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French agency for food, environmental and occupational health safety
Investigate, evaluate, protect

Veterinary Pharmacovigilance: Introduction

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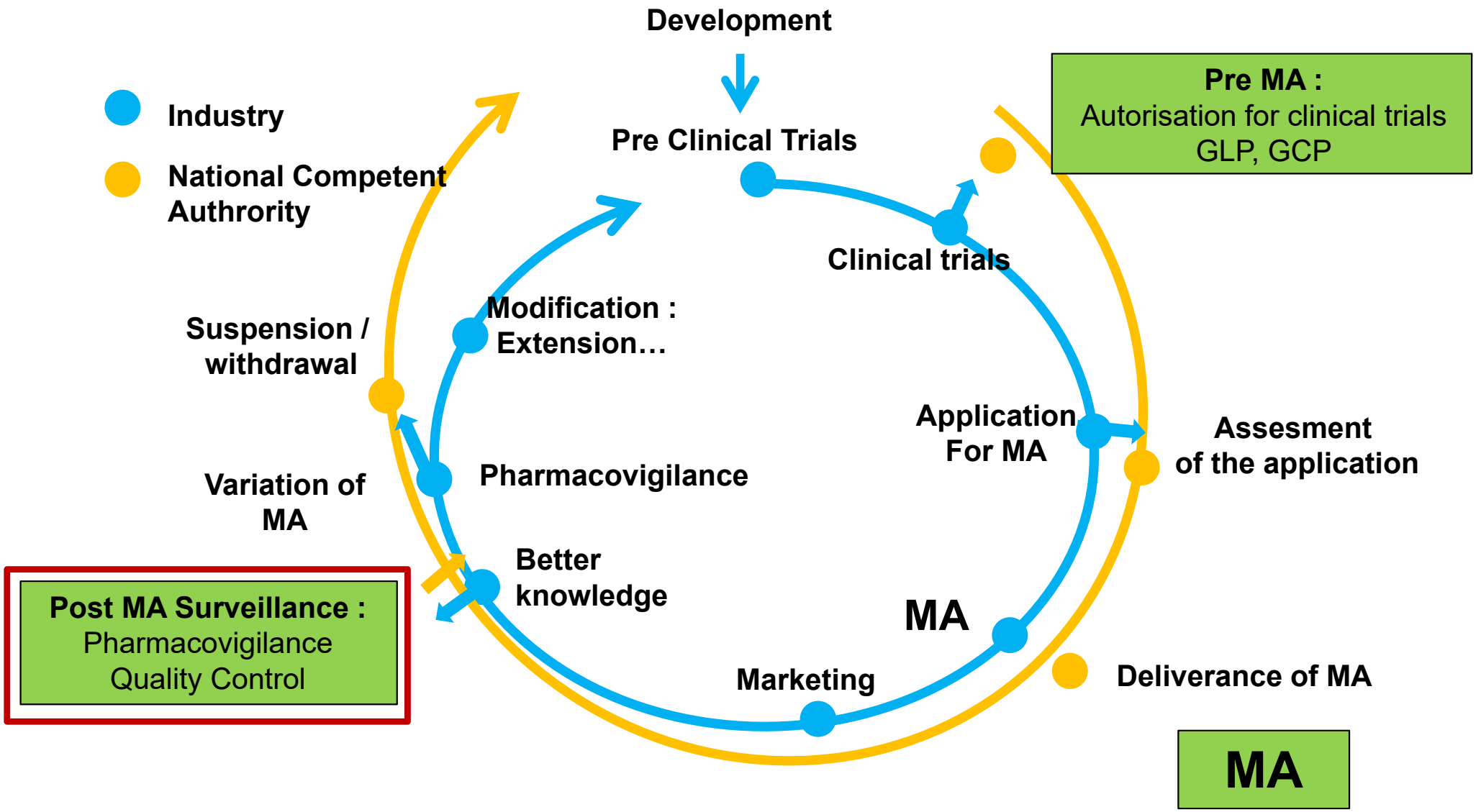
Marketing Authorisation Cycle



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.

