

# OPERATING MANUAL

## A basic pharmacovigilance system veterinary medicinal products



### How to use the Operating Manual?

VICH does not:

- **establish regulations**
- tell how to **set up a pharmacovigilance center**
- set **record keeping/reporting timelines**
- prescribe how to **analyze individual adverse event reports**
- suggest how to conduct **signal detection activities**
- propose a **reporting form for consumers**

**Objective today: to describe how to use the manual to address some of these topics .**

### Contents of the Operating Manual

1. Introduction
2. Veterinary pharmacovigilance – roles and responsibilities
3. Defining the scope of pharmacovigilance
4. Drafting appropriate national legislation and additional guidance
5. Setting up a pharmacovigilance system
6. How to promote pharmacovigilance and encourage reporting
7. Submission, reception and processing of spontaneous reports
8. How to code the data
9. How to store and archive pharmacovigilance data
10. Standardised periodic update reports
11. How to analyse aggregated data
12. Risk management and follow-up regulatory measures
13. What and how to communicate pharmacovigilance outcomes
14. Inspections and ensuring compliance

## A basic pharmacovigilance system

### Establishing a pharmacovigilance center

#### Scope of Pharmacovigilance

**Ambitions and scope**  **available resources**

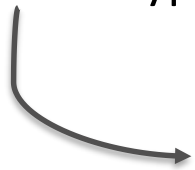
- Form of IT/People
- Budget (funding)
- Number of anticipated adverse event reports
- Number of products on the market
- Local culture of reporting


**What adverse events will be in scope**

- Treated animal
- The user
- Residues
- Environmental

**What products will be in scope:**

- Veterinary Medicinal products
- Other types of products

 Separate systems  
and AER forms

Can it be traced to an  
individual product ? 

### Setting up a Pharmacovigilance System

#### **Define, scope, obtain funding, draft legal and guidance**

- Plan implementation of the system within the Agency
- Estimate scale & volume of AER's - how many products & volume of sales
- Responsibilities - Who does what - adequate staff
- Documentation-report form, filing system
- Process, SOP's, language
- Paper, spreadsheet or database system
- Define responsibilities and obligations of companies

#### **Standard formats**

- VICH GL24 + 30 for standard AE forms and definitions
- VEDDRA standardised terminology for report data entry
- Set up a spreadsheet with VEDDRA term and local term

## A basic pharmacovigilance system

### **Responsibilities and obligations of the national competent authority (Agency)**

- To establish a pharmacovigilance system:
  - collect information
  - scientific evaluation and product group analysis
  - collate with data on sales or use, and local epidemiology
    - ✓ For local context and incidence rate
  - monitor compliance of companies
  - do risk-based inspections and perform controls
  - take corrective actions where necessary
- Initiate further investigation and assessment of identified safety concerns
- Implement conditions and restrictions on products
- Encourage reporting
- Make companies and veterinarians aware of their obligations

# A basic pharmacovigilance system

## Responsibility of Marketing Authorisation Holder (MAH)

Responsible for ensuring an appropriate system of pharmacovigilance surveillance and risk management

- Ensure action can be taken, when necessary

Responsibilities and obligations of MAHs should be defined, covering information collection format, language, timelines, rules, and communication plans

Are responsible for collecting, storing and analysing the pharmacovigilance data on their products

- Signal detection
- Further communication of adverse event information

Potentially designate a Pharmacovigilance Responsible Person.

## A basic pharmacovigilance system

### Establishing regulations Legislation and Guidance

#### Need a legal basis to impose requirements and rules

- Establish structures and systems
- Obtain government funding
- Enforce regulatory measures
- Provide legal clarity on responsibilities of each actor

#### Legal requirement to report → carrot or stick ?

#### Unadvisable to put operational details in legislation

- Keep legislation high level
- Put details in guidance
- Consult all stakeholders



More flexible  
System can evolve and grow  
Can adapt with experience  
Easier to update  
Increase engagement



