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Surveillance

Workshop for OIE national Focal Points for Veterinary Products
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Market surveillance

- Control laboratories
- Pharmacovigilance
- Residues

Control laboratories

- 1 - Have a database of authorized vet medicines (and those really marketed) and if possible quantities (volumes)
- 2 - Elaborate a programme of surveillance with a risk analysis and in cooperation with other services (assessment, pharmacovigilance, inspection)

Risk based programme

- Products used for food producing animals
- Products that present a risk for the users (vet, farmers, etc.)
- Focus on antibiotics and antiparasitics
- Any other risk specific to the concerned area (temperature, manufacturer, product largelly used, product that can be counterfeited….)

Sampling

⇨Done by inspectorates (in wholesalers but also anywhere on the market depending of the area)

⇨Make as much as possible series : all solutions for injection with benzylpenicillin for example

- To have an idea of the market for this kind of products
- To be able to test with the same method (as much as possible)
- To avoid imbalance between rival Marketing Authorization

Testing

⇨Active ingredient content

most often by HPLC (High performance Liquid Chromatography)

- Reference method is the method from the Marketing Authorization dossier as soon as it has been validated (i.e. following VICH guidelines)
- Possibility to use one generic methods to be able to test all products with the same method.

Reference substance

- Possibility to use the one given by the Marketing Authorization as soon as it has been tested following a compendial method (pharmacopoeia) or with a Marketing Authorization method validated with VICH guidelines (= certificate supplied with the reference and with a shelf life)

- Use reference substances in case of doubts (for example: from EDQM-European Directorate for the Quality of Medicines & HealthCare)

Other tests

- Density (may be needed for calculation of active ingredient content)

- pH (pH meter also useful for preparing aqueous part for buffered mobile phases for HPLC)

- …

Quality

- Apply a quality management system (QMS) in line with ISO17025 : quality reference for control laboratories
- Depending of the area, air conditioning may be needed (for testing and for sample storing)

Out Of Specification : OOS

- In case of Out Of Specification
- - check list of the analyse done (Is there anything I did wrong ?)
- If anything is wrong throw away the result and do again.
- If everything is OK look the reference method
- Avoid testing until compliance.

Strategy for quality control of IVMPs (immunologicals)

- Possibly based on a risk analysis :
  - biologicals involved in the control of zoonosis
  - biologicals involved in the control of regulated diseases
  - live vaccines
  - recombinant vaccines
- ➔ Example official batch control :
  - rabies vaccines (live and inactivated)
  - bovine and avian tuberculins
  - brucellosis vaccine
  - brucelline

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Quality control for IVMPs: examples

Control Authority Batch Release

- Review of manufacturer's control reports

  and
- Testing

Or

- Harmonised procedure
- System for exchange of information (not complying batch)

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Market surveillance

- ⇨ Control laboratories
- ⇨ Pharmacovigilance
- ⇨ Residues

Pharmacovigilance

objective

safe and effective veterinary medicinal products

- protect animal health and welfare
- minimise losses and distress to companion animal owner
- avoid economic consequences to farmers

Pharmacovigilance

primary objective : collect and evaluate information

on suspected adverse drug reactions (ADRs):

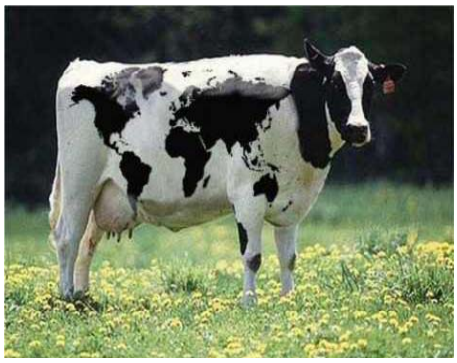
serious, non-serious, expected, unexpected

Pharmacovigilance

Veterinary Pharmacovigilance may cover:

- clinical safety in animals
- lack of expected efficacy
- extra label use / misuse / abuse
- insufficient withdrawal periods
- potential environmental problems
- adverse reactions in humans to veterinary medicines (user safety aspects)

Particularities of Veterinary Pharmacovigilance



insufficient withdrawal period: food safety problem

residues of drugs in food, violation of Maximum Residue Limits (MRL)

Particularities of Veterinary Pharmacovigilance

environmental problems

Case example: Sheep dip residues contaminated small river which irrigated nearby aqua culture and lead to fish death.

Particularities of Veterinary Pharmacovigilance

environmental problems

Case Example: Diclofenac, used in southern Asia as a livestock treatment, is toxic to vultures when they feed on contaminated carcasses, causing kidney failure and death. 3 vulture species nearly extinct.

