GOOD FARM MANAGEMENT PRACTICES AND INFORMED USE OF DRUGS

1. A CHOICE OF ETHICS AND SOCIAL RESPONSIBILITY

In recent years, the massive use of antimicrobials in human and veterinary medicine has accelerated the emergence and spread of resistant microorganisms. The situation has grown worse due to a lack of investment in new effective antibiotics development. The scale of the problem is evidenced by the fact that more than 25,000 people in the European Union die each year from infections caused by antibiotic-resistant bacteria.

Antibiotic resistance is a natural biological phenomenon that occurs due to the emergence and propagation of bacterial resistance factors to antibiotics and is triggered and amplified by the selective pressure exerted on microbial populations through the use of these drugs.

At national level, sectoral legislation has already intervened by making punishable the improper use of veterinary medicinal products (the use of a veterinary medicinal product in a way that does not comply with what is indicated in the product characteristics' summary; the term also refers to serious abuse or incorrect use of a veterinary medicinal product) pursuant to art. 108, paragraph 9 of Legislative Decree 193/2006 (*Unless the fact constitutes a crime, anyone who does not comply with the requirements imposed with the authorisations issued pursuant to this decree is subject to the payment of a pecuniary administrative sanction from € 2,582.00 to € 15,493.00*). Any drug for veterinary use must be used responsibly, based on a visit to the animal by the veterinarian who establishes the diagnosis and prescribes with his own prescription the type of drug authorised for that animal species, necessary to treat the ascertained pathology. Responsible use of the drug involves several subjects: pharmaceutical companies, the manufacturer, the public veterinary service, the freelance veterinarian and the breeder.

Responsible use therefore concerns all those who intervene, in different ways, in the administrative cycle.

- It is the responsibility of veterinarians to choose the most appropriate medicines carefully and to monitor their use.
- It is the farmer's duty to promptly identify situations of disease and ensure the correct use of prescribed medicines. The breeder must in fact regularly monitor the health and well-being of their animals; taking note of any changes in their health is essential for an early diagnosis by the veterinarian.

2. DEFINITION OF ANTIMICROBIAL

The term "antimicrobial" has been used in general and includes antibiotics and antibacterial agents, but excludes antivirals and pesticides. This definition is consistent with the wording adopted by the European Food Safety Authority, the European Centre for Disease Prevention and Control, the European Medicines Agency and the Scientific Committee on Emerging Health Risks; definitions recently included in the joint scientific opinion on antimicrobial resistance focused on infections transmitted to humans by animals and food (zoonosis). See notes 1-2-3.

(1) "Antimicrobial agents: any substance of natural, semi-synthetic or synthetic origin which in live concentrations kills microorganisms or inhibits their growth by interacting with a specific target". Guidelines for the analysis of risks related to resistance to antimicrobials of food origin (CAC / GL 77-2011).

(2) "By antimicrobial agent we mean a substance present in nature, semi-synthetic or synthetic which in live concentrations shows an antimicrobial action (kills microorganisms or inhibits their growth). Anthelmintics and substances classified as disinfectants or antiseptics are excluded from this definition". Terrestrial Animal Health Code http://web.oie.int/eng/normes/mcode/en_glossaire.htm#terme_antibiotique.

(3) An active substance of synthetic or natural origin that destroys bacteria, inhibits their growth or the ability to reproduce in animals or humans, excluding antivirals and pesticides. http://www.efsa.europa.eu/it/efsajournal/pub/1372.htm

3. PURPOSE

Given that antimicrobials are essential for health care and the health of animal and livestock populations, these guidelines aim to provide operational directives for the implementation of strategies to promote the prudent use of antimicrobials, in particular antibiotics, whilst reducing their use.

The ultimate goal is to reduce the need to use antimicrobials for disease prevention. Animal diseases and infections must be prevented in the first place by ensuring biosecurity, following good production and management practices, and implementing integrated disease control programs to minimise their occurrence and eradicate endemic diseases.

The cornerstones on which the aforementioned plan focuses are as follows:

- Staff training; Health management of the farm: prevention of viral and bacterial infections by drawing up a vaccination plan;
- Adoption of good farming-biosecurity practices;
- Respect for animal welfare;
- Prudent use of antimicrobials;
- Pharmacovigilance.