### Guidelines

#### **Provide operational details in guidelines**

- Reference the legal basis
- Guidelines for Agency operational details
- Management of adverse event cases - process timelines, receipt and filing procedures, storage and archiving
- Evaluation of cases - how are cases going to be assessed
- Communication with the MAH - timeline, methods, expectations
- Investigation of identified issues and subsequent risk management measures

### Guidelines

#### **Guidelines for compliance of MAH**

- Details on requirements
- Details on expectations for the MAH staff training and frequency of retraining
- Details on reporting adverse event cases

#### **Consult all stakeholders**

- System must work for everybody = smooth running
- Raising awareness
- Builds “buy-in”- facilitate smooth implementation

### *Record-keeping / Reporting timelines* **Reception & Processing of Spontaneous AERs**

#### **Starting point:**

- Reports must use standard definitions & terminology (VICH)

#### **Standard content:**

- An identifiable reporter, including name and contact details
- An affected animal (defined by species at minimum) or human being
- An identifiable veterinary medicinal product
- One or more adverse signs or description of the event

#### **Language:**

- Worldwide reporting - English

## Data process for spontaneous AEs

### Reception of the AER:

- Assign case number
- Confirmation of receipt
- Follow up to obtain missing info or for personal response

### Handling and storage:

- Paper format - must be archived-paper or electronic format (scan)
- Electronic format - must be archived
- Security of storage-controlled access, fire/water/theft, longevity of storage media, data privacy/protection

## Data process for spontaneous AEs

### Data entry and records:

- Data entry to computer system-aids storage and analysis
- Verification of data entry
- Data fields (International standards - VICH GL 30 & 42)

### Coding and assessment:

- Medical review-evaluation of the data
- Causality assessment

### Submission of Individual AERs

#### **Timeline:**

- Too short = incomplete reports - no time to obtain missing data
- Several follow up submissions = more work

#### **Timeline examples:**

- Expedited/serious 15 days
- Other 30 days

#### **Or**

- All reports 30 days
- Agency to be alerted to significant safety concern ASAP

## A basic pharmacovigilance system

### More on data storage/archiving

- Depends on the chosen system-paper-based, electronic
- Adverse event reports using electronic data storage
  - a. facilitates analysis
  - b. is access-controlled and prevents unauthorised access
  - c. is protected against fire, water, data privacy (loss and theft)
- A simple (vet-specific) pharmacovigilance database compatible with international standard format is preferable
  - a. Facilitates easier reporting
  - b. Facilitates exchange of data
- Prepare operating procedures for storage and archiving

