

Veterinary Pharmacovigilance: Introduction

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Pharmacovigilance: An Important Step in the Drug Development Process



- Despite the rigor of the pre-approval drug development process, it is impossible to have complete information about the safety of a drug at the time of approval.
- A drug product's safety profile can evolve over time.
- Ongoing collection and evaluation of post-market adverse event reports and other safety information is essential to ensure safe use of a product over its lifetime in the marketplace.

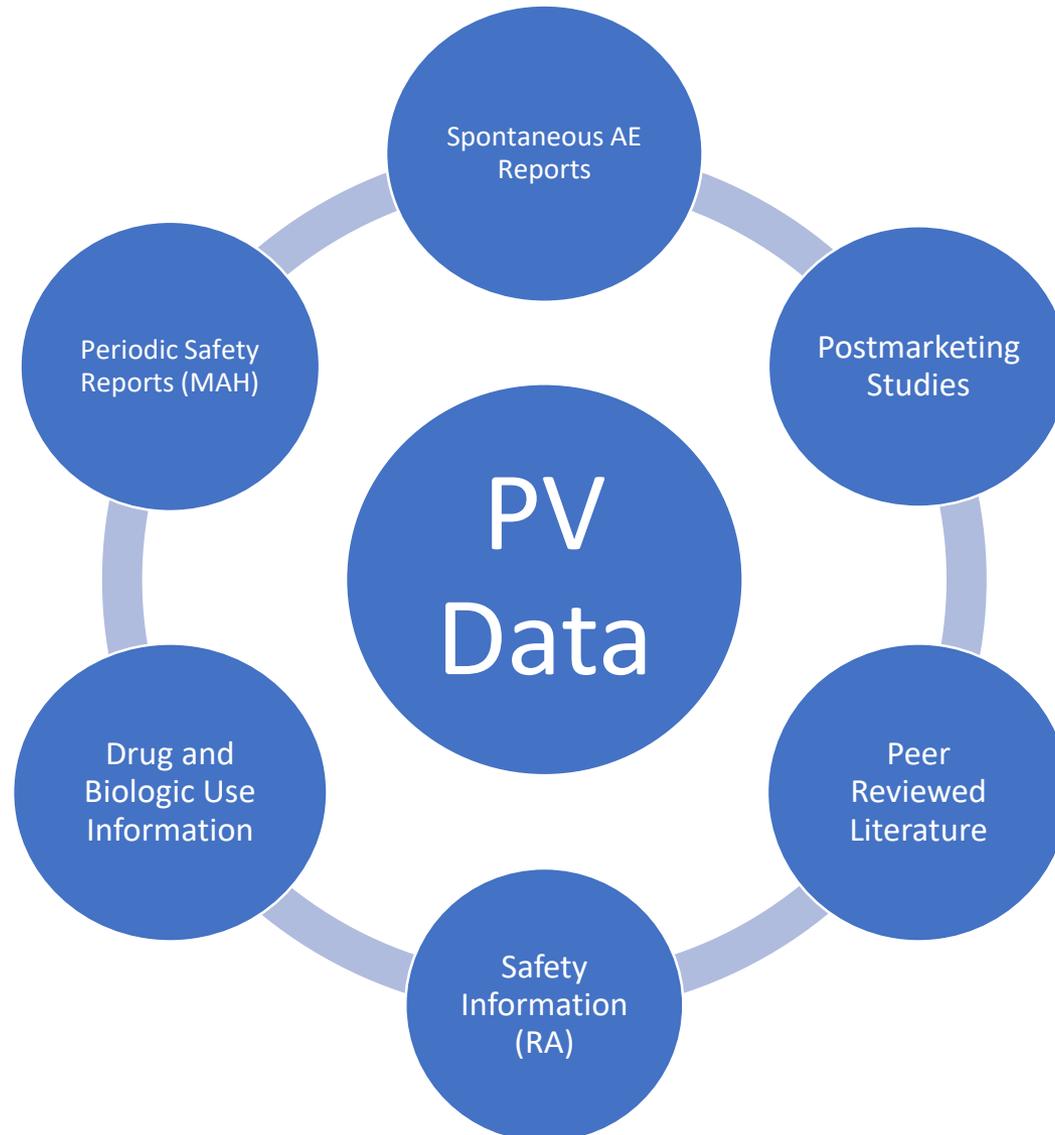
An effective pharmacovigilance system...

