CHAPTER 6.10.

RESPONSIBLE AND PRUDENT USE OF ANTIMICROBIAL AGENTS
IN VETERINARY MEDICINE

# Article 6.10.1.

### Purpose and scope

This document provides guidance for the responsible and prudent use of *antimicrobial agents* in veterinary medicine for treatment, control and prevention of diseases in food and non-food producing *animals*, with the aim of protecting both *animal* and human health as well as minimising and containing antimicrobial resistance risks in the relevant *animal* ~~the~~ environment, as part of a One Health approach.

It defines the respective responsibilities of the *Competent Authority* and stakeholders such as the veterinary pharmaceutical industry, *veterinarians*, *animal* *feed* manufacturers, distributors, and ~~food~~ *animal* ~~producers~~ breeders, owners and keepers, who are involved in any or all of the following activities:~~the authorization~~ regulatory approval, production, control, importation, exportation, sales, advertising, distribution and use of *veterinary medicinal products* ~~(~~*~~VMPs~~*~~)~~ containing *antimicrobial agents*.

Responsible and prudent use is determined by taking into account the specifications detailed in the relevant regulatory approval ~~marketing authorization and their implementation~~ when *antimicrobial agents* are administered to *animals* and is part of good veterinary and ~~good agricultural~~ *animal* husbandry practices. All measures to prevent infectious *animal* diseases contribute to a decreased need of using *antimicrobial agents* in *animal*s, thus reducing the risk for development of antimicrobial resistance.

Activities associated with the responsible and prudent use of *antimicrobial agents* should involve all relevant stakeholders.

Coordination of these activities at the national or regional level is recommended and may support the implementation of targeted actions by the stakeholders involved and enable clear and transparent communications.

# Article 6.10.2.

### Objectives of responsible and prudent use

Responsible and prudent veterinary medical use of *antimicrobial agents* includes implementing ~~practical~~ measures ~~and recommendations~~ intended to improve *animal* health and *animal welfare* while preventing or reducing the selection, emergence and spread of antimicrobial-resistant bacteria and resistance determinants in *animals*, humans and the relevant *animal* environment; ~~in~~[*~~animals~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_animal)~~and humans. S~~such measures include:

1) ensuring the responsible and prudent ~~rational~~ use of *antimicrobial agents* ~~in~~[*~~animals~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_animal) with the purpose of optimising both their effectiveness ~~efficacy~~ and safety in *animals*;

2) complying with the ethical obligation and economic need to keep *animals* in good health;

3) preventing or reducing ~~the~~ transfer of resistant micro-organisms or resistance determinants within *animal* populations, between *animals*, humans, and the relevant *animal* environment ~~the environment and between~~[*~~animals~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_animal)~~and humans~~;

4) contributing to the maintenance of the effectiveness ~~efficacy and usefulness~~ of *antimicrobial agents* used in *animal* and human medicine;

5) protecting consumer health by ensuring the safety of food of *animal* origin with respect to residues of *antimicrobial agents*.

# Article 6.10.3.

### Responsibilities of the Competent Authority

1. National Action Plan

The *Competent Authority* should design and oversee the implementation of the relevant part of their National Action Plan. The *Competent Authority* in cooperation with *animal* health, plant health, and public health professionals should adopt a One Health approach to promote the responsible and prudent use of *antimicrobial agents* as an element of a national strategy to minimise and contain antimicrobial resistance. Furthermore, the *Competent Authority* should allocate budgetary resources for the design and implementation of the relevant part of their National Action Plan including communication strategies. The *Competent Authority* should also conduct regular monitoring and evaluation of the National Action Plan. National Action Plans should incorporate best management practices, including disease prevention and control measures, *biosecurity* policies and development of *animal* health programmes to reduce the burden of *animal* disease thereby reducing the need for antimicrobial use. As part of National Action Plans for antimicrobial resistance, the C*ompetent Authority* should ensure that surveillance for antimicrobial use and antimicrobial resistance in the *animal* health sector are in place and should work closely together with human, plant and environmental sectors on the harmonisation, analysis and integration of *surveillance* across sectors.

