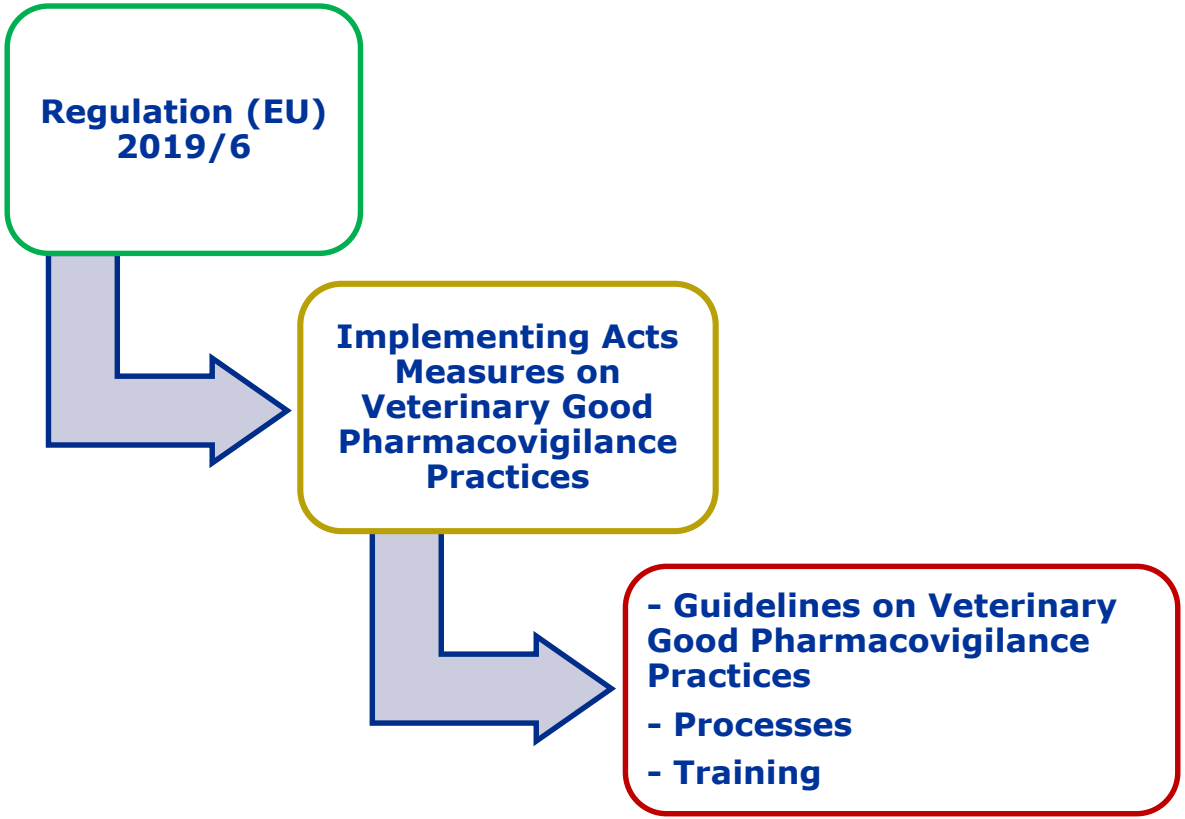
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update on pharmacovigilance, signal detection and surveillance

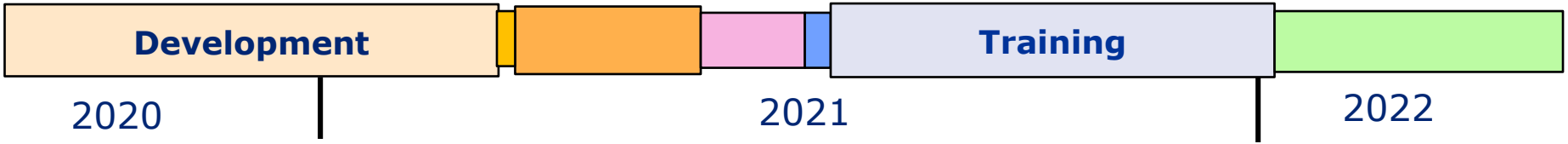
Veterinary Medicines Info Day 2021

Presented by Jos Olaerts on 25 March 2021
Veterinary Risk and Surveillance Service