4. STAFF TRAINING

The staff handling the animals must be in sufficient numbers and must be properly trained so that their knowledge and competence skillset is professionally adequate.

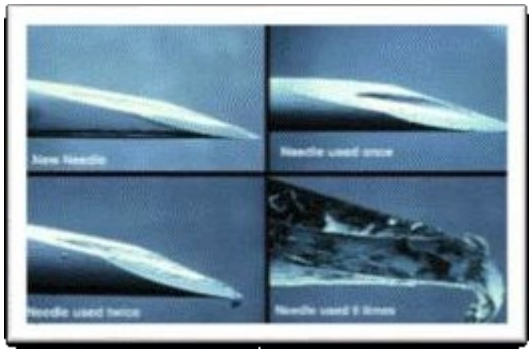
We do not recommend the use of occasional inexperienced labour due to liability court actions in the management of animals; the person in charge of hiring the animal guardians must first make sure that the staff have received instructions and guidance on the main requirements related to the good running of the farm, both in the legal and livestock areas.

All staff must be supervised during training.

The correct practices are recalled through special forms compiled by the company veterinarian and affixed near the pharmaceutical cabinet.

The workers are also appropriately trained in the administration of drugs:

- *Proper storage of the drug, preferring the use of disposable materials or otherwise*:
  - change the needle frequently in order to always perform the treatments with a well sharpened needle;



  - rinse the syringe when the active ingredient is changed in order to avoid mixing;
  - disassemble and wash the syringe daily only with hot water without using soap or other disinfectants that
    could exert interactions on the active ingredients used;
  - do not use the same syringe for vaccines and other types of veterinary drugs.

- *Adding drugs to milk in the case of a group treatment*:
  - Always dissolve medications first before adding them to milk
  - Do not mix more than one medication in the blender at a time.
  - Do not add drugs when the milk temperature exceeds 50°C.
  - Mix for at least 1 minute after adding the drugs into the milk.
  - After treatment, wash the equipment in which the drug was prepared adequately before administering the untreated milk to another group of animals.

5. HEALTH MANAGEMENT OF BREEDING FARMS: PREVENTION OF VIRAL AND BACTERIAL INFECTIONS THROUGH THE DRAFTING OF A VACCINAL PLAN.

In order to control the spread of infectious diseases, each farm should be equipped with a vaccination plan drawn up by the company veterinarian, taking into account the viruses and bacteria isolated in the farm.

Vaccines have 2 main effects, both decisive, for the purpose of reducing the consumption of antimicrobials:

- *they make animals less susceptible to contracting the infection and manifesting the disease, with a consequent improvement in production and reproductive performance;*
- *They increase the immunity of the herd, with less circulation of infectious agents and consequent improvement in the general health of the animals.*

In this case, at least the following etiological agents must be taken into account, which may be the primary cause of disease or as a door opener for the irruption of secondary microorganisms:

Parainfluenza 3
Infectious bovine rhinotracheitis
Viral diarrhoea
Respiratory syncytial virus
Histophilus somni
Mannheimia haemolytica
Pasteurella multocida
Clostridium spp.

In drafting the plan, it is strongly recommended for the first vaccination intervention to use, where possible, vaccines with live-attenuated values, which guarantee greater immune stimulation and in shorter times than the deactivated counterparts, recalling after 3-4 weeks as provided by AIC.

The vaccines will be stored according to the temperatures indicated on the information leaflet respecting the cold chain, that is, procuring from authorised suppliers and equipping company workers with suitable isothermal containers to reduce thermal stress to the products during routine vaccination operations.

It would be advisable, in order to guarantee the best conservation, to buy vaccines in the quantity suitable for the supposed vaccination intervention to avoid storing high quantities for long periods.

6. ADOPTION OF GOOD FARMING PRACTICES- BIOSECURITY

Supplier farms are required to adopt a Good Practice Manual for proper farm management.

Particular attention is required to the hygiene of the facilities (including the animal housing stalls) and to the daily inspection of all the animals present.