National Action Plans should include recommendations to relevant professional organisations as appropriate to develop evidence-based, species or sector-specific antimicrobial use guidelines.

~~1~~2. Regulatory approval~~Marketing authorisation~~

~~All Member Countries should combat the unauthorised manufacture, compounding, importation, advertisement, trade, distribution, storage and use of unlicensed, adulterated and counterfeit products, including bulk active ingredients, through appropriate regulatory controls and other measures.~~

The [*Competent Authority*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_autorite_competente) is responsible for granting relevant regulatory approval ~~marketing authorisation~~ which should be done in accordance with the provisions of the *Terrestrial Code*. The *Competent Authority* ~~It~~ has a significant role in specifying the terms of this ~~authorisation~~ approval and in providing the appropriate information to *veterinarians* and all other relevant stakeholders.

The *Competent Authority* should establish and implement efficient statutory registration procedures that evaluate the quality, safety and efficacy and proposed post-marketing surveillance programmes for ~~of VMP~~ *veterinary medicinal products* containing *antimicrobial agents*. According to Article 3.2.2., the *Competent Authority* should be free from any commercial, financial, hierarchical, political or other pressures which might influence ~~affect~~ its judgement or decisions.

Member Countries lacking the necessary resources to implement an efficient registration procedure for ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents*, and which are importing them, should undertake the following measures:

a) evaluate the effectiveness ~~efficacy~~ of administrative controls on the import of these ~~VMP~~ *veterinary medicinal products*;

b) evaluate the validity of the registration procedures of the exporting ~~and~~ or manufacturing country as appropriate;

c) develop the necessary technical co-operation with an experienced ~~relevant authorities~~ *Competent Authority* to check the quality of imported ~~VMP~~ *veterinary medicinal products* as well as the validity of the recommended conditions of use.

The *Competent Authority~~ies~~* of *importing countries* should request the pharmaceutical industry to provide quality certificates prepared by the *Competent Authority* of the exporting or ~~and~~ manufacturing country as appropriate.

Regulatory approval ~~Marketing authorisation~~ is granted on the basis of the data submitted by a ~~the~~ pharmaceutical company ~~industry~~ or other applicant and only if the criteria of quality, safety~~, quality~~ and efficacy are met.

~~Member countries~~ The *Competent Authority* ~~are~~ is encouraged to apply or require the use of the existing guidelines established by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH).

An evaluation of the ~~potential~~ risks and benefits to both *animals* and humans resulting from the use of *antimicrobial agents* in ~~with particular focus on use in food-producing~~ *animal*s~~,~~should be carried out. The evaluation may ~~should~~ focus on each individual *antimicrobial agent* and the findings from one agent should not be generalised to the antimicrobial class to which the particular active ingredient belongs. Guidance on use ~~usage~~ should be provided for all target species, route of administration, dosage regimen~~s,~~ (dose, dosing interval and duration of the treatment), and withdrawal period as relevant ~~and different durations of treatment that are proposed~~.

The *Competent Authority* should ~~expedite~~ implement timely the regulatory approval process for new *antimicrobial agents* in order to address ~~a~~ specific needs for the treatment of *animal* diseases and should take into account recommendations included in the OIE List of Antimicrobials of Veterinary Importance.

~~2~~3. Quality ~~control~~ of antimicrobial agents and ~~VMP~~ veterinary medicinal products containing antimicrobial agents

The *Competent Authority* should make sure that the quality of the *veterinary medicinal products* was determined by the applicant in accordance with national and international guidance to ensure that:

~~Quality controls should be performed:~~

a) the specifications of *antimicrobial agents*~~in compliance with the provisions of~~[*~~good manufacturing practices~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_creton)~~;~~

~~b)~~ ~~to ensure that analysis specifications of~~[*~~antimicrobial agents~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique) used as active ingredients comply with the provisions of registration documentations (such as monographs) approved by the relevant *Competent Authority;*

~~c~~b) ~~to ensure that~~ the quality of *antimicrobial agents* in the marketed dosage forms is maintained until the expiry date, established under the recommended storage conditions;

~~d~~c) ~~to ensure~~ the stability and compatibility of *antimicrobial agents* when mixed with *feed* or ~~drinking~~ water;

~~e~~d) ~~to ensure that~~ all *antimicrobial agents* and the ~~VMP~~ *veterinary medicinal products* containing them are manufactured to the appropriate quality and in compliance with the provisions of *good manufacturing practices* ~~purity in order to guarantee their safety and efficacy~~.