An agency of the European Union



Guidelines on Veterinary Good Pharmacovigilance Practices - timeframe



Meetings on Guidelines on Veterinary Good Pharmacovigilance Practices since October 2020

- Weekly experts groups meetings on
  - Reporting and recording of suspected adverse events Communication
  - Signal detection
  - Communication
  - PhV Inspections – PSMF
- Joint meetings EMA with NCA members of the PHVWP-V – **11** meetings
- Stakeholders meetings EMA, NCA members and industry – **7** meetings

Modules

1. Overview: Veterinary Pharmacovigilance in the EU
2. Reporting and recording of suspected adverse events
3. Pharmacovigilance data analysis – signal management
4. Inspections – PSMF – Quality management system
5. Pharmacovigilance communication
6. Annexes
    i. EudraVigilance Veterinary
    ii. Pharmacovigilance Data Warehouse
    iii. List of Medically important VeDDRA terms

NVR PhV Pillars

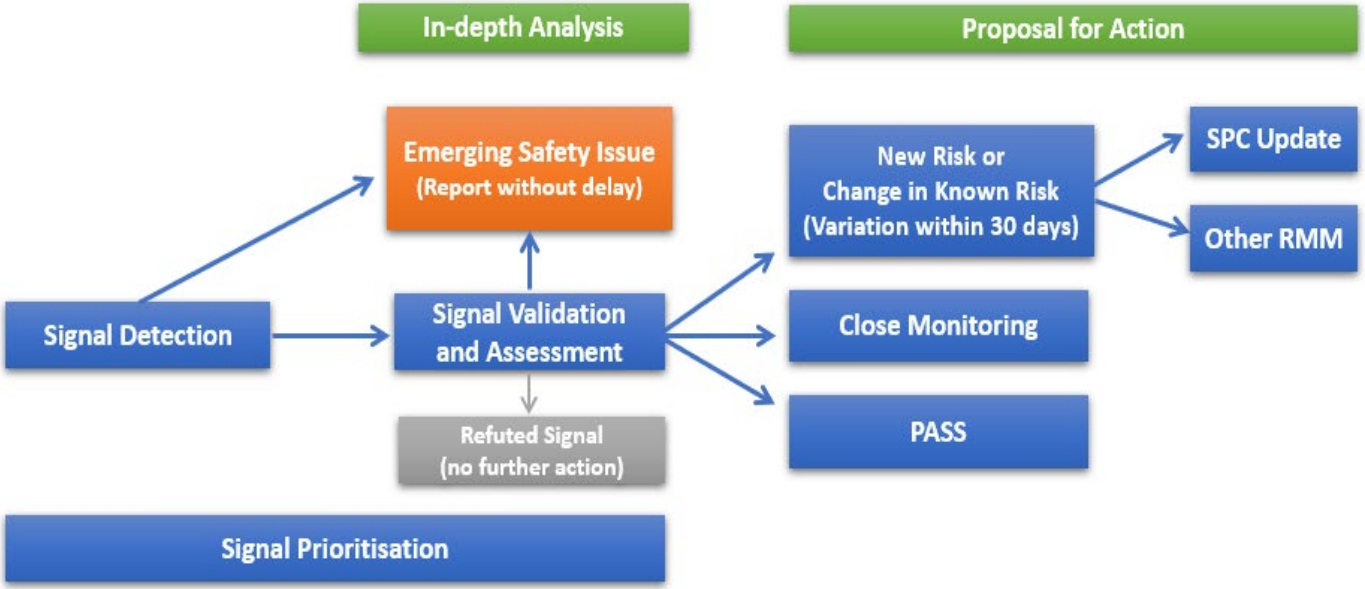
- **AE collection and recording**
  - 30 days + non-serious cases
  - Yearly sales (+ estimation of exposed Number of target species)
- **Continuous AE analysis by MAH (signal management)**
  - Using EVVET database or own database (+ 1 yearly SD analysis on EVVET)
  - Yearly MAH statements + SM outcomes submitted to database
- **Regulator oversight through**
  - PhV Inspections
  - Risk based signal surveillance by regulators
  - Ad-hoc targeted surveillance
- **Pharmacovigilance Master File (+ Quality Management System)**

