Pharmacovigilance
Benefits of reporting adverse events

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WHAT IS PHARMACOVIGILANCE?

The combined efforts of

- authorities
- industry
- veterinary profession
- end-users

to evaluate safety and efficacy of veterinary medicines in practical use situations and to incorporate these findings in product availability and documentation in order to optimise animal health, welfare and public health

Adverse Event

- Any observation in animals, whether or not considered to be product-related, that is unfavorable and unintended and that occurs after any use of VMP (off-label and on-label uses)
- Included are events related to a suspected lack of expected efficacy according to approved labelling or noxious reactions in humans after being exposed to a VMP

VICH GL24

SCOPE

- Lack of efficacy
- Off-label use
- Human Reactions
- Potential environmental problems
- Investigation of the validity of the withdrawal period

arising from the use of the product ...which may have an impact on the evaluation of their benefits and risks

WHY DO WE NEED PHARMACOVIGILANCE?

The frequency of adverse events is defined using

the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 in 100 animals)
- uncommon (more than 1 but less than 10 in 1,000 animals)
- rare (more than 1 but less than 10 in 10,000 animals)
- very rare (less than 1 in 10,000 animals)

Table 1. Number of exposed animals needed to detect true frequencies of adverse events (AEs)

	Statistical power			
Frequency of AE	95%	90%	80%	63%
1 in 100	300	231	161	100
1 in 500	1,500	1,152	805	500
1 in 1,000	3,000	2,303	1,610	1,000
1 in 5,000	15,000	11,513	8,048	5,000
1 in 10,000	30,000	23,026	16,095	10,000
1 in 50,000	150,000	115,130	80,472	50,000

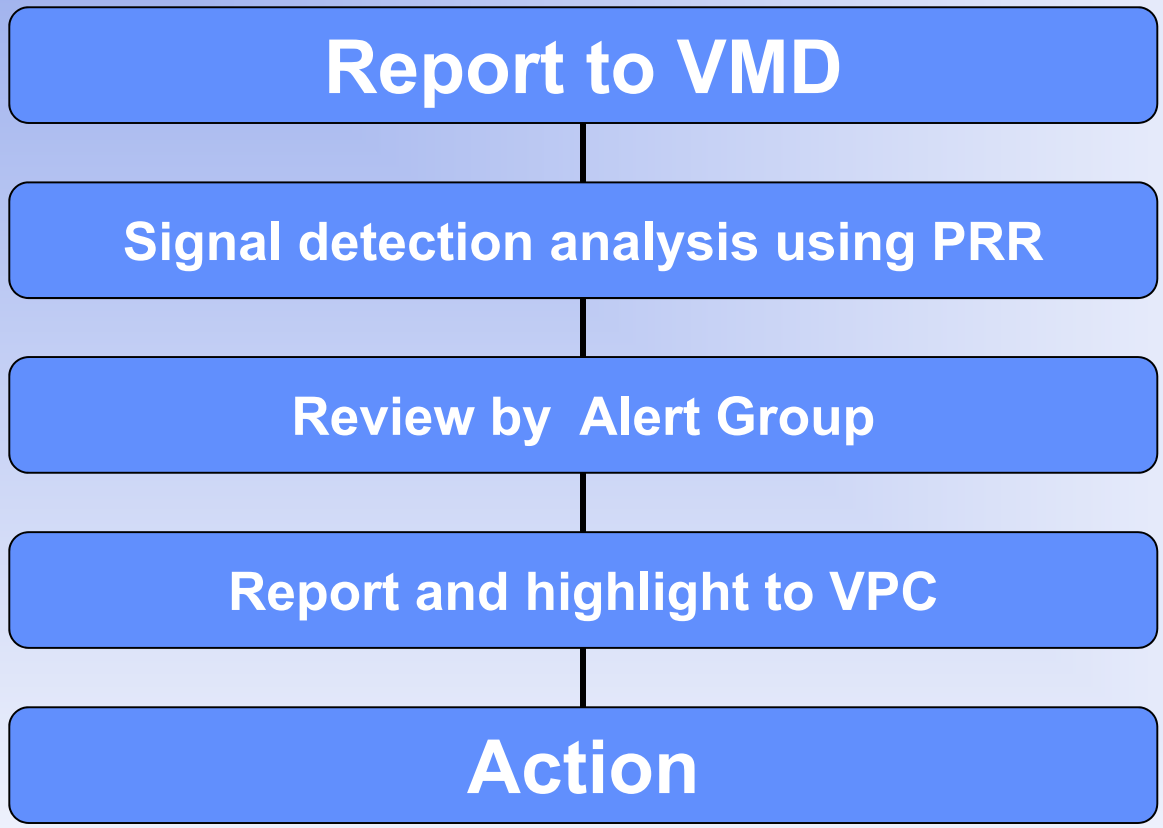
O'Rourke, D.J. (2016) Adverse events – vets have a key role. *Veterinary Practice Today*, 4(2):23-26.