In order to lower and contain the bacterial concentration, avoiding the spread of infectious diseases, it is desirable to keep both the litter and the manger clean, paying particular attention to the scrupulous cleaning of the drinking troughs.

It would be advisable, where possible, before restocking new garments to carry out a sanitary vacuum accompanied by careful disinfection of the stall through the use of suitable disinfectants (see Table 1.).

Table 1. Disinfectant characteristics

Active principles	Usage	Effectiveness	Disadvantages
Chlorhexidine	Equipment, premises, foot baths	Active on some species of bacteria and viruses	Reduced activity against some agents (some viruses, Pseudomonas)
Phenols	Equipment, premises, foot baths	Active on many species of bacteria	Limited effect on fungi, viruses and bacterial spores. Possible environmental damage
Formaldehyde and other aldehydes	Equipment, premises, foot baths	Active on many species of bacteria, bacterial spores, fungi and viruses	Use regulated for high toxicity
Iodophores	Clean equipment	Active on bacteria and fungi	Inactivate by organic material. limited effect on bacterial spores and viruses
Inorganic compounds of hydrogen peroxide	Clean equipment and surfaces	Active on many species of bacteria, virus, fungi and bacterial spores	Inactivate by organic material
Quaternary salts of ammonium	Clean equipment	Active on many species of bacteria	Inactivate by organic material. limited effect on bacterial spores and viruses
Chlorine, hypochlorite, chloramines	Clean equipment	Active on bacteria and fungi	Inactivate by organic material. Irritating and corrosive. Limited effect on bacterial spores and viruses
Hydrated lime	Premises, litter boxes, cracks in the floors	Active on bacteria and viruses	Caustic for wet skin (especially nipple skin)

In order to efficiently control the development of infectious/diffusive diseases, a careful inspection of all the animals on the farm at least twice a day is required, ensuring adequate therapy for all sick animals.

The biosecurity measures must provide for the protection of the company from biological agents that can be of a viral, bacterial, fungal or parasitic nature.

It is based on the implementation of written plans and the application of good rules, both for company operators and for visitors and for all vehicles that pass through the company itself.

Specifically, access to the company centre is allowed only to authorised personnel, any guests must park their vehicles outside the entrance gate and be accompanied wearing, before entering the stables, disposable shoes and gowns.

The trucks that load the dead animals must wait outside the company boundaries; where possible, the dead animal destined for destruction is carried in closed containers to the outside of the company.

The biosecurity measures must also include the pest control plan, with particular reference to rodents, flying and crawling insects.

7. RESPECT FOR ANIMAL WELLBEING

The application of the legislation on animal welfare is the basis for good farm management. In addition to the legislative elements described in detail in the community regulations, animal welfare is promoted through the following foundations:

- establishing groups of animals as homogeneous as possible, based on sex, age, breed, morphology origin, etc.
- Reduce animal density as much as possible: remember that as the number of animals increases, there is a simultaneous increase in competitiveness; it is therefore advisable to form small groups that never exceed 20 head.
- Avoid stressful events or practices during handling.

To these managerial elements are added structural elements that should not be underestimated such as:

- number of drinking troughs. Sufficient space in the feeding trough to allow all animals to eat at the same time.
- Appropriate ventilation.
- Suitable room temperature.

8. PRUDENT USE OF ANTIMICROBIALS

The use of antimicrobials in animals must comply with the requirements of national and EU standards.

In particular, the use of antimicrobials must comply with what is specified in the information of the authorised product [summary of product characteristics (SPC), instruction sheet and labelling].

One of the fundamental aspects underlying the prudent and responsible use of antimicrobials is based on targeted use, modelled on a clinical and possibly etiological diagnosis, with the aim of:

- improving the effectiveness of antimicrobial therapy;
- reduce the consumption of antimicrobials, avoiding their unjustified use;
- avoid unnecessary and unjustified expenses for the breeder;
- contribute to the containment of antimicrobial resistance.

For this purpose, the breeder and the breeding staff must regularly observe the animals for early detection of signs of disease, injuries or abnormal behaviour.

