OPERATING MANUAL

A basic phamacovigilance system veterinary medicinal products

How to use the Operating Manual?

As already described VICH do 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**

What I aim to do is describe how to use the manual to address some of these topics .

Contents of the Operating Manual

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

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

Responsibility of Marketing Autorisation 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

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

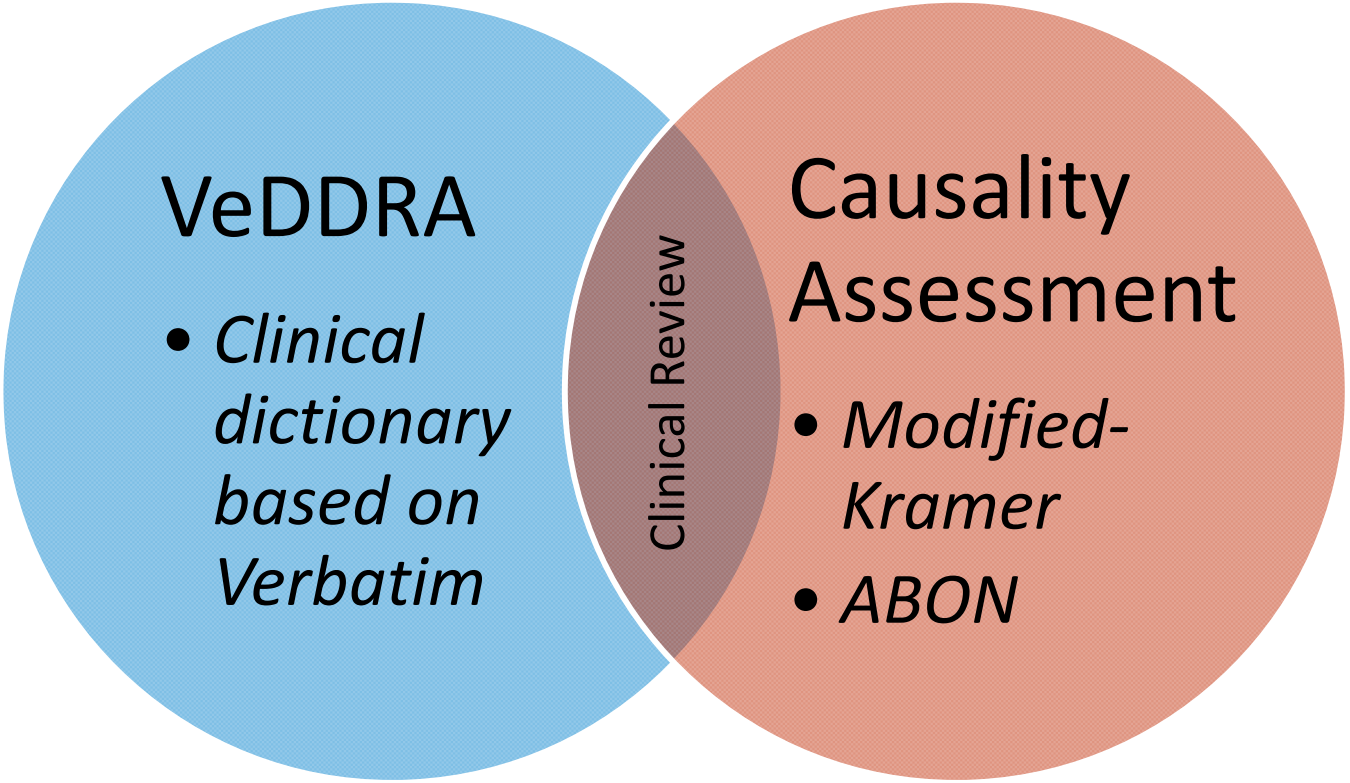
Archive periods

- **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

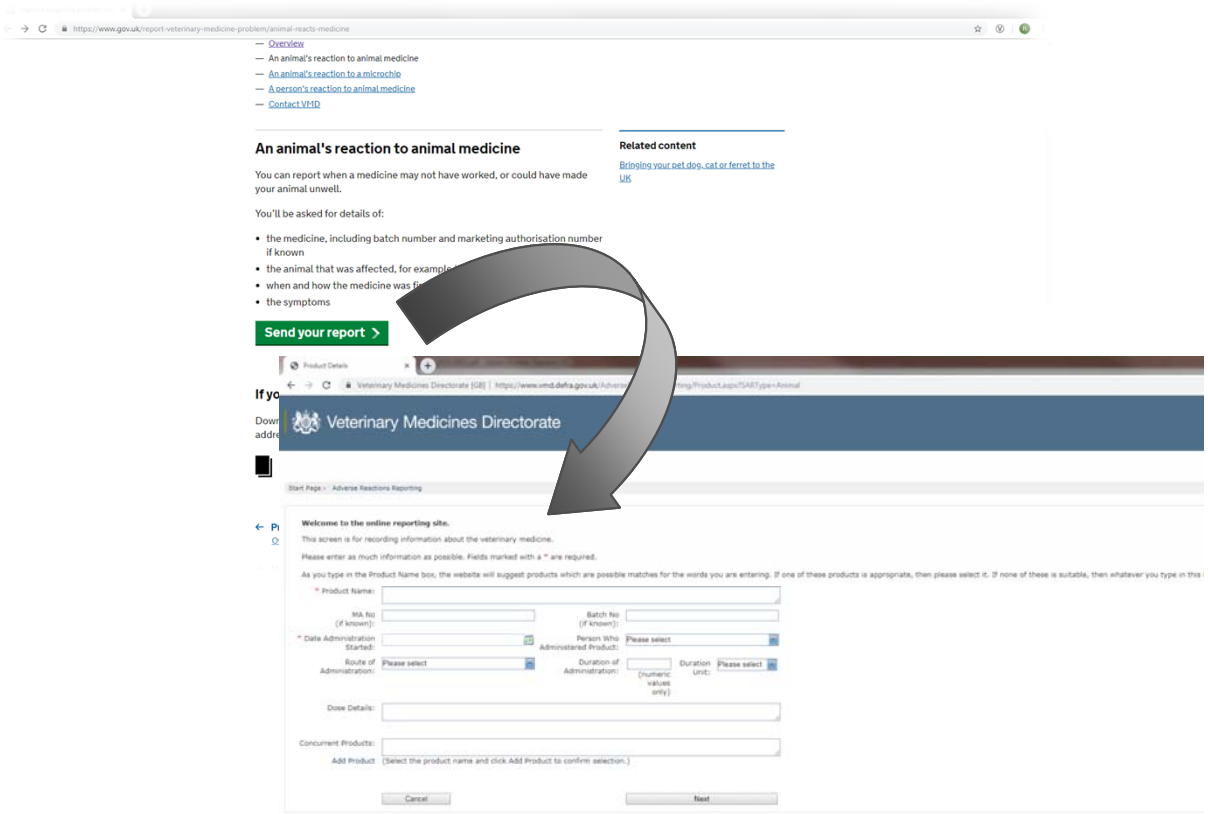
- A signal is defined as the detection of a new AE or a change in the rate of a known AE
- Signals should be prioritised based on their potential severity. All detected potential signals need to be validated, evaluated
- A confirmed signal is considered a risk
  a) either a potential risk
  b) or as 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

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: Initial report ☐ / Follow-up report ☐
Fax:	Phone:	
E-mail:	Website:	

IDENTIFICATION	NAME AND ADDRESS OF SENDER	NAME & ADDRESS / REF. OF PATIENT