But then….Practice….

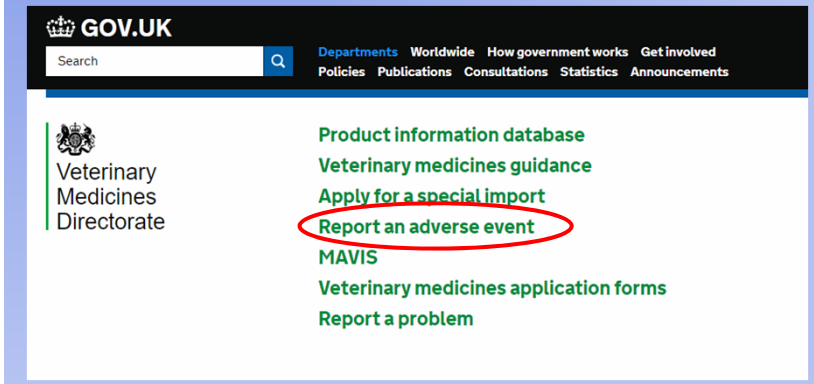
- larger number of animals
- combinations with ….
- other environmental conditions
- other species
- off label use: dosage/time
- age/condition
- ..sometimes….product failures

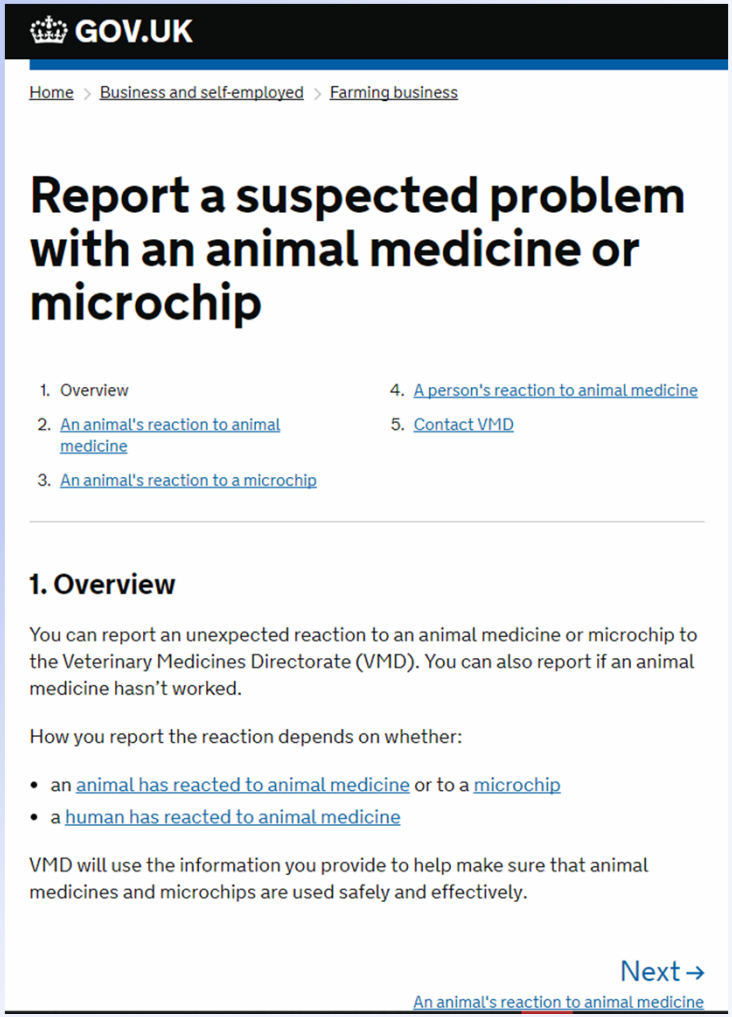
The safety profile of a VMP evolves over its lifetime on the market

Pharmacovigilance – the process



How are reports received?





