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## **Definition of a serious adverse event in intensive food animal production**

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

In this context, the collection and assessment of serious adverse reactions is ANSES-ANMV's principal objective in order to quickly take appropriate measures in cases where public health is at risk.

French regulations are above all geared to the management of serious adverse reactions. In particular:

- veterinarians must report all serious adverse reactions they observe (as well as any unexpected reactions)
- pharmaceutical companies must inform ANSES-ANMV of all serious adverse reactions within 15 days of them being brought to their attention

Article R. 5141-92 3 of the French Public Health Code, which transposes into French law Article 1 (paragraph 12) of Directive 2001/82/EC, as amended, defines a serious adverse reaction as "An adverse reaction which results in death, is life-threatening, results in significant disability or incapacity, is a congenital anomaly/birth defect, or which results in permanent or prolonged signs in the animals treated". "

In 2007, the French Veterinary Pharmacovigilance Commission, then in 2013 the French Veterinary Drug Commission, worked on this definition by providing clarifications with regard to non-lethal cases (see the ANSES website, [https://www.anses.fr/fr/system/files/Avis-CNMV-classification-cas-graves-052013\\_1.pdf](https://www.anses.fr/fr/system/files/Avis-CNMV-classification-cas-graves-052013_1.pdf) (In French))

However, the legal definition of a serious adverse reaction applies first and foremost to an individualised type of medicine. When treatments are administered to production animals managed in groups, it is recommended to take clinical signs into consideration at the level of the treatment group. They also note that reduced zootechnical performance can be considered a serious adverse reaction.

Since these zootechnical criteria can vary from one species to another, a review of the subject was conducted by ANSES-ANMV and its partners in the pig, poultry and rabbit sectors in order to define objective, quantifiable criteria for evaluating whether a given adverse reaction in intensive food animal production should be considered serious. The two goals of this review were:

- to promote reporting in the various intensive food animal production sectors and at the same time help veterinarians to fulfil their reporting obligations;
- to harmonise the classification practices of the authorities and MA holders.

With regard to mortality and reproductive problems, levels were set, by sector and by the animals' physiological stages, beyond which an event should be considered as serious.

Potentially life-threatening individual clinical signs that are permanent or prolonged, or which result in significant incapacity, are difficult to observe in large groups of animals. These signs however often have an indirect effect on water and/or feed consumption, with repercussions on growth and zootechnical performance.

In addition to the fatal cases, it was decided that these indirect criteria would also be taken into account by setting, for each sector, specific levels for reduced water consumption, feed consumption and/or growth beyond which the consequences of the adverse reactions should be considered as serious, and should therefore lead to reporting.

The following annexes provide the sector-based seriousness criteria chosen to describe a serious adverse event in intensive food animal production sectors.

## Annex 1: Seriousness criteria for pig farming

### Mortality

	Mortality rate	Calculation reference
Sows	X 4 during 1 month	Average annual rate for farm*
Suckers	X 2	Average of the 3 previous batches
Post-weaning	X 1.5	
Fattening	X 1.5	

#### \* Example for sows

6% annual mortality in a farm with 100 sows represents an average of 0.5 death/month. A loss of 2 sows over a one-month period would therefore be considered a serious event.

### Reproduction

	Criteria	Calculation reference
Late-term abortions	≥ 10% of the animals in the batch, or ≥ 10% of the animals in several batches over a month with a minimum of 4 sows	Average of the 3 previous batches
Artificial Insemination success rate	20% decrease	
Perinatal mortality	2X the average rate	
Live births	20% decrease of the average number	

### Consumption

	Daily decrease	Calculation reference
Feed	≥ 30%	Previous days
Water	≥ 50%	

### Growth

	Growth rate	Calculation reference
Post-weaning	20% decrease	Average of the 3 previous batches
Fattening	20% decrease	