Reporting and recording of suspected adverse events

Elements that have been particularly discussed:

- Literature reports, internet and social media reports, reports from post-authorisation studies
- Causality assessment
- Data quality management
- Special situations (e.g. off-label use, homeopathic VMPs)
- Reporting AEs following the use of human medicinal products
- Human adverse reactions

Pharmacovigilance data analysis – Signal management



Medically Important Events (MIE) list

MIE PTs	Species association #	Excluded LLTs ¤
Abdominal pain	Horse	Abdominal cramp, Abdominal discomfort, Praying position, Stomach cramp, Tense abdomen
Abomasitis	Ruminant, Camelid	
Abortion	All	
Acute mastitis	Ruminant, Camelid, Horse	
Anaphylaxis	All	
Anorexia	Horse	
Apnoea	All	
Birth defect	All	
Blindness	All	
Bone marrow hypoplasia	All	
Cardiac arrest	All	
Cardiac insufficiency	All	
Circulatory shock	All	
Collapse NOS	All	
Coma	All	
Convulsion	All	
Deafness	All	
Death	All	Unexplained death, Unrelated death
Diabetes mellitus	All	
Dyspnoea	All	
Epileptic seizure	All	
Fish asphyxia	Fish	
Fish body deformity	Fish	
Haemolytic anaemia	All	
Haemorrhagic gastroenteritis	All	
Heart block	All	
Hepatic failure	All	
Hypersensitivity reaction	All	Allergic pruritus, Allergic reaction, Allergic skin reaction, Allergy NOS
Hypocalcaemic condition	Ruminant, Camelid	
Hypomagnesaemic condition	Ruminant, Camelid	
Impaired hearing	All	
Impaired vision	All	
Ketosis	Ruminant, Camelid	
Laminitis	Horse	
Loss of consciousness	All	
Lying down	Horse, Ruminant, Pig, Camelid	
Metastatic neoplasia	All	
Metritis	Horse, Ruminant, Camelid	
Moribund	All	
Multi-organ failure NOS	All	
Myoglobinuria (Horses only)	Horse	
Paralysis	All	
Paresis	All	
Perinatal mortality	All	
Recumbency	Horse, Ruminant, Pig, Camelid	
Renal insufficiency	All	
Reticulitis	Ruminant, Camelid	
Stillbirth	All	
Suspected infectious agent transmission	All	

Dashboards	Reports
Signal Detection	**Overview of AERs per product/active substance/ATC Vet code**
	Signal detection with 2 RORs up to date 2 and up to date 1
	Static ROR Evaluation
Signal evaluation	**Animal Data** (species/breed, age, weight analysis, pharmaceutical form, regional distribution, time to onset)
	Product information (product used without other products)
	Product association (product used in association with another product)
	Associated VedDRA (where VedDRA term appears in conjunction with another VedDRA terms)
	Link to VPhS
Adverse Events comparison between 2 period (previous name: reaction monitoring)	**Adverse Events comparison between 2 periods**