Online since September 2010

Type of reports received

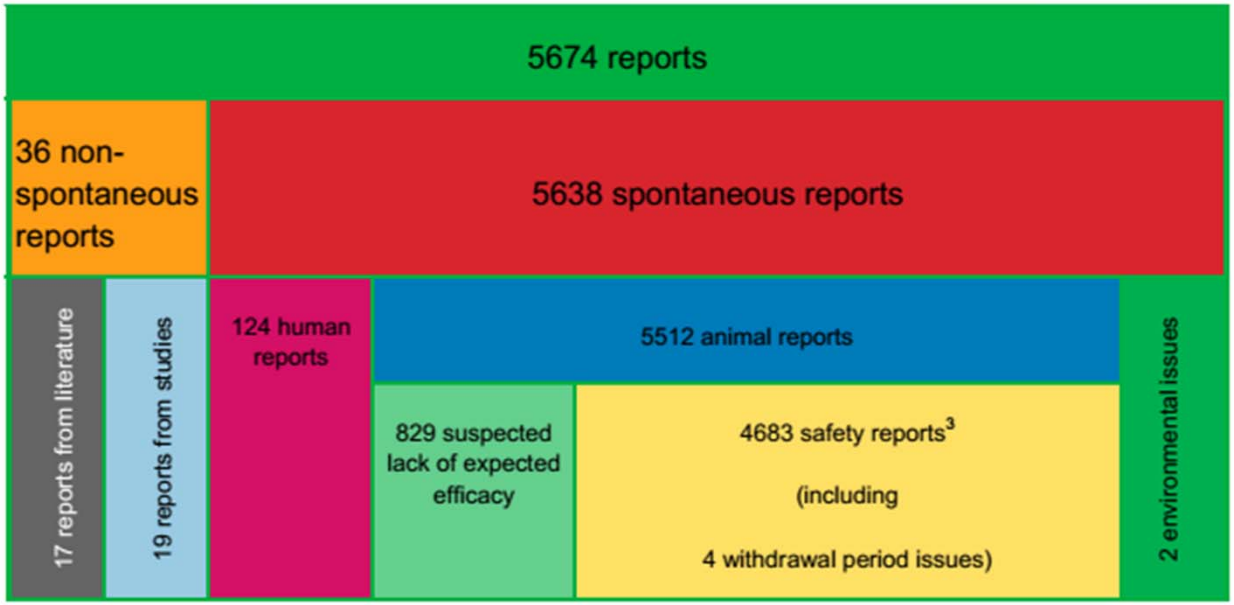


Figure 3 Different types of adverse event report received

Veterinary Pharmacovigilance in the United Kingdom: Annual Review 2015
(https://www.gov.uk/government/publications/veterinary-medicinespharmacovigilance-annual-review-2015).

Products involved in reports

- Treatments for internal and external parasites (52%)
- Vaccines (30%)
- Others (18%):
  - Antibiotics
  - Anaesthetics
  - Treatments for vomiting
  - Treatments for inflammation
  - Treatments for hormone regulation