Adverse reactions in humans

Unintended

⇨close contact with animal i.e. antiparasitic spot on products, collars

⇨contact (skin / eye)

⇨accidental injection

⇨confusion with human medicinal product

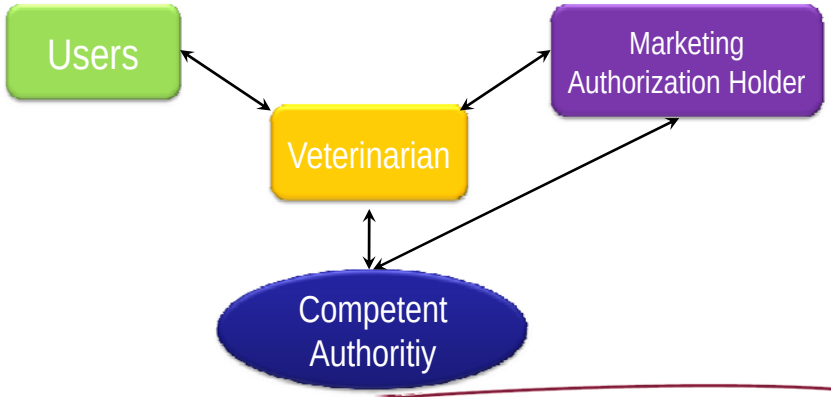
Adverse reactions in humans

Micotil (Tilmicosin)

Problem : accidental self injection by farmers

What are the needs for a good Pharmacovigilance system

A system based on interaction between interested parties : Network



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What are the needs for a good Pharmacovigilance system

A system based on interaction between interested parties

As a minimum, relying on:

- ✓ A national database
- ✓ An assessment by experts in pharmacovigilance (scientific Committee)
  - To assess data related to adverse effects
  - To issue opinions
- ✓ A scientific secretariat

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What are the needs for a good Pharmacovigilance system

Information / Communication / Transparency

- Modification of MA (SCP)
- Pharmacovigilance general information

newsletters to health professionals

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Market surveillance

⇨ Control laboratories

⇨ Pharmacovigilance

⇨Residues

Residues origin

⇨Volontary usage

- Correct usage of the VMP
- Strict respect of the withdrawal period
- Usage in another species
- Respect of the legislation

⇨Fraudulent usage

- Forbidden substance
- Starting material
- No respect of the legislation

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Residues origin

⇨Unvolontary usage

- Administration mistake
  - ✓Animals identification
  - ✓No respect of the prescription
  - ✓Use without prescriber's advice
- Animals management mistake
  - ✓Bad recording of treated animals
- Cross contamination
  - ✓Medicated feeding stuff
  - ✓Distribution system (feed, water)

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Residues

- A regulation is necessary to:
  - Assess risks associated to residues
  - Manage risks : LMR definition, classification of products

- Implementation of Auto-control and surveillance by Countries :
- Sampling plans
- Reference laboratories at national and regional level

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Surveillance plans organisation

⇨Comptetent authority :annual control plans to put in place

- Designation of a person responsible for sampling
  - ➢ Veterinary Services
- Sampling points
  - ➢ Farm level
  - ➢ Primary transformation (slaughter, dairy, etc…)
- Analysis
  - ➢ Reference laboratory
  - ➢ Authorised routine laboratory
  - ➢ Official methods

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Residues control: an example

⇨Forbidden substances (in European Union)

- Chloramphenicol, Nitrofuranes

⇨Authorised substances

- Antimicrobials as Betalactamins, Cephalosporins …
- Antiparasitics : Avermectines, Benzimidazoles
- Anesthesics

⇨ Malachit green

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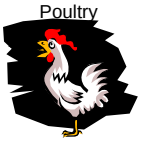
Residue Monitoring : Animals and products concerned

Bovines

Aquaculture

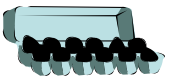
Milk

Poultry

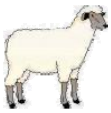


Farmed game
Wild game

Eggs



Sheep/goats



Horses (food)

Honey

Residue Monitoring : Frequencies, level of the control

Species	Number of controlled animals (% of annual production)	Unauthorised substances		VMPs
Bovine	0.4%	0.25%	50% live animal	0.15%
			50% slaughterhouse	
Porcine	0.05 %	0.02%		0.03%
Sheep and Goat	0.05 %	0.01%		0.04%
Equine	In relation to the problems identififed			
Poultry	1 per 200 tons	50% of samples		50% of samples
Aquaculture	1 per 100 tons	1/3 of samples		2/3
Milk	1 per 15000 tons	1/3 of samples		2/3
Eggs	1 per 1000 tons	1/3 of samples		2/3
Honey	10/300 tons (3000 tons) + 1/300 tons			

Results and follow-up : Non compliance

⇨ If the result exceeds the maximum residue limit (MRL)

➡ Investigation on farm

- Find the cause of non compliance (not respect of the latency).
- Checking the register of breeding.
- Recall of the obligations.
- Correct measurements to implement.
- Withdrawal of the market of the food products if new non compliant results.
- Targeting of the breeding for the plan of the year n+1.

Thank you for your attention

Organisation mondiale
de la santé animale

World Organisation
for Animal Health

Organización Mundial
de Sanidad Animal

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