In the event that an individual or breeding problem is highlighted, the company veterinarian must be involved promptly for the necessary investigations, which include at least:

- clinical examination of the affected subjects;
- specific diagnostic tests, aimed at identifying the cause (in the case of infectious diseases, the etiological agent).

In cases where it is necessary to use antimicrobials to safeguard the health and welfare of animals, the following principles must be respected.

- Where it is necessary to prescribe an antimicrobial, the prescription must be based on a diagnosis made following a clinical examination of the animal by the prescribing veterinarian.
- Use laboratory investigations as much as possible.
- Antimicrobial metaphylaxis (4) should only be prescribed when there is a real need for medical treatment. Antimicrobial metaphylaxis should never be used as a substitute for good management practices.
  (4) The term "metaphylaxis" refers to the simultaneous administration of the product to a group of clinically healthy (but presumably infected) contact animals, to prevent them from developing clinical symptoms and prevent further spread of the disease. The presence of the disease in the group/herd must be ascertained before using the product. A metaphylaxis request should always be associated with a treatment request (EMA / CVMP / 414812/2011-Rev.1).
- Whenever possible, the administration of antibiotic medicinal products to an entire herd or herd should be avoided. Sick animals must be isolated and treated individually (e.g. by administering injectable preparations).
- Prefer molecules with a more limited spectrum. (*Broad spectrum antimicrobials in fact lead to the development of resistance in non-target microorganisms more rapidly than antimicrobials with a narrower spectrum of action. Use only molecules considered "of critical importance" (CIAs) in human therapy as a last resort (cephalosporins of third and fourth generation, macrolides, fluoroquinolones and colistin*).
- The storage of the drug must take place away from sources of heat, intense light and humidity in a suitably clean place with limited access.

Correct use of AM involves the compliance with:

- pharmacological criteria:
  - pharmacokinetics (ability of the drug to penetrate live into the tissue site of infection) –
  - pharmacodynamics (bacteriostatic/bactericidal) association of several active ingredients (See Table 2.)

Table 2. Association of active ingredients

ASSOCIATIONS	MAJOR EFFECT
Betalactamines + Aminoglycosides	Synergy
Amoxicillin + Ac. Clavulanic	Synergy
Sulfamidco + Diaminopyrimidine	Synergy
Betalactamines + Fluoroquinolones	Synergy / indifference
Betalactamine + Phenicol	Antagonism
Betalactamines + Tetracyclines	Antagonism
Fluoroquinolones + Phenicol	Antagonism
Fluoroquinolones + Tetracyclines	Antagonism

(Ref.: Antibiotic resistance: pharmacovigilance and the role of the veterinarian. Turin 8/10/15 Prof. Giovanni Re. Modified)

AM associations make it possible to guarantee the animal a broader spectrum antibiotic coverage and reduce the toxicity of some principles active (e.g. sulfonamides) and, more importantly, can limit the onset of AMR.

To this end, extemporaneous AM associations not based on compliance with the pharmacokinetic and pharmacodynamic criteria must be avoided by resorting to the dictates suggested by pharmacology or preparations already available on the market.

According to what has been said, it is good practice to associate AM with the same pharmacodynamics (bacteriostatic with bacteriostatic and bactericide with bactericide) since bacteriostatic agents antagonise the effect of bactericides, especially if the latter act on bacteria in the logarithmic phase of growth (e.g.: beta-lactamines).

In addition, the combination of a time-dependent bactericide and a concentration-dependent one with a post-antibiotic effect (PAE) and with advantageous kinetics can develop a synergistic effect.

The association of AMs that present antagonism in addition to favouring the onset of AMR and not being ethically correct, constitutes a worthless use of the drug, therefore a direct economic cost for the farmer linked to the use of a greater quantity of product, as well as indirect, as the reduction in effectiveness causes the onset of subclinical or chronic infections (greater losses in the barn).

- Compliance with the dosage of use and the provisions of the AIC ("intra-label" use)

  Each antibiotic-based veterinary medicinal product should be used only according to the dosage and methods of administration indicated in the information leaflet and limited to the microorganisms indicated (Legislative Decree No. 193 of 6th April 2006).

  It is therefore requested that the treatment cycles provided for by the drug's dosage of use is followed.