Pharmacovigilance data analysis – Signal management

Roles, responsibilities and procedural aspects

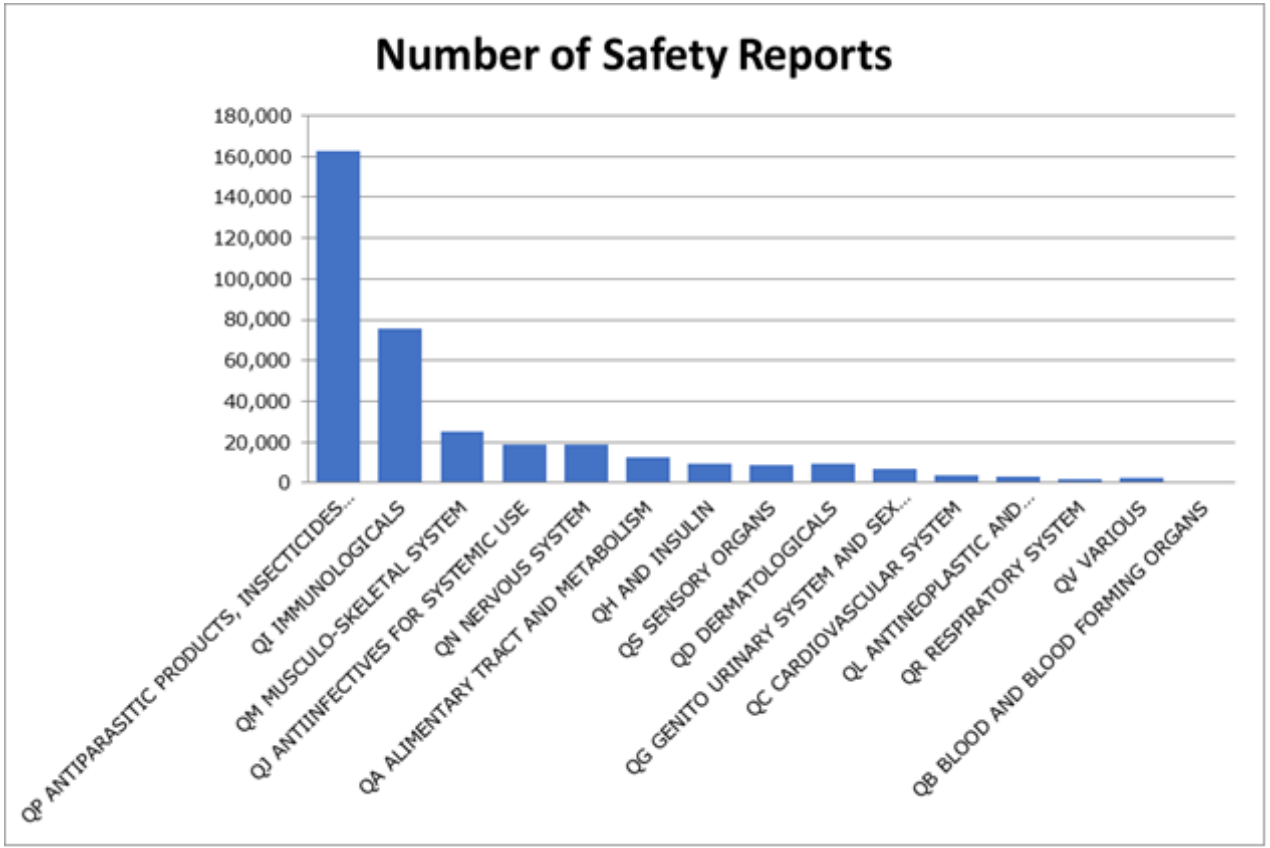
- Central role of PhVWP-V

Two different approaches are considered and still to be agreed:

1. Workshare similarly to PSURs and lead authorities
2. Central Member States Expert group on signal management

Reports per active substance

Active Substance	Number of Safety Reports	%
IVERMECTIN	49,607	11.9%
PYRANTEL PAMOATE	48,715	11.7%
AFOXOLANER	43,945	10.5%
MELOXICAM	16,215	3.9%
FLURALANER	14,916	3.6%
SPINOSAD	14,252	3.4%
MILBEMYCIN OXIME	14,148	3.4%
CANINE DISTEMPER VACCINE (LIVE), FREEZE-DRIED	11,739	2.8%
CANINE ADENOVIRUS VACCINE (LIVE)	11,624	2.8%
CANINE ADENOVIRUS TYPE 2	9,499	2.3%