~~3~~4. Assessment of therapeutic efficacy

The *Competent Authority* should conduct an assessment of the therapeutic efficacy based on data provided in the relevant regulatory approval application submitted by the applicant to enable marketing:

a) Preclinical trials

i) Preclinical trials should:

‒ establish the spectrum of activity of *antimicrobial agents* against relevant pathogenic agents and non-pathogenic agents (commensals);

‒ assess the capacity of the *antimicrobial agents* to select for resistance *in vitro* and *in vivo*, taking into consideration intrinsically resistant ~~and pre-existing resistant~~ strains and strains with acquired resistance;

‒ establish an appropriate dosage regimen ~~(dose, dosing interval and duration of the treatment)~~ and route of administration necessary to ensure the therapeutic efficacy of the *antimicrobial agents* and limit the selection of antimicrobial resistance. Pharmacokinetic and pharmacodynamic data and models can assist in this appraisal. Such data together with clinical data could be used by independent experts to establish clinical breakpoints per *animal* species, antimicrobial agent and pathogen combination.

ii) The activity of *antimicrobial agents* towards the targeted microorganism should be established by pharmacodynamic~~s~~ investigations. The following characteristics ~~criteria~~ should be taken into account:

‒ spectrum of activity and mode of action;

‒ minimum inhibitory and bactericidal concentrations against recent isolates;

‒ time-kill kinetics when appropriate;

‒ time- or concentration-dependent activity or co-dependency;

‒ activity at the site of *infection*.

iii) The dosage regimens allowing maintenance of effective antimicrobial concentrations ~~levels~~ should be established by pharmacokinetic~~s~~ investigation~~. The following criteria~~ and should ~~be~~ take~~n~~ into account:

‒ ~~bio-availability in accordance with the route of administration;~~

‒ absorption, distribution, [~~of the~~ *~~antimicrobial agents~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique) ~~in the treated~~ [*~~animal~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_animal) ~~and~~ concentration at the site of *infection*, metabolism and elimination;

‒ ~~metabolism;~~

‒ ~~excretion routes.~~

‒ any potential routes of administration proposed by the applicant.

Any proposed u~~U~~se of combinations of *antimicrobial agents* should be scientifically supported.

b) Clinical trials

Clinical trials in the target *animal* species should be performed to confirm the validity of the claimed therapeutic indications and dosage regimens established during the preclinical phase. The following criteria should be taken into account:

‒ diversity of the clinical cases encountered when performing multi-centre trials;

‒ compliance of protocols with good clinical practice;

‒ eligibility of studied clinical cases, based on appropriate criteria of clinical and bacteriological diagnoses;

‒ parameters for qualitatively and quantitatively assessing the efficacy of the treatment.

45. Assessment of the potential of antimicrobial agents to select for resistance

Other studies may be requested in support of the assessment of the potential of *antimicrobial agents* to select for resistance. The applicant for regulatory approval ~~The party applying for market authorisation~~ should, where possible, supply data derived in target *animal* species under the intended conditions of use.

For this assessment the following may be considered:

a) the concentration of ~~either~~ active *antimicrobial agents* ~~or~~ and, where appropriate, active metabolites in the gut of the *animal* (where the majority of ~~potential foodborne~~ pathogenic and commensal bacteria ~~agents~~ reside) at the defined dosage level;

b) the antimicrobial activity of the *antimicrobial agents* and metabolites in the intestinal environment;

~~b~~c) the pathway for ~~the~~ human exposure to antimicrobial resistant microorganisms and antimicrobial residues in the environment;

~~c~~d) the presence of and potential ~~degree~~ for co-resistance and cross-resistance;

~~d~~e) the intrinsic and pre-existing, baseline level of resistance in the pathogenic ~~agents~~, commensal and food-borne bacteria of human health relevance ~~concern~~ in both *animals* and humans.