  The main good practices are:
  - To discourage the use of antibiotics in ways other than those indicated in the dosage ("extra-label");
  - Avoid mixing products in the same syringe unless otherwise specified by the AIC;
  - Respect the correct time interval between administrations;
  - Respect the duration of the treatment; Respect the quantity of active ingredient;
  - Carefully estimate the animal's live weight.

  Under-dosage, reducing the effective dose, leads to a drop below the MIC90 (the lowest concentration of antibiotic capable of respectively inhibiting the development of 90% of bacterial strains tested), aggravating the AMR phenomenon. Nevertheless, it is necessary to realise that overdose can have even worse consequences by selecting resistant, often pathogenic bacteria.

  The use of electronic systems for the management of registers of use of veterinary medicines on the farm is recommended. They have the following advantages:
  - Reduction of the margin of error in checking suspension times;
  - Alignment with the new rules of electronic prescriptions in the implementation phase;
  - Possibility of collecting and aggregating data for the processing of statistics and reduction targets.

- Antimicrobial sensitivity test.

In order to define suitable therapeutic protocols, it is important to implement a constant collection of data relating to circulating microbial agents in the farm, evaluating the sensitivity spectrum towards antimicrobials.
The evaluation of sensitivity to antimicrobials in vitro is based on both qualitative (diffusion in agar according to the Kirby-Bauer method) and quantitative methods, with evaluation of the minimum inhibitory concentration (MIC, methods with dilution in agar or micro-dilution in broth).
Regardless of the method used, the interpretation of the results of the sensitivity test requires the availability of break-points, provided by international organisations such as the Clinical Laboratory Standard Institute (CLSI).
The method of diffusion in agar (Kirby-Bauer), currently the most used in the diagnostic routine to obtain useful indications to orient the therapeutic choice, classifies the pathogen as sensitive (S), intermediate (I) or resistant (R) towards antimicrobial molecules tested.
With quantitative tests, where the result is expressed as MIC, it is also possible to make a comparison between the different molecules to which the pathogen is sensitive (evaluation of the break-point/MIC ratio), preferring the one with the highest result.

One of the problems, both for the requesting veterinarian and for the laboratory, given the large number of specialties registered by animal species, production line and system, is to define which active ingredients to include in the antibiogram.

For a greater standardisation of the methods it is advisable to test a limited number of antimicrobials avoiding, when possible, to test molecules of the same antimicrobial class with similar behaviour in vitro.
For this purpose, the so-called "prototype" molecules, which better predict live efficacy through their use in vitro, have been identified on the recommendation of the Reference Centre for Antimicrobial Resistance (CRAB) - IZS Lazio Toscana.
Some examples of "antimicrobial panels" that can be used in bovine according to the different pathologies and related etiological agents are reported (see Table 3). Together with the outcome of the antibiogram, the laboratory must provide a legend that relates the prototype molecule with the related molecules represented (see Table 4).

Table 3. Panel of antimicrobials for the evaluation of the sensitivity of isolated bovine bacterial strains

Gram + mastitis	Gram – mastitis	Gram + Other pathologies *	Gram – Other pathologies§	Gram – respiratory
mpicillin	Ampicillin	Nalidixic Acid	Nalidixic Acid	Nalidixic Acid
Cephalothin	Cephalothin	Ampicillin	Ampicillin	Ampicillin
Ceftiofur	Cefazolin	Cephalothin	Cephalothin	Ceftiofur
Enrofloxacin	Ceftiofur	Ceftiofur	Cefazolin	Enrofloxacin
Erythromycin	Enrofloxacin	Clindamycin	Enrofloxacin	Florfenicol
Kanamycin	Kanamycin	Enrofloxacin	Florfenicol	Gentamicin
Oxacillin	SXT	Erythromycin	Gentamicin	Kanamycin
Penicillin	Sulfamethoxazole	Florfenicol	Kanamycin	Spectinomycin
Pirlimycin	Tetracycline	Kanamycin	SXT	SXT
Rifampicin	Ampicillin	Oxacillin	Tetracycline	Tetracycline
SXT	Cephalothin	Penicillin	Tilmicosin	Tilmicosin
Sulfamethoxazole	Cefazolin	SXT		
Tetracycline	Ceftiofur	Tetracycline		
Tilmicosin		Tilmicosin		

*Respiratory pathologies included

§With the exception of respiratory diseases

Table 4. Prototype molecules used in bovine pathology.