## Annex 2: Seriousness criteria for poultry farming

### Mortality

		% mortality over a single day	% mortality per day over two consecutive days	
			D	D + 1
TURKEYS*	Confined broilers	≥ 4	≥ 1	≥ 1
	Free-range broilers	≥ 4	≥ 0.5	≥ 0.5
	Future Breeders	≥ 4	≥ 0.25	≥ 0.25
	Layer breeders	≥ 4	≥ 0.25	≥ 0.25
BROILER CHICKEN SECTOR	Confined broilers	≥ 4	≥ 1	≥ 1
	Free-range broilers	≥ 4	≥ 0.5	≥ 0.5
	Future Breeders	≥ 4	≥ 0.25	≥ 0.25
	Layer breeders	≥ 4	≥ 0.25	≥ 0.25
TABLE EGG SECTOR	Pullets	≥ 4	≥ 0.5	≥ 0.5
	Laying hen	≥ 4	≥ 0.5	≥ 0.5
	Future Breeders	≥ 4	≥ 0.25	≥ 0.25
	Layer breeders	≥ 4	≥ 0.25	≥ 0.25
GUINEA FOWL	Confined broilers	≥ 4	≥ 0.5	≥ 0.5
	Free-range broilers	≥ 4	≥ 0.25	≥ 0.25
	Future Breeders	≥ 4	≥ 0.25	≥ 0.25
	Layer breeders	≥ 4	≥ 0.25	≥ 0.25
QUAILS	Confined broilers	≥ 4	≥ 0.5	≥ 0.5
	Free-range broilers	≥ 4	≥ 0.25	≥ 0.25
	Future Breeders	≥ 4	≥ 0.25	≥ 0.25
	Layer breeders	≥ 4	≥ 0.25	≥ 0.25
DUCKS	Broilers	≥ 2	≥ 0.5	≥ 0.5
	Ready-for-gavage	≥ 2	≥ 0.25	≥ 0.25
	Future Breeders	≥ 2	≥ 0.25	≥ 0.25
	Layer breeders	≥ 2	≥ 0.5	≥ 0.5
GEESE	Broilers	≥ 2	≥ 0.5	≥ 0.5
	Ready-for-gavage	≥ 2	≥ 0.25	≥ 0.25
	Future Breeders	≥ 2	≥ 0.25	≥ 0.25
	Layer breeders	≥ 2	≥ 1	≥ 1
PHEASANTS	Any stage	≥ 4	≥ 0.25	≥ 0.25
Red-legged PARTRIDGES	Any stage	≥ 4	≥ 0.25	≥ 0.25
Grey PARTRIDGES	Any stage	≥ 4	≥ 0.25	≥ 0.25

MALLARDS	Reproduction and breeding	≥ 4	≥ 0.25	≥ 0.25
PIGEONS	Future Breeders	≥ 4	≥ 1	≥ 1
	Breeders	≥ 4	≥ 0.25	≥ 0.25

**\* Example for a confined broiler turkey farm:**

With a mortality rate equal to or higher than 4% over a one-day period, or a mortality rate of between 1% and 4% the first day and remaining at between 1% and 4% for 2 days or more, the veterinarian who was called in, after having excluded any pathological cause or a farming or feed accident, concluded that there was a possible connection between the administration of a veterinary medicinal product and the signs observed, and therefore filed a serious adverse event report.

**Reproduction/Laying**

	Decrease in laying over a single day	Decrease over 3 successive days			Calculation reference
		D0	D1	D2	
Laying	≥ 15%	≥ 5%	≥ 5%	≥ 5%	Previous days

**Consumption**

	Daily decrease over a single day	Decrease over 3 successive days			Calculation reference
		D0	D1	D2	
Feed	≥ 50%	≥ 25%	≥ 25%	≥ 25%	Previous days
Water	≥ 50%	≥ 25%	≥ 25%	≥ 25%	

Example for water or feed consumption:

With a reduction equal to or higher than 50% over a one-day period, or between 25% and 50% the first day (D0) and remaining at between 25% and 50% D1 and D2, the veterinarian who was called in, after having excluded any pathological cause or a farming or feed accident, concluded that there was a possible connection between the administration of a veterinary medicinal product and the signs observed, and therefore filed a serious adverse event report.

### Annex 3: Seriousness criteria for rabbitry

#### Mortality

	Mortality over a single day	Total mortality/batch
Does	≥ 4%	≥ 2%/average mortalities of the 3 previous batches X% + 2% With X = average mortalities of the 3 previous batches
Unweaned young	≥ 5%	
Fattening rabbits	≥ 5%	
Future breeder rabbits	≥ 4%	

#### \* Examples for does

- If the mortality rate for does over a single day is 4% or more, the event is considered serious.
- If the average mortality rate for does is 3.5% in the 3 previous batches and the rate is 5.5% in the following batch, the event is considered serious.

#### Reproduction

	Decrease	Calculation reference
-		Average of the 3 previous batches
Birth/palpation difference	≥ 20%	
Parturition rate	≥ 20%	
Still births	≥ 50%	
Live births	≥ 30%	

#### Consumption

	Daily decrease	Calculation reference
Feed	≥ 30%	Previous days
Water	≥ 50%	