- Is a key component of drug regulation systems
- Promotes public health through early identification, assessment and risk mitigation of drug safety issues not identified pre-approval
- Informs communications (labels, product information sheets, safety alerts) that help ensure approved products remain safe and effective
- Promotes public trust/confidence

Pharmacovigilance Defined

Pharmacovigilance (PV) is defined by the World Health Organization as the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

What Pharmacovigilance Data is Available for Assessment?



A Note about Challenges with Assessing Spontaneous Reports



- Assessment of spontaneously reported adverse events is the primary post market surveillance method for veterinary medicinal products.
- Analysis of individual case reports can be challenging. Training is necessary.
 - With small numbers of reports, individual case review and assessment may be feasible.
 - Large volumes of AE reports may necessitate implementing signal detection/management tools; however, assessment of individual cases contributing to a “signal” remains necessary.

A Note about Challenges with Assessing Spontaneous Reports (continued)

- Spontaneous adverse event reporting is passive surveillance and has limitations:
 - Cannot reliably determine incidence of events.
 - Underreporting of adverse events is considered significant.
 - Individual Case Reports may provide limited information.
 - Causality cannot be *definitively* determined for most reports.

Encourage Good Case Reports

- In spite of the challenges with spontaneous reporting, it remains our primary post market surveillance method
- Good case reports should be encouraged, including:
 - Description of adverse event
 - Suspected and concomitant product therapy details (e.g., dose, dates of therapy)
 - Patient characteristics (e.g., species, breed, age, sex), baseline medical condition, co-morbid condition, relevant medical history, other risk factors
 - Documentation of the diagnosis
 - Clinical course and outcomes
 - Relevant therapeutic measures and laboratory data
 - Dechallenge and rechallenge information
 - Reporter contact information
 - Any other relevant information

The Complex Scope of Veterinary Pharmacovigilance World Wide:

A list of ten topics related to veterinary pharmacovigilance, presented in white text within a large, light blue, cloud-like shape. The topics are: Spontaneous Adverse Event Reports, Solicited Reports (e.g., post market clinical studies), Medication Errors, Product Quality Issues, Environmental Issues, Validity of Withdrawal Period, Off-label Use, Therapeutic Failures/Lack of Effect, Human Exposures to Veterinary Products, and Reports of Adverse Events in Unapproved Products.

- Spontaneous Adverse Event Reports
- Solicited Reports (e.g., post market clinical studies)
- Medication Errors
- Product Quality Issues
- Environmental Issues
- Validity of Withdrawal Period
- Off-label Use
- Therapeutic Failures/Lack of Effect
- Human Exposures to Veterinary Products
- Reports of Adverse Events in Unapproved Products

Global Harmonization Helps Navigate the Complexity

The VICH Pharmacovigilance Guidelines (GLs) were developed to facilitate information exchange of any type of adverse event report between manufacturers and regulatory authorities. If you are developing a PV system, start small:

- GL24 AE Terms, Definitions, Management
- GL29 PSUR Standardization, Management



Note: Some regional legislation has evolved since implementation of the above two Management GLs and may impact pharmacovigilance requirements referenced in the above two GLs

- GL42 Data Elements for Submission of AE
- GL30 Controlled Lists of Terms (24 lists!)
- GL35 Electronic Standards (Data Transfer)