Prototype molecule	Molecules represented by the prototype
Nalidixic Acid	Nalidixic Acid, Flumequine
Ampicillin	Ampicillin, Amoxicillin
Cephalothin (Enterobacteriaceae)	Cephalothin, Cefalexin, Cefapirin, Cefazolin, Cefacetrile, Cefalonio
Cefazolin	Cephalothin, Cefalexin, Cefapirin, Cefazolin, Cefacetrile, Cefalonio
Ceftiofur	Ceftiofur, Cefoperazone, Cefquinome
Enrofloxacin	Enrofloxacin, Danofloxacin, Marbofloxacin
Erythromycin	Erythromycin, Spiramycin, Tilosin, Tilmicosin, Tulathromycin
Florfenicol	Florfenicol
Gentamicin	Gentamicin
Kanamycin	Kanamycin, Neomycin, Framicetin
Oxacillin (Staphylococcus)	Oxacillin, Cloxacillin, Dicloxacillin, Nafcillin
Penicillin	Penetamate
Pirlimycin	Pirlimycin, Clindamycin, Lincomycin
Rifampicin	Rifampicin, Rifaximin
Spectinomycin	Spectinomycin
Sulfamethoxazole	All sulfonamides
SXT	All sulfonamides boosted with Trimethoprim
Tetracycline	All tetracyclines (Chlortetracycline, Oxytetracycline)
Tilmicosin (Pasteurella and Mannheimia)	Tilmicosin, Spiramycin, Tilosin, Tildipirosina

➢ Antimicrobial selection criteria.

On the basis of the WHO classification and the commercial products registered for the bovine species, indications for use have been drawn up by pathology, and the antimicrobials have been categorised in antimicrobials "first, second and last choice" (see Table 5). Reference: *"Critically important antimicrobials for human medicine, 5th revision Ranking of antimicrobial agents for risk management of antimicrobial resistance due to non-human use (http://apps.who.int/iris/bitstream/handle/10665/255027/9789241512220-eng.pdf?sequence=1)*.

- *"First choice antimicrobial"*: can be used based on the clinical diagnosis of the company veterinarian. However, the diagnosis should be confirmed on an etiological basis, so as to be able to confirm the accuracy of the prescription and to be able to intervene effectively in the event of therapeutic failure. Although individual therapy, limited only to sick animals, is always to be considered preferable, it is possible to use the antimicrobial also for mass therapies (metaphylaxis), only when there is real need and not as a substitute for good breeding practices. Prophylactic use must be avoided and/or limited to exceptional cases and be justified by the prescribing veterinarian.
- *"Second choice antimicrobial"*: must be used following a precise etiological diagnosis and an in vitro sensitivity test that demonstrates the ineffectiveness of "first choice" drugs and/or a proven therapeutic failure of all first choice drugs. Although the individual route is always to be considered preferable, it can also be used for mass therapies (metaphylaxis) only when there is real need and not as a substitute for good breeding practices. Prophylactic use must be avoided and in any case limited to exceptional cases and justified by the prescribing veterinarian.
- *"Third choice antimicrobial"*: must be used following a precise etiological diagnosis and an in vitro sensitivity test that demonstrates the ineffectiveness of first and second choice drugs and/or a proven therapeutic failure of all first and second choice drugs. These drugs should only be used for the individual treatment of sick animals. The use through water or feed should be limited to the therapeutic use of the group of sick animals. The metaphylactic use must be limited to exceptional cases and justified by the prescribing veterinarian. Prophylactic use is not acceptable.

It should be remembered that antimicrobials have recently been categorised by the OIE in classes of importance,

- Veterinary Critically Important Antimicrobials,
- Veterinary Highly Important Antimicrobials,
- Veterinary Important Antimicrobials.