Safety issue in animals ☐ in humans ☐ Lack of expected efficacy ☐ Withdrawal period issues ☐ Environmental problems ☐	Veterinarian ☐ Pharmacist ☐ Other ☐ Name: Address: Phone: Email:	(according to national law) Name: Address: Ref.:

PATIENT(S) Animal(s) ☐ Humans (for humans fill only age and sex below) ☐

Species	Breed	Sex	Status	Age	Weight	Reason for treatment
		Female ☐ Male ☐	Neutered ☐ Pregnant ☐			

VETERINARY MEDICINAL PRODUCTS ADMINISTERED BEFORE THE SUSPECTED ADVERSE REACTION

(if more products are administered concurrently than the number of boxes available, please duplicate this form)

	1	2	3
Name of the veterinary medicinal product (VMP) administered			
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 ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
Has the Marketing Authorisation Holder (MAH) been informed?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐

Duration of the adverse reaction in minutes, hours or days

nimals or Safety issues in
eriod/environmental problems)

the animal prior to the product
, how and with what and what
drawn and what happened
ed with the product(s) and what
en treated, how and with what

ERS IF NECESSARY e.g.
edical report for human cases)

ase also complete the details of

☐ joint ☐ other

address are send to
the MAH if further information requested, please tick the box. ☐

Date: Place: Name and signature of sender:

Contact point (Phone):
(if different from the number on page 1)

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