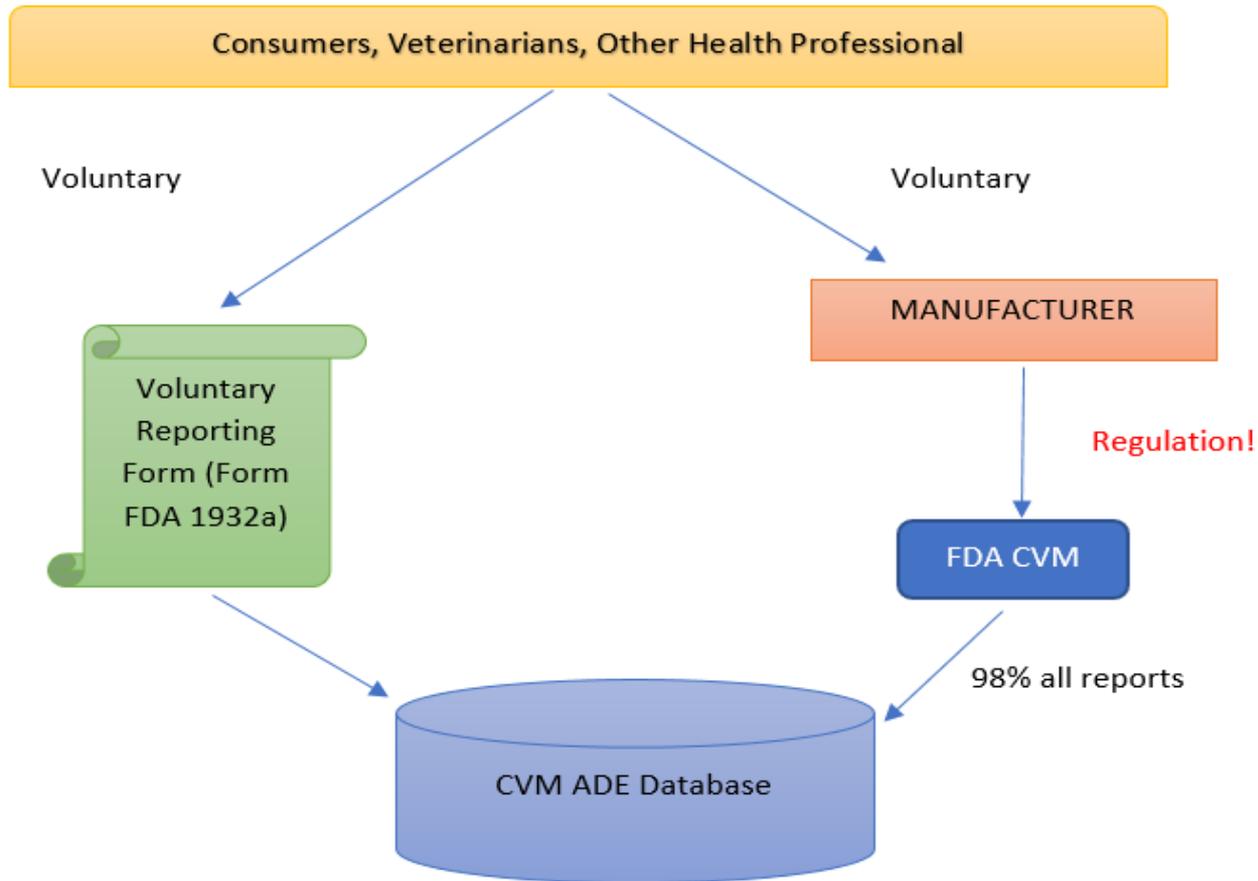


<https://vichsec.org/en/guidelines/pharmacovigilance/vich-gls-24-29-35-42.html>

VICH Technical Guidelines **do not**...

- Provide information on establishing regulations or describe how to set up a pharmacovigilance center
- Establish record keeping/reporting timelines (those currently exist in regional regulations)
- Provide instructions on how to analyze individual adverse event reports or conduct signal detection activities
- Provide guidance on developing a reporting form for consumer to report directly to agency (although some data elements could be leveraged to develop this). The existing technical guidelines DO advise on *electronic* exchange of individual case reports from manufacturer to regulatory authority *or* between regulatory authorities.

Regulatory Perspective: How FDA CVM Receives Adverse Event reports



Regulatory Perspective: Subject Matter Experts at FDA



Safety Evaluators:

- Clinical Veterinarians (large and small animal experience represented)
- Epidemiologists
- Statisticians
- Pharmacist

Multidisciplinary teams collaborate and evaluate any potential safety issues

Causality Assessments

- Several algorithms (ABON, modified Kramer) are used world-wide, but they have similar underlying principles of assessment, including evaluations of:
 - Temporal association
 - Dechallenge/rechallenge
 - Comorbid conditions
 - Biologic plausibility
 - Concomitant medications



Regulatory Perspective: Risk Management Activities and Communications

- Label revisions – Post Approval Experience (PAE) sections, warnings, product packaging
- Publicly available ADE data on CVM website
- Dear Doctor letters
- Client information sheet
- Freedom of Information (FOIA) requests
- Post-approval risk minimization programs
- Journal articles
- CVM Updates (FDA website)

Thank you!

