e.g. variations, urgent safety restrictions and as appropriate, communication to veterinary professionals)

5.3.1.3 Ensure that there are appropriate processes, resources, communication mechanisms and access to all sources of relevant information in place for the fulfilment of the QPPV's responsibilities and tasks.

5.3.1.4 Notify the Authority of the absence of the QPPV not later than 30 days after the position becomes vacant.

5.3.1.5 Have a written contract with the QPPV.

5.3.2 Responsibilities of QPPV

5.3.2.1 The QPPV should have oversight of the pharmacovigilance system in relation to structure and proper functioning and be able to ensure that all responsibilities are performed well and to ensure the following system components and processes, either directly or through supervision.

5.3.2.2 The QPPV should act as a point of contact for the applicant on all matters relating to pharmacovigilance and safety of marketed VMPs.

5.3.2.3 Establishment and maintenance of a system which ensures that information about all suspected adverse drug reactions/ events which are reported to the

personnel of the applicant and to the veterinarians is collected, collated and assessed for onward submission to the Authority.

5.3.2.4 The QPPV should have access to the pharmacovigilance system master file (PSMF) and be in a position of authority to ensure and to verify that the information contained in the PSMF is an accurate and up-to-date reflection of the pharmacovigilance system under the QPPV's responsibility.

5.3.2.5 Providing input into the preparation of regulatory action in response to emerging safety concerns (e.g. variations, urgent safety restrictions, and communication to veterinary professionals)

5.3.2.6 Prepare the following documents for submission to the Authority:

i. Adverse Drug Reaction reports/ individual case safety reports (ICSRs)
ii. Periodic Safety Update Reports (PSURs)/Periodic Benefit-Risk Evaluation Report PBRER), when necessary

5.3.2.7 Ensure that any request from the Authority for additional information deemed necessary for the evaluation of the risk–benefit afforded by a marketed product, is provided to MCAZ promptly and fully.

5.3.2.8 Ensure safety monitoring oversight of the marketed VMPs and any emerging safety concerns.

5.3.3 Training of personnel for pharmacovigilance

All personnel involved in the performance of pharmacovigilance activities shall receive initial and continued training. For applicants, this training shall relate to the roles and responsibilities of the personnel. The organisation shall keep annual training plans and records for documenting, maintaining and developing the competences of personnel. Training plans should be based on training needs assessment and should be subject to monitoring.

The training should support continuous improvement of relevant skills, the application of scientific progress and professional development and ensure that staff members have the appropriate qualifications, understanding of relevant pharmacovigilance requirements as well as experience for the assigned tasks and responsibilities. All staff members of the organisation should receive and be able to seek information about what to do if they become aware of a safety concern.

6.0 KEY RELEVANT DOCUMENTS

6.1 VICH GL24 on pharmacovigilance of veterinary medicinal products: management of adverse event reports (AERs)

6.2 VICH GL29 on pharmacovigilance of veterinary medicinal products: management of periodic summary update reports (PSUs)

6.3 VICH GL35 on pharmacovigilance of veterinary medicinal products: electronic standards for transfer of data

6.4 VICH GL42 on pharmacovigilance of veterinary medicinal products: data elements for submission of adverse event reports (AERs)

6.5 MCAZ PVCT Guidelines GL02

7.0 HISTORY

DOCUMENT HISTORY		
Revision Number	Date Approved	N/a
N/A	N/A	

ANNEX I: Veterinary Adverse Drug Reactions Reporting Form

Medicines Control Authority of Zimbabwe

EVALUATIONS AND REGISTRATION DIVISION

EVRF 77

VETERINARY ADVERSE DRUG REACTIONS REPORTING FORM

Tel: +263 772 145191
Email: vetevr@mcaz.co.zw

Reporting Veterinarian/Practice/Owner

Facility/Practice:	
District/City:	Tel:
Province:	Email:

Patient Details

Patient Name				File/Ref#		Owner					
Sex		Species		Breed		Age		☐ Pregnant			
Allergies				Estimated Gestational Age at time of reaction							

Suspected Medicine(s)-Medicines suspected to have caused the ADR

Trade Name and Manufacturer	Route of Administration	Dose and Interval	Date started/given	Date stopped	Reason for use	Batch#	Expiry Date

All other medicines patient was taking at the time of ADR

(incl. over-the-counter and complementary medicines)

Trade Name and Manufacturer	Route of Administration	Dose and Interval	Date started/given	Date stopped	Reason for use	Batch#	Expiry Date

Adverse Drug Reaction/Product Quality Problem

Date and Time of onset:	Date reaction resolves/duration:

Describe ADR/Quality Control Problem-add as much clinical information as possible.

Adverse Drug Reaction/Product Quality Problem

Intervention (tick applicable boxes)		
☐ No intervention		
☐ Intervention unknown		
☐ Owner informed		
☐ Discontinued suspect drug	Replaced with	
☐ Decreased suspect drug dosage	New dose	
☐ Treated ADR	Treatment	
☐ Referred to veterinarian	Name of veterinarian	
☐ Other intervention	Describe	

Patient outcomes (tick applicable boxes)		
☐ Recovered/Resolved	☐ Recovering/Resolving	
☐ Not recovered/not resolved		
☐ Died	Date of Death	
☐ Impaired/Disability		☐ Congenital anomaly
☐ Patient hospitalized/ Hospitalization prolonged		
☐ Life threatening	☐ Other	
☐ ADR reappeared after restarting suspect drug/similar drug/re-challenge?		

Lab result and name of laboratory

Lab test	Test result	Test date	Lab test	Test result	Test date

Co-morbidity/ Other medical conditions

Description

Reported by:

(ADR report is not confirmation that the reporter or the suspect medicine(s) caused the ADR)

Name:			Email:			
Designation:	☐ Veterinarian	☐ Manufacturer	☐ Owner	☐ Other		Telephone:
Date Reported				Signature		

What must be reported

Types of products to be reported on
-medications (pharmaceuticals and vaccines)
-medical devices and in-vitro diagnostics
-complementary / alternative medicines

For

-adverse drug reactions to registered/unregistered products
-adverse drug reactions to off-label used products
-serious reactions and interactions with other products
-adverse drug reactions which are not in the label
-lack of expected efficacy
-adverse reactions to humans exposed
-violation of residues
-environmental problems

Report product quality problems such as
-suspected contamination
-questionable stability
-defective components and presentation
-poor packaging
-changes to labelling/product information

Report even if
-you're not certain the product caused the event
-or you don't have all the details

Important numbers:
-phone: +263772 145191
-E-mail: vetevr@mcaz.co.zw

Confidentiality: Identities of the reporter and patient will remain strictly confidential

Your support of the veterinary adverse drug reaction monitoring programme is appreciated