6. Establishment of clinical breakpoints

In order to interpret the result of a susceptibility test, there is a need for clinical breakpoints for each bacteria-antimicrobial-*animal* species combination. Those clinical breakpoints should be established by independent experts.

~~5~~7. Establishment of acceptable daily intake (ADI), maximum residue limit (MRL) and withdrawal periods in food-producing animals

a) When setting the ADI and MRL for an *antimicrobial agent*, the safety evaluation should also include the potential microbiological ~~biological~~ effects on the intestinal ~~flora~~ microbiome of humans to derive ADI.

b) The establishment of an ADI for each *antimicrobial agent*, and an MRL for each *animal*-derived food, should be undertaken before a ~~VMP~~ *veterinary medicinal product* containing it is granted ~~marketing authorization~~ regulatory approval.

c) For all ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* for use in food-producing *animal*s, withdrawal periods should be established for each *animal* species in order to ensure compliance with the MRLs, taking into account:

‒ the MRLs established for the *antimicrobial agent* in the target *animal* edible tissues;

‒ the composition of the product and the pharmaceutical form;

‒ the dosage regimen;

‒ the route of administration.

d) The applicant should describe methods for regulatory testing of residues in food based on the established marker residues.

~~6~~8. Assessment ~~Protection~~ of the impact on the relevant animal environment

An assessment of the impact of the proposed antimicrobial use on risks to the relevant environment should be conducted in accordance with national or international guidelines.

The *Competent Authority* should consider the results of an antimicrobial resistance environmental risk assessment. For both food and non-food producing *animal*s the following risk factors should be taken into consideration as appropriate: reuse of wastewater for irrigation, use of manure, other waste-based fertilizers for soil fertilization, transfer of antimicrobial resistant genes or bacteria in veterinary practice. When a significant antimicrobial resistance risk is determined the need for monitoring and proportionate risk management measures should be discussed.

~~7~~9. Establishment of a summary of product characteristics or equivalent for each ~~VMP~~ veterinary medicinal product containing antimicrobial agents

~~The summary of product characteristics contains~~ The *Competent Authority* should ensure that the Summary of Product Characteristics (SPC) or equivalent, the package insert and labelling includesthe information necessary for the appropriate use of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents.*~~and constitutes the official reference for their labelling and package insert. This~~ The SPC or equivalent summary should contain the following items as appropriate:

a) name of the *veterinary medicinal product*;

~~a~~b) active ingredient and class;

c) pharmaceutical form;

d) quantitative composition;

~~b~~e) pharmacological properties;

~~c~~f) any potential adverse effects;

~~d~~g) target *animal* species and, as appropriate, age or production category;

~~e~~h) therapeutic indications;

~~f~~i) target micro-organisms;

~~g~~j) dosage regimen and route of administration;

~~h~~k) withdrawal periods;

~~i~~l) incompatibilities and interactions;

~~j~~m) storage conditions and shelf-life;

~~k~~n) operator safety;

~~l~~o) particular precautions before use;

p) precautions for the protection of the environment;

q) use during pregnancy, lactation or lay;

~~m~~r) particular precautions for the proper disposal of unused ~~un-used~~ or expired products;

~~n~~s) information on conditions of use relevant to the potential for selection of resistance;

~~o~~t) ~~C~~contraindications.