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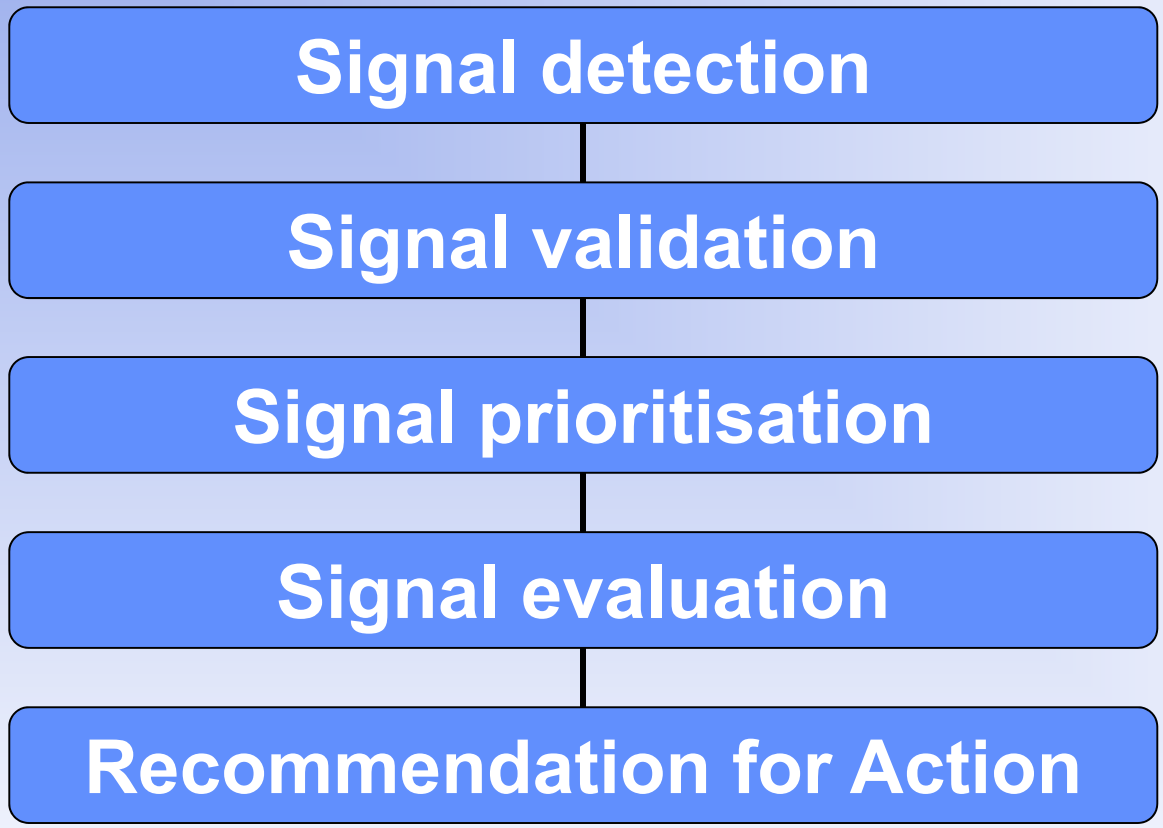
How are reports assessed?

- All reports are reviewed to assess:
  - the severity of the reaction
  - whether there have been any previous reports to the same or similar products
  - whether any further information is required and what follow up action is required
  - all animal reports are assessed for **causality**.

Signal Detection

- Historically based on case-by-case causality assessment.
- Long-term analysis depends on the personal experience of each assessor
- Becomes more difficult as the number of reports received increases.

Signal management



Proportional Reporting Ratio

- PRR enables assessment over time
- Can produce lots of false positives
- BUT will flag up possible associations
- It does NOT replace the assessor

Proportional Reporting Ratio

- Analysis run every 4 months to monitor for any new or unexpected signals
- Split by:
  - Companion animals
  - Production animals
  - Suspected Lack of Efficacy

What happens next??

- Monitoring
- Recommend changes to product literature, labels or package leaflets
- Suspend sale and supply of product or batch
- Revoke Marketing Authorisation