Pharmacovigilance inspections and PSMF

Module focus: Planning, conduct, reporting, follow-up and operation of pharmacovigilance inspections

- Topics where additional guidance is required:
  - PSMF (summary of PSMF and content/access/maintenance)
  - Quality Management System for Pharmacovigilance

Communication

- Part I: Principles for good practice on communication
- Part II: Components of overarching communication plan
- Part III: Communication procedures & operation within the Union regulatory network
  - General principles for information exchange
    - Use of Union pharmacovigilance database for PhV alerts [I and non-urgent info
    - Cooperation between MAHs/CAs/Agency
    - Coordination of communication :
  - Regulatory review of veterinary pharmacovigilance communication (& individual communication plan)
    - Procedure for regulatory review of communication (e.g. DaHPC)

- Annex: DaHPC template; Individual communication plan

“EMA to organise meetings or network for groups of veterinarians..” (Art. 79)

EUROPEAN MEDICINES AGENCY

Specialised Veterinary Practices

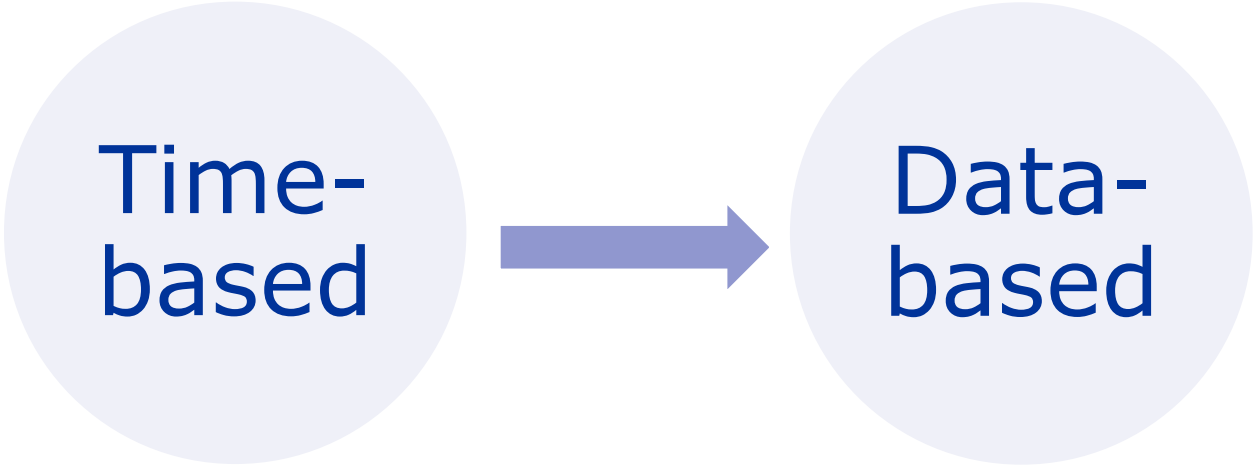
EU regulators

Direct exchange of know-how




Dependencies

- EVVET 3 + simple signal management workflow (first iteration based on legislative requirements only) by 28 January 2022; additional functionalities and an improved signal management workflow will be delivered in 2022.
- UPD (Union Product Database)
- availability of product data in UPD + recoding the AERs in EVVET3 against products.



PhV - basics

- **Clinical judgment:**
  - Injection site reaction, anaphylactic type reaction.
  - Rare events, long-term effects, confounding factors concomitant products, underlying disease, possible interaction
  - Observational data versus prospective study
- Signal Detection advantage:
  - facilitates lifecycle overview
  - Relative comparison (however skewed dataset)

PhV related activities (“Burden”)

EUROPEAN MEDICINES AGENCY

- Systems
- Processes
- Training
- Signals

Any questions?

Further information

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Telephone +31 (0)88 781 6000
Send us a question Go to www.ema.europa.eu/contact

Follow us on **@EMA_News**