~~8~~10. Post-marketing antimicrobial resistance surveillance

The *Competent Authority* should assess ~~T~~the information collected through existing pharmacovigilance and surveillance programmes, including reporting of lack of response ~~efficacy~~, and any other relevant scientific data. These information sources should form part of the comprehensive strategy to detect and minimise antimicrobial resistance. In addition to this, the following should be considered:

a) General epidemiological surveillance

The *surveillance* of *animal* microorganisms resistant to *antimicrobial agents* is essential. The *Competent Authority* ~~relevant authorities~~ should implement a programme in accordance with Chapter 1.4.

b) Specific surveillance

*Specific surveillance* to assess the impact of the use of a specific [*~~antimicrobial agent~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique) *veterinary medicinal product* may be implemented after the granting of the relevant regulatory approval ~~marketing authorisation~~. The *surveillance* programme should evaluate not only resistance in target *animal* pathogens ~~pathogenic agents~~, but also in foodborne and other relevant zoonotic pathogens ~~pathogenic agents~~, and commensals if relevant and possible. This will also contribute to general epidemiological *surveillance* of antimicrobial resistance.

~~9~~11. Distribution ~~Supply~~ and administration of ~~the~~ antimicrobial agentsor ~~VMP~~ veterinary medicinal products containing antimicrobial agents

~~The relevant authorities~~ The *Competent Authority* should ensure that all th*e antimicrobial agents* and *veterinary medicinal products* containing *antimicrobial agents* used in *animals* including through *feed* and water are:

~~a)~~ ~~prescribed by a~~[*~~veterinarian~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_veterinaire)~~or other suitably trained person authorised to prescribe VMP containing~~[*~~antimicrobial agents~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique)~~in accordance with the national legislation and under the supervision of a~~[*~~veterinarian~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_veterinaire)~~;~~

~~b~~a) supplied only through licensed or authorised distribution systems;

b) not illegal, substandard, falsified medicines or unapproved formulations and that these are prevented from entering distribution systems;

c) prescribed by a *veterinarian* or other suitably trained person authorised to prescribe *veterinary medicinal products* containing *antimicrobial agents* in accordance with the national legislation;

~~c~~d) administered to *animals* by a *veterinarian* or under the supervision of a *veterinarian*, ~~or~~ by other ~~authorised~~ suitably trained persons, *animal* breeder, owners or keepers as appropriate.

The *Competent Authority* should encourage the availability of authorised products on the market and in collaboration with the pharmaceutical industry follow-up any potential drug shortages.

~~The relevant authorities~~The *Competent Authority* should develop effective procedures for the safe collection and disposal or destruction of unused or expired ~~VMPs~~ *veterinary medicinal products* containing *antimicrobial agents*. Their labels should have appropriate instructions for disposal and destruction.

~~10~~12. Control of advertising

All advertising of *antimicrobial agents* should be compatible with the principles of responsible and prudent use and should be controlled by codes of advertising standards. The *Competent Authority* ~~relevant authorities~~ must ensure that the advertising of these products:

a) complies with the regulatory approval ~~marketing authorisation~~ granted, in particular regarding the content of the summary of product characteristics or equivalent;

b) is restricted to a *veterinarian* or other suitably trained person authorised to prescribe ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* in accordance with the national legislation ~~and under the supervision of a~~ *~~veterinarian~~*.

~~11~~13. Training related to the use ~~on the usage~~ of antimicrobial agents and antimicrobial resistance

The *Competent Authority* should take a key role in promoting training for responsible and prudent use of antimicrobials and on antimicrobial resistance. The target audiences for t~~T~~he training on the ~~usage~~ use of *antimicrobial agents* should include all the relevant stakeholders and organisations, such as the [*~~Competent Authority~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_autorite_competente)~~,~~ pharmaceutical industry, veterinary ~~schools~~ and paraprofessional education establishments, research institutes, veterinary professional and paraprofessional organisations and other approved users such as food *animal* owners and manufacturers of medicated *animal* *feed*. The~~This~~ training may ~~should focus on preserving the effectiveness of~~[*~~antimicrobial agents~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique)~~and~~ include:

~~a)~~ ~~information on disease prevention, management and mitigation strategies;~~

~~b~~a) the ability of *antimicrobial agents* to select for resistant microorganisms in *animals* and the ~~relative~~ importance of that resistance to public and *animal* health and the environment;