Recommend changes to product literature, labels or package leaflets

- 2015 – 22
- 2016 – 28
- 2017 (Jan to Apr) – 14

Benefits of Reporting

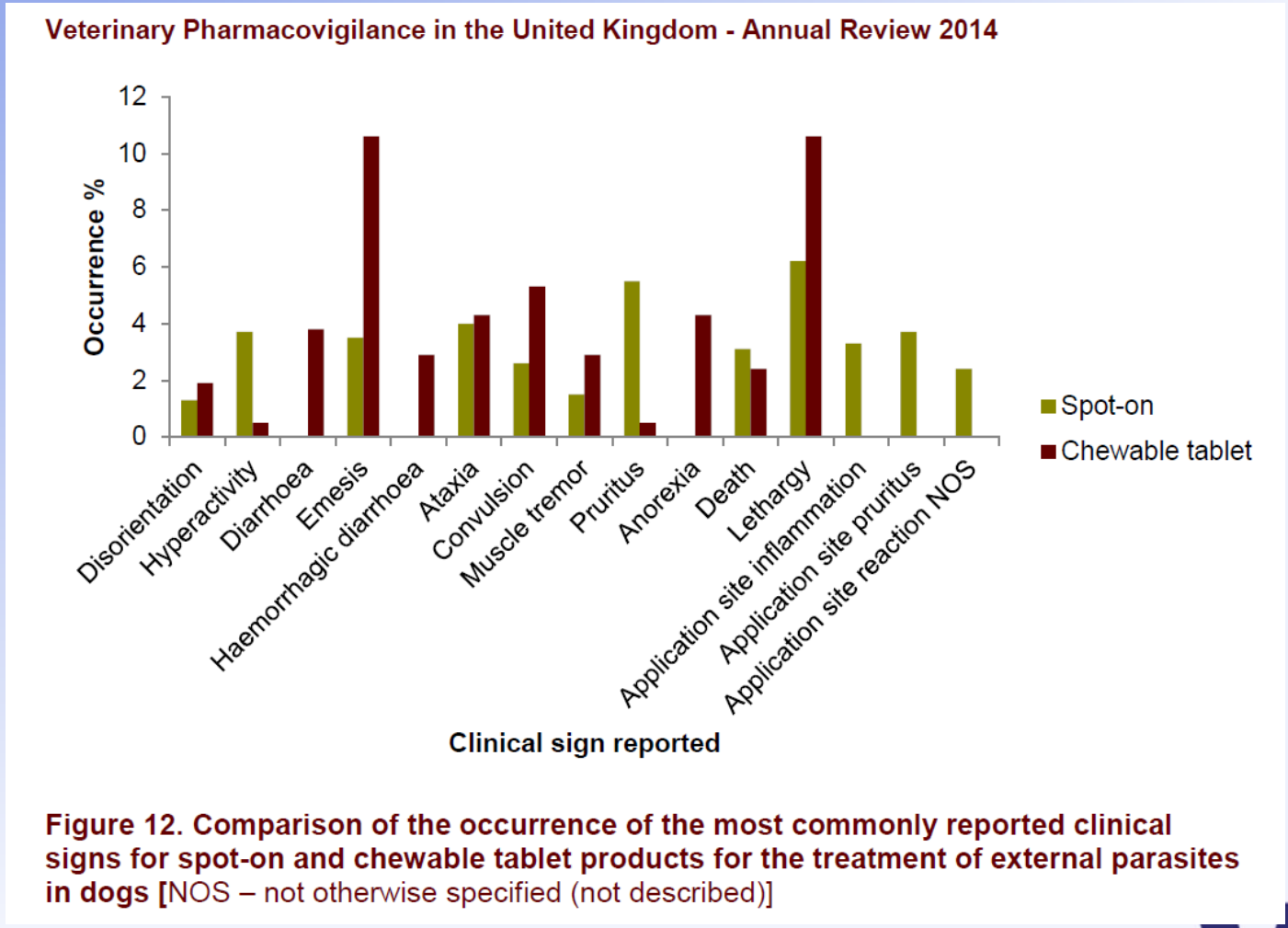


Figure 12. Comparison of the occurrence of the most commonly reported clinical signs for spot-on and chewable tablet products for the treatment of external parasites in dogs [NOS – not otherwise specified (not described)]