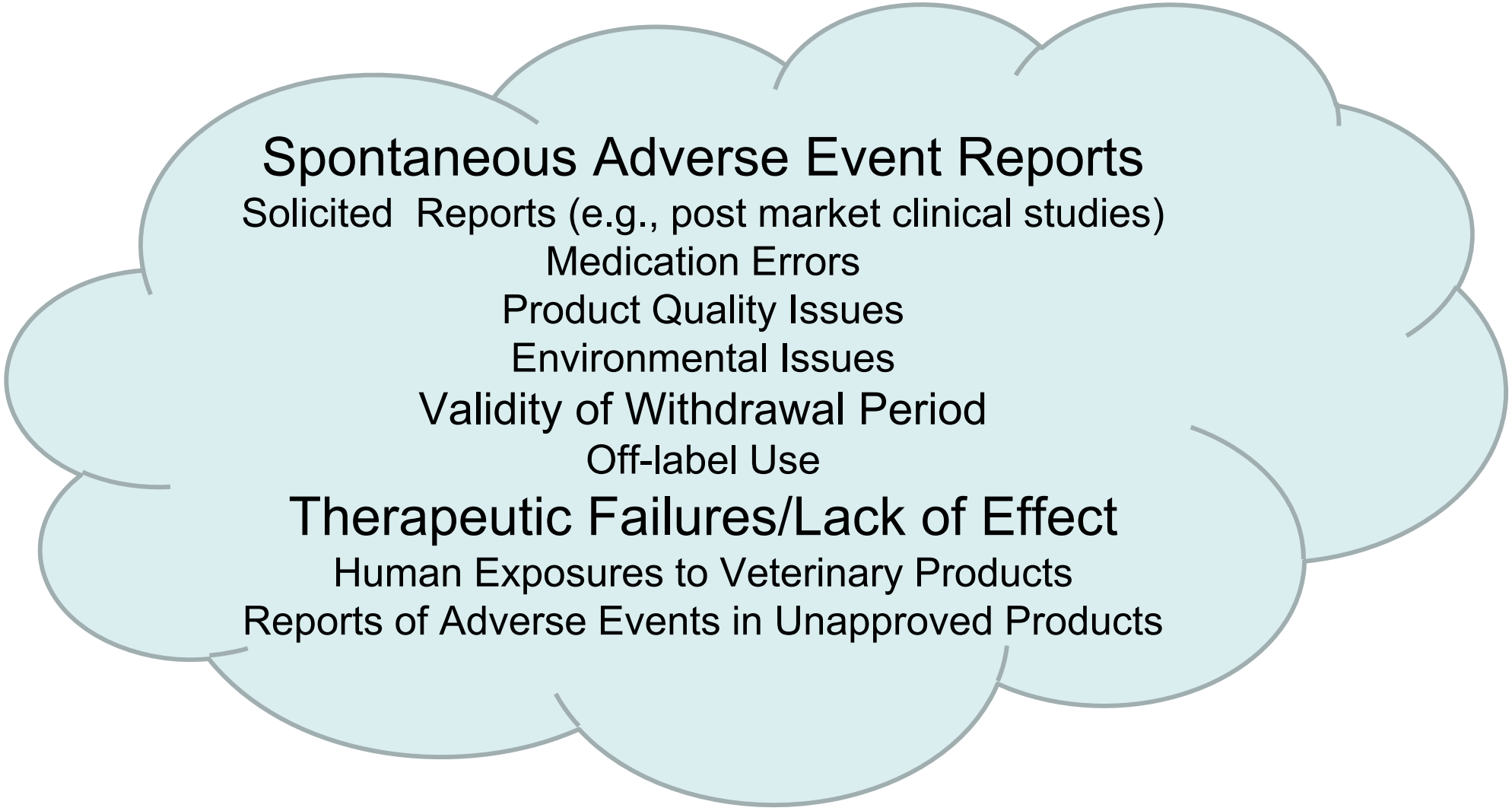
An effective pharmacovigilance system…

- 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

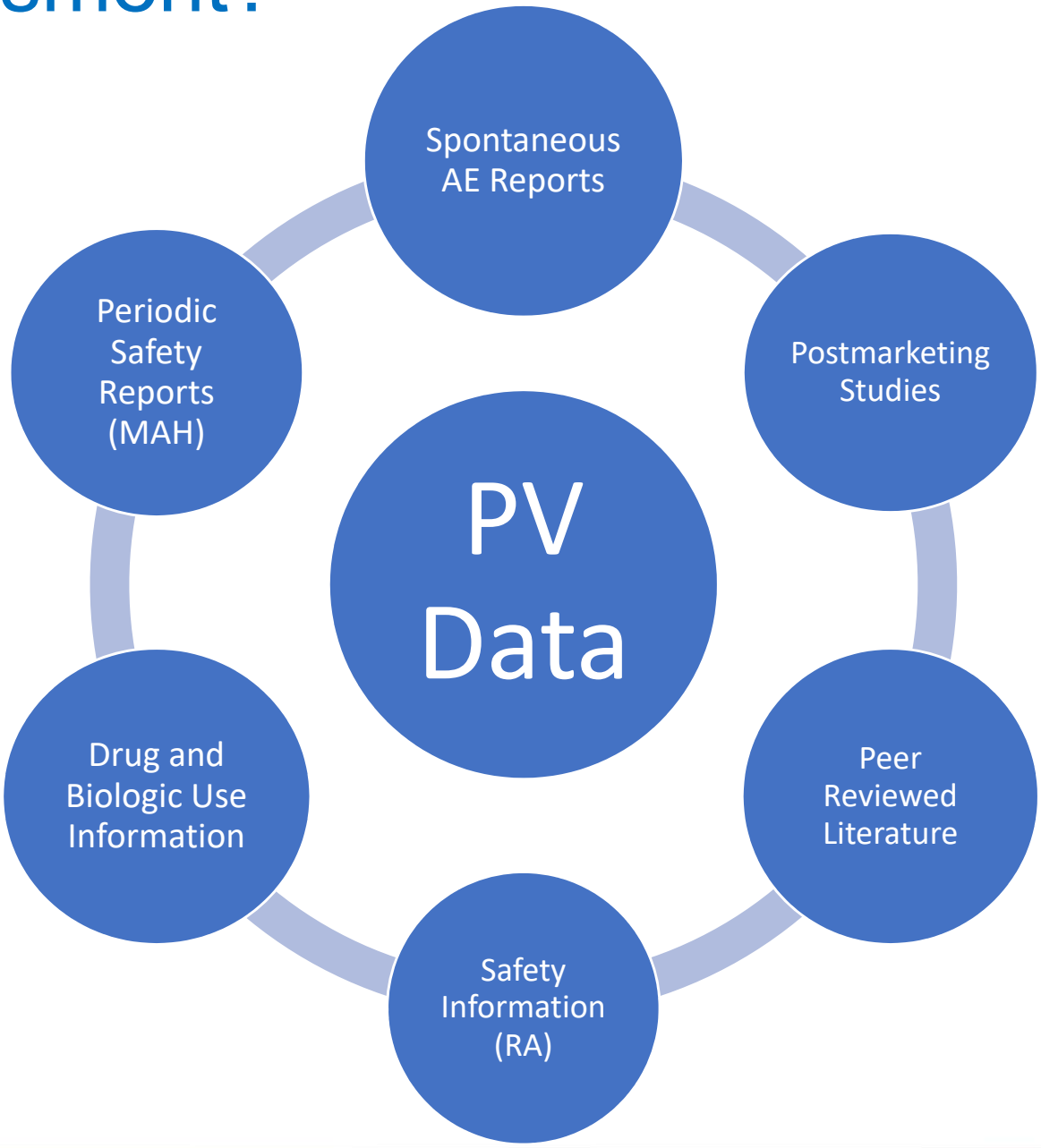
Pharmacovigilance - Definition

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.

The complex scope of veterinary pharmacovigilance world wide:



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

Adapted from: Guidance for Industry -Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, March 2005

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

Start with GL24 and GL29

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)