~~c~~b) the need to observe responsible and prudent use principles ~~recommendations~~ for the use of *antimicrobial agents* in *animal* husbandry in agreement with the provisions of the ~~marketing authorisations~~ regulatory approval, national and international guidelines and recommendations from the OIE List of Antimicrobial Agents of Veterinary Importance

~~d~~c) information on the appropriate storage conditions before and during use and proper disposal of unused or expired ~~VMP~~ *veterinary medicinal products*;

~~e)~~ ~~record keeping;~~

d) training in new methodologies for molecular detection of resistance, understanding methods and results of antimicrobial susceptibility testing and molecular analysis;

e) interpretation of relevant risk assessment outputs of antimicrobial resistance derived from the use of *veterinary medicinal products* containing *antimicrobial agents* in *animals* and how to use these outputs to inform the development of *risk communication* and *risk management* strategies;

f) the collection and reporting of antimicrobial resistance and antimicrobial use data to the *Competent Authority* to complement existing national and international surveillance programmes;

g) information on disease prevention, management and mitigation strategies that can contribute to reducing the need to use *antimicrobial agents* in *animal*s.

14. Monitoring of antimicrobial use

The *Competent Authority* should collate antimicrobial use in a harmonised manner to improve the understanding of the extent and trends of antimicrobial use and antimicrobial resistance in *animal* populations at national level and identify areas for further research. The data collected on antimicrobial use at country level should:

a) give an indication of the trends in the use of *antimicrobial agents* in *animals* over time and potential associations with antimicrobial resistance in *animals;*

b) help in the interpretation of antimicrobial resistance *surveillance* data and assist in responding to problems of antimicrobial resistance in a precise and targeted way;

c) assist in *risk management* to evaluate the effectiveness of efforts and mitigation strategies;

d) inform *risk communication* strategies.

The *Competent Authority* should provide the antimicrobial use data to the ‘Animal Antimicrobial Use Global database of the World Organisation for Animal Health’ on a yearly basis.

~~12~~15. Knowledge gaps and r~~R~~esearch

The *Competent Authority* ~~relevant authorities~~ should encourage coordination of public- and industry-funded research, in the following areas but not limited to: ~~for example on methods to identify and mitigate the public health risks associated with specific~~[*~~antimicrobial agent~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique)~~uses, or on the ecology of antimicrobial resistance.~~

a) improve the knowledge about the mechanisms of action, pharmacokinetics and pharmacodynamics of *antimicrobial agents* to optimize the dosage regimens for veterinary medical use and their effectiveness;

b) improve the knowledge about the mechanisms of transmission, selection, co-selection, emergence and dissemination of resistance determinants and resistant microorganisms in *animal* populations and along the food chain;

c) develop practical models for applying the concept of *risk analysis* to assess the *animal* and public health concerns linked to the development of antimicrobial resistance in *animal*s and *animal*-derived foods;

d) further develop protocols to predict, during the authorization process, the impact of the proposed use of the *antimicrobial agents* in *animals* on the rate and extent of antimicrobial resistance development and spread to *animals*, humans, plants and the environment, following a One Health approach;

e) assess the primary drivers leading to use of *antimicrobial agents* in *animals*, and the effectiveness of different interventions to change behaviour and reduce the need to use *antimicrobial agents* in *animals*;

f) develop safe and effective alternatives to *antimicrobial agents*, new *antimicrobial agents*, rapid diagnostics, and vaccines for infectious diseases to reduce the need for antimicrobial use in *animals*;

g) improve knowledge on the role of the environment on the persistence of *antimicrobial agents*, and the emergence, transfer and persistence of antimicrobial resistance determinants and resistant microorganisms resulting from antimicrobial use in *animals*.

# Article 6.10.4.

### Responsibilities of the veterinary pharmaceutical industry with regards to ~~VMP~~ veterinary medicinal products containing antimicrobial agents

1. Regulatory approval~~Marketing authorisation~~

The veterinary pharmaceutical industry has responsibilities to:

a) ~~Supply~~ provide all the information requested by the national *Competent Authority* as specified in Article 6.10.3;

b) guarantee the quality of this information in compliance with the provisions of good manufacturing, laboratory and clinical practices;

c) implement and regularly report on a pharmacovigilance programme and on request, *specific surveillance* for bacterial susceptibility and resistance data;~~.~~

d) isolate and identify bacteria, and collect relevant data and submit them to the *Competent Authority*. The data will enable independent experts to establish clinical breakpoints for use in the laboratory to guide antimicrobial therapy.