## Archiving

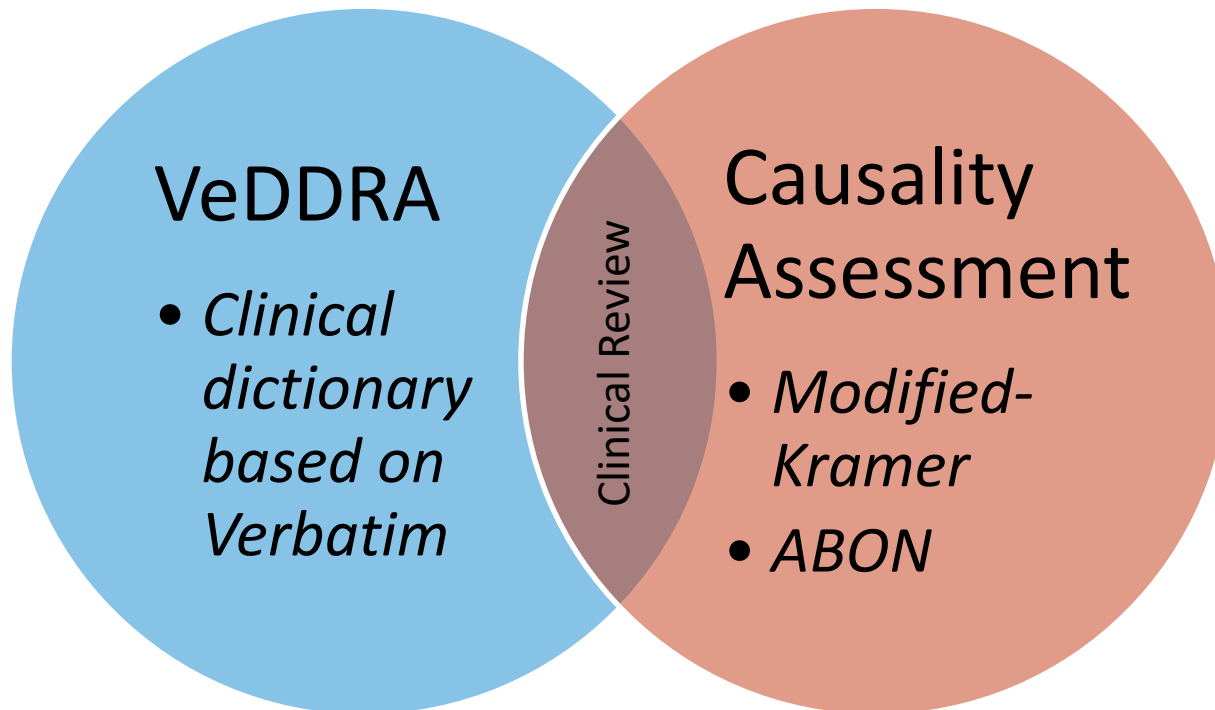
### Archive periods

- **For the MAH:**  
should be retained for a period of 2 years after the *expiration date of a product*
- **For the Agency:**  
for at least 3 years after *the marketing authorisation* has expired



# A basic pharmacovigilance system

## Analysis of individual adverse event reports



### Analysis of Aggregated Data

#### Analysis at meaningful intervals

- By product
- By group of similar products  
e.g. same active substance
- By species
- By AE type

#### Periodicity of analysis

- Risk-based approach - see PSR frequency

#### Method

- Depends on number of AER's involved
- Line listing review for few cases
- Spreadsheet analysis for large number of cases
- Database with statistical tools and software
- Detect trends and potential signals (threshold trigger)

#### Put data into context

- Incidence rate-increase in sales
- Reporting rate

### Signal Management

- A signal is defined as the detection of a new AE or a change in the rate of a known AE
- Signals should be prioritised based on their potential severity. All detected potential signals need to be validated, evaluated
- A confirmed signal is considered a risk
  - a) either a potential risk
  - b) or as identified risk
- The risk level is defined based on its severity
  - low risk - no risk mitigation measures are considered to be necessary
  - important risk - risk mitigation measures are considered necessary.
- The time frame for implementing the measures should reflect the level of risk

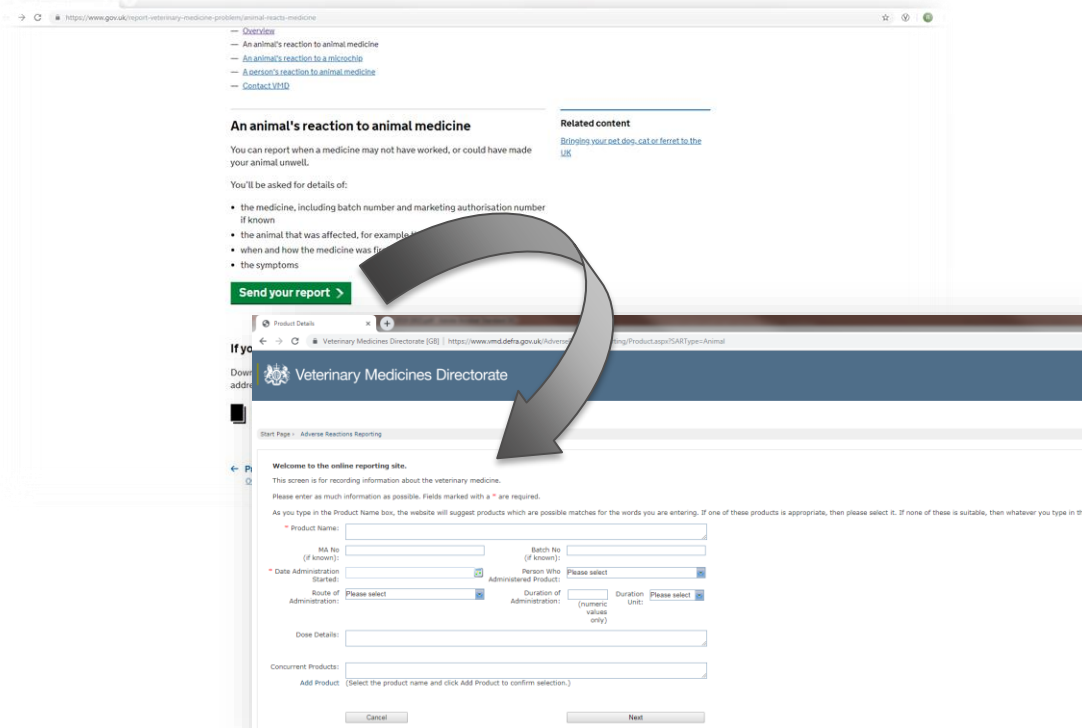
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## A basic pharmacovigilance system