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Benefits of Reporting

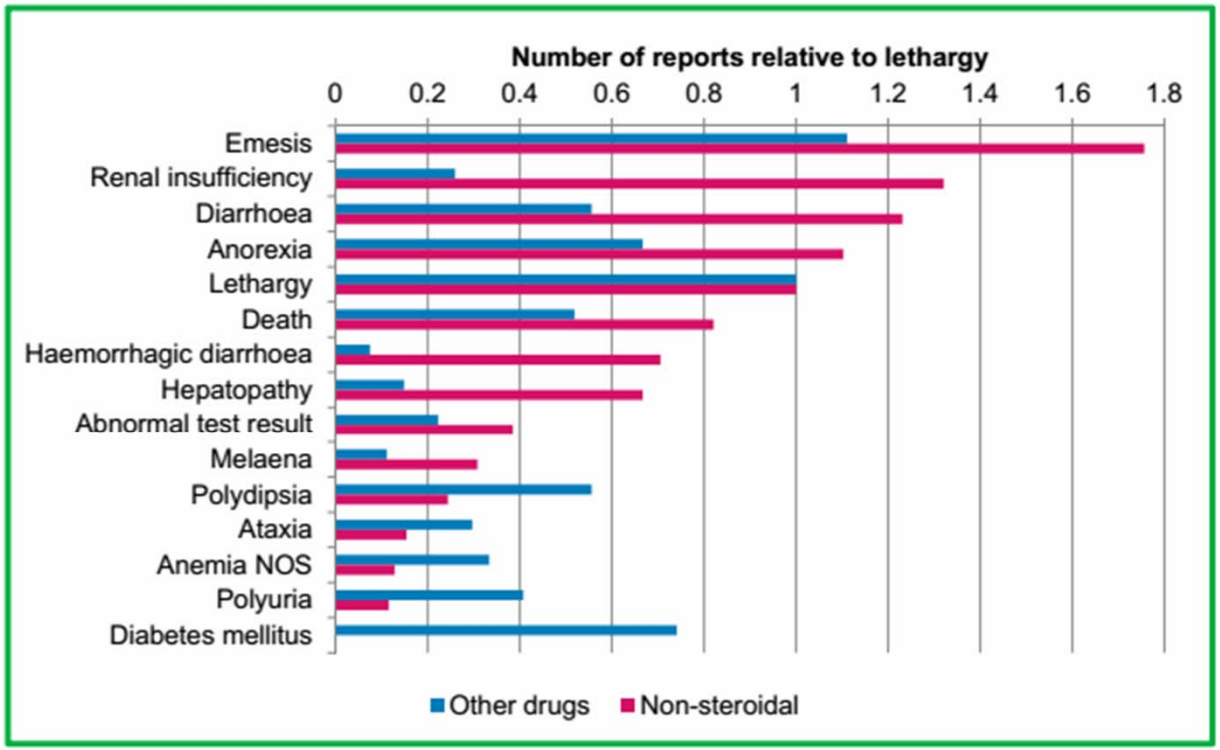

Figure 20 Comparison of clinical signs observed following the use of non-steroidal and other medicines for the treatment of inflammation

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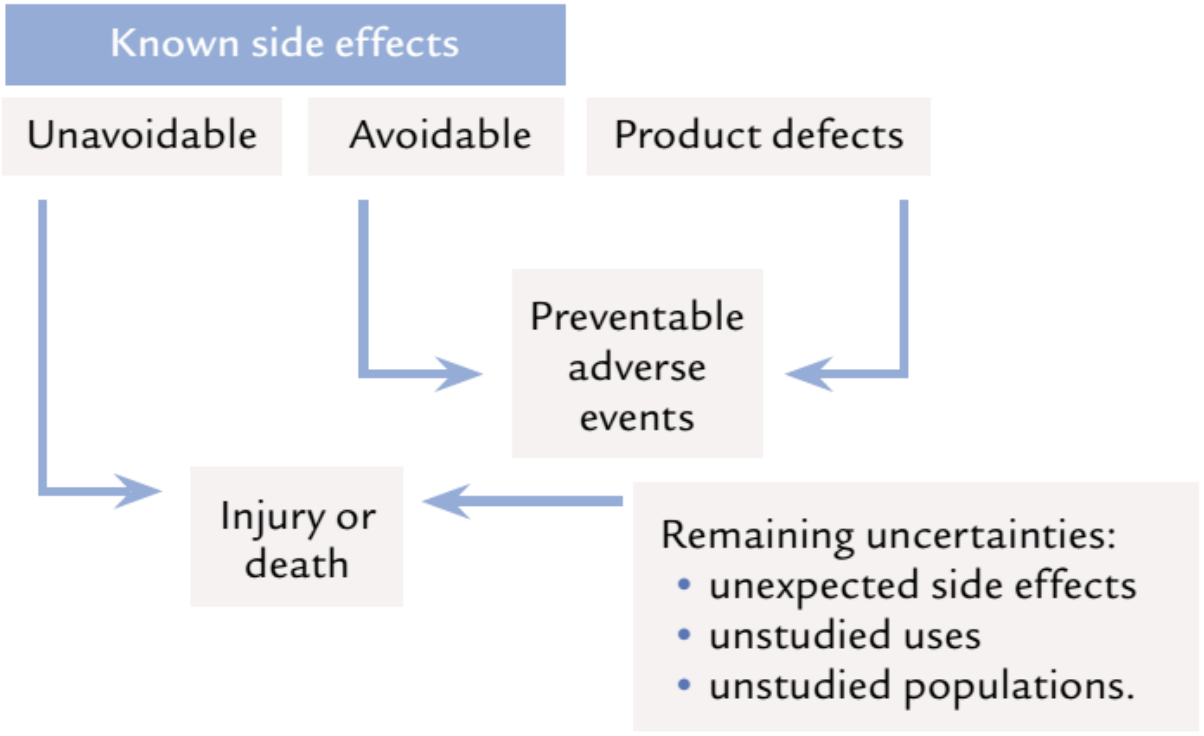
Adverse events are preventable

Figure 3. *Sources of risk from veterinary medicinal products. (Adapted from FDA, 1999)*



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I ♥ PHARMACOVIGILANCE