1. Marketing and export

For the marketing and export of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents*:

a) only licensed and officially approved ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* should be sold and supplied, and then only through ~~licensed/~~authorised distribution systems;

b) the pharmaceutical industry should provide quality certificates prepared by the *Competent Authority* of the exporting or ~~and~~ manufacturing countries to the *importing country*;

c) the pharmaceutical industry should endeavour to guarantee the availability of authorised products and cooperate with the *Competent Authority* to forecast and avoid any drug shortage;

~~c~~d) the *Competent Authority* ~~national regulatory authority~~ should be provided with the information necessary to evaluate the amount of *antimicrobial agents* marketed.

1. Advertising

The veterinary pharmaceutical industry should respect principles of responsible and prudent use and should comply with established codes of advertising practices ~~standards~~, including to:

a) distribute information in compliance with the provisions of the granted ~~authorization~~ approval;

b) not advertise ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* directly to the food *animal* ~~producer~~ breeder, owner and keeper.

1. Training

The veterinary pharmaceutical industry should participate in training programmes as defined in point 13~~1~~ of Article 6.10.3.

1. Research

The veterinary pharmaceutical industry should contribute to research as defined in point 1~~2~~5 of Article [6.10.3.](#_bookmark0)

# Article 6.10.5.

### Responsibilities of wholesale and retail distributors

1) Distributors ~~of VMP containing~~[*~~antimicrobial agents~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique) should only distribute *veterinary medicinal products* containing *antimicrobial agents* ~~do so~~ on the prescription of a *veterinarian* or other suitably trained person authorised to prescribe ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* in accordance with the national legislation ~~and under the supervision of a~~ *~~veterinarian~~*. All products should be appropriately labelled.

2) The recommendations on the responsible and prudent use of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* should be reinforced by retail distributors who should keep for an appropriate period detailed records of:

a) date of supply;

b) name of prescriber;

c) name of user;

d) name of product;

e) batch number;

f) expiration date;

g) quantity supplied;

h) copy of prescription~~.~~;

i) other information as required by national legislation.

3) Distributors should also be involved in training programmes on the responsible and prudent use of ~~VMP~~ *veterinary medicinal products* containing antimicrobial agents, as defined in point 13~~1~~ of Article [6.10.3.](#_bookmark0)

# Article 6.10.6.

### Responsibilities of veterinarians

The *veterinarian*'sresponsibility is to promote public health, antimicrobial stewardship, *animal* health and *animal welfare*, including detection, diagnosis ~~identification~~, prevention and treatment of *animal* diseases. The promotion of sound *animal* husbandry methods, hygiene procedures, *biosecurity* and *vaccination* strategies can help to minimise the need for antimicrobial use in ~~food-producing~~ *animal*s.

The *veterinarian~~s~~* should only prescribe *antimicrobial agents* for *animals* under their care. The v*eterinarian* should consider non-antimicrobial options or alternatives to antimicrobials before prescribing *antimicrobial agents.*

Some of the responsibilities described in this article may be applicable to *veterinary paraprofessionals* or other suitably trained persons according to the national legislation.

1. ~~Use of antimicrobial agents~~Pre-requisites for using antimicrobial agents

The responsibilities of *veterinarians* are to obtain a detailed history and carry out a proper clinical examination of the *animal(s)* ~~and then~~, taking appropriate samples for further testing as necessary.If the provisional or definitive diagnosis is a microbial infection, then the *veterinarian* should:

a) ~~administer, or~~ prescribe, dispense or administer *antimicrobial agents* only when necessary ~~and taking into consideration the OIE list of~~ *~~antimicrobial agents~~* ~~of veterinary importance~~ to treat