### Reporting form for consumers

Simplified form for Agency and/or MAH

- Paper-based
- Electronic



Form to be sent to (Name and address of the relevant Regulatory authority)		IN CONFIDENCE For official use only Ref. Number:	
Fax:	Phone:	Initial report <input type="checkbox"/> / Follow-up report <input type="checkbox"/>	
E-mail:	Website:		
<b>IDENTIFICATION</b>	<b>NAME AND ADDRESS OF SENDER</b>	<b>NAME &amp; ADDRESS / REF. OF PATIENT</b>	
Safety issue in animals <input type="checkbox"/>	Veterinarian <input type="checkbox"/>	(according to national law)	
Safety issue in humans <input type="checkbox"/>	Pharmacist <input type="checkbox"/>	Name:	
Lack of expected efficacy <input type="checkbox"/>	Other <input type="checkbox"/>	Address:	
Withdrawal period issues <input type="checkbox"/>	Name:	Ref.:	
Environmental problems <input type="checkbox"/>	Address:		
	Phone:		
	Email:		
PATIENT(S) / Animal(s) <input type="checkbox"/>		Humans (for humans fill only age and sex below) <input type="checkbox"/>	
Species	Breed	Sex	Status
		Female <input type="checkbox"/>	Neutered <input type="checkbox"/>
		Male <input type="checkbox"/>	Pregnant <input type="checkbox"/>
			Age
			Weight
			Reason for treatment
<b>VETERINARY MEDICINAL PRODUCTS ADMINISTERED BEFORE THE SUSPECTED ADVERSE REACTION</b> (If more products are administered concurrently than the number of boxes available, please duplicate this form.)			
Name of the veterinary medicinal product (VMP) administered	1	2	3
Pharmaceutical form & strength (ex: 100 mg tablets)			
Marketing Authorisation number			
Batch number			
Route/site of administration			
Dose / Frequency			
Duration of treatment / Exposure			
Start Date			
End Date			
Who administered the VMP? (veterinarian, owner, other)			
Do you think that the reaction is due to this product?	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>
Has the Marketing Authorisation Holder (MAH) been informed?	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>	Yes <input type="checkbox"/> No <input type="checkbox"/>
Address to be sent to the MAH if further information requested, please tick the box. <input type="checkbox"/>			
Date:	Place:	Name and signature of sender:	
Contact point (Phone): (if different from the number on page 1)			

## A basic pharmacovigilance system

### Summary

- ✓ The Operating Manual provides a clear, concise description of creating a basic pharmacovigilance system
- ✓ Promotion of pharmacovigilance is key
- ✓ Creation of a PhV system which focusses on a risk-based approach
- ✓ Adopt an incremental approach to building a PhV system (scalable)
  - Start small and simple → time/progress → large and sophisticated
- ✓ You are not alone. Work together in the harmonisation of PhV systems
- ✓ Adopt VICH guidelines