Reporting forms can be developed/structured using these elements

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

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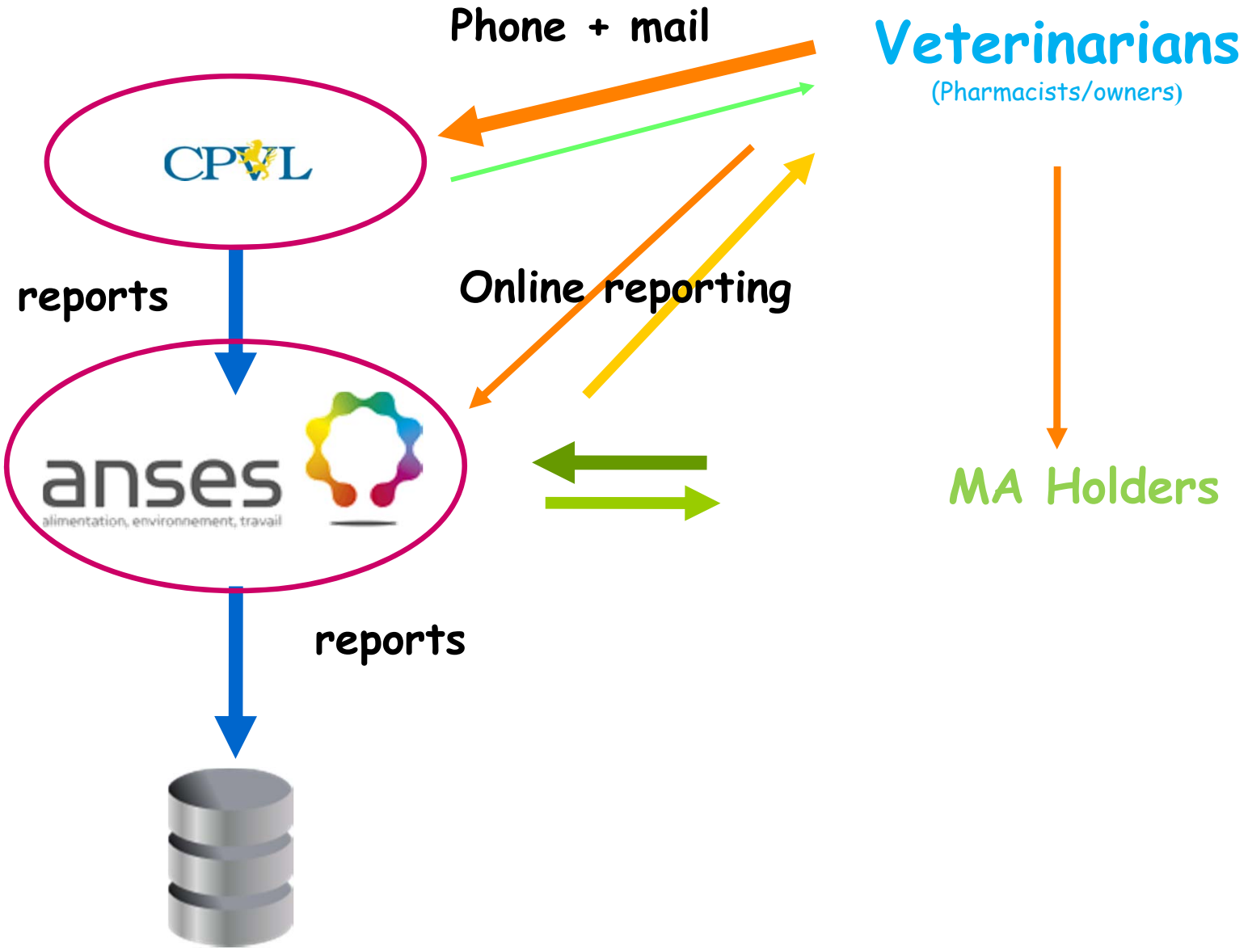
VICH Technical Guidelines **do not**…

- 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.

The French veterinary PhV system



Healthcare professionals

- Veterinarians and health care professionals
  - ✓Unexpected and/or serious adverse events (even expected) = Mandatory reporting
  - ✓Other events = Possible reporting

Marketing Authorization Holders

- Implementation of a Pharmacovigilance System+/- Risk Management Plan
- Trained staff and designation of a responsible person
- Adverse event reporting

  => Recording, assessment and transmission ANMV (15 days for serious cases)

- Periodic safety update reports (PSURs)
  - Benefit/risk assessment for each VMP
  - Transmission to Anses-ANMV

National Competent authority

« Animates and coordinates the national system»

- **Adverse event reports**
  - Recording (national database)
  - Individual assessment and scientific analysis
  - Response to reporter
- **Other activities**
  - Assessment of MAH's pharmacovigilance systems and risk management plans and inspection
  - Assessment of periodic safety update reports(PSURs) submitted by MAHs
  - Assessment of the benefit/risk ratio of VMPs during renewal procedures
- **Actions of promotion and communication**
  - Publications, annual report….
  - Education of vets

Competencies of experts and training

Safety Evaluators:

- Clinical Veterinarians (large and small animal experience represented)
- Epidemiologists
- Toxicologist (residues, eco-toxicologist, …)
- 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

Promotion and communications

To promote PVce feedback and regular exchanges with health care professionals are very important

- Feedback to professionals after notification
- Publicly available ADE data on NCAs website
- Annual report
- Label revisions – Post Approval Experience (PAE) sections, warnings, product packaging
- Dear Doctor letters or other warning information
- Client information sheet
- Journal articles
- Participation to professional congress
- Particiaption to education and training of veterianrians and other health care professional….

Thank you!