For a more accurate choice of the different molecules, see the document "OIE list of antimicrobials of veterinary importance" present at the following link: https://www.oie.int/doc/ged/D9840.PDF

Table 5. Categorisation of the antibiotic I°, II° and III° choice

Antimicrobial	DIAGNOSIS	INDIVIDUAL treatment	MASS treatment	
			Metaphylactic*	Prophylactic*
I° CHOICE (empirical)	Clinic: symptomatology	To be preferred	Possible	Avoided and/or limited to exceptional cases
II° CHOICE	Etiological diagnosis + sensitivity test; antimicrobial resistance and / or ineffectiveness I° choice	To be preferred	Possible	Avoided and/or limited to exceptional cases
III° CHOICE	Etiological diagnosis + sensitivity test; resistance and / or ineffectiveness of antimicrobial I°/° II choice	Exclusively	Only in exceptional cases	Not acceptable

* only if provided for in AIC

9. VETERINARY PHARMACOVIGILANCE.

Definition: *set of activities carried out to monitor, evaluate and improve the quality, safety, efficacy of the medicine after commercial authorisation*.

Pharmacovigilance allows you to monitor the safety of veterinary medicines, including antibiotics after commercial authorisation.

The task of pharmacovigilance is to ensure:

- the safe use of veterinary medicines in animals;
- the safety of food of animal origin; safety for humans who come into contact with veterinary medicines;
- safety for the environment.

Pharmacovigilance requires that any suspected adverse reaction, including for example a decrease in efficacy or loss of appetite, must be reported by veterinarians and pharmacists to the Ministry of Health and regional pharmacovigilance centres, using a special report form.

The reporting form (Annex II of Legislative Decree 193/2006) is the fundamental element for the transmission of information. The type of information subject to pharmacovigilance is described below:

Negative side effect: any unintended effect of a drug that occurs at normal doses and is connected to the chemical-physical properties of the drug.

Unexpected negative side effect: harmful and unexpected reaction that is not mentioned among the pharmaco-toxicological characteristics of the product (it is the most important reaction to report).

Decrease in efficacy: decrease in the clinical efficacy of treatment with the veterinary medicinal product compared to that expected according to the indications for use reported by AIC.

Objectives of pharmacovigilance, definition: *the set of preventive control actions exercised in the context of the production, distribution, possession, supply and use of veterinary medicines*, they include:

- the study of the side effects of veterinary medicines on animals;
- the study of the negative side effects on humans who (accidentally) come into contact with them;
- the study of the phenomena of low efficacy of medicines;
- verification of the validity of waiting times;the study of any problems relating to the environment (ecotoxicity);
- the collection of information on the methods of prescription and use of drugs (off-label);
- New therapeutic indications.

For an adequate evaluation of the adverse reaction it is crucial that the report form is completed in its entirety in as much detailed and that any available laboratory data, results of post-mortem examinations, photographs and other relevant information, are attached to the form itself. Reporting forms should normally be submitted within six working days for adverse reactions considered to be serious and within fifteen working days for all others. The Ministry of Health, moreover, to facilitate the transmission of the reporting forms of all adverse reactions on animals and humans has set up a new dedicated e-mail address: pharmacovigilanzavet@sanita.it.
The reporting forms must be sent to:
OFFICE IV former DGSA - Veterinary medicines and medical devices for veterinary use
DIRECTORATE-GENERAL OF ANIMAL HEALTH AND VETERINARY DRUGS
DEPARTMENT OF VETERINARY PUBLIC HEALTH, FOOD SAFETY AND COLLEGIAL BODIES FOR THE PROTECTION OF HEALTH
Ministry of Health
Via Giorgio Ribotta n.5,
00144 ROME
Tel. +39 06 59946255 Tel.+39 06 59946932 Fax +39 06 59946949
E-mail: Pharmacovigilanzavet@sanita.it

This document represents a guide for the practical application of the principles for the responsible use of antibiotics, identified by the Ministry of Health.

PRINCIPLES FOR RESPONSIBLE USE OF ANTIBIOTICS IN REVENUE ANIMALS

Correct diagnosis.
Known pharmacokinetics.
Known state of immunocompetence.
Choice of the appropriate antibiotic.
Correct dosage.
Verification of results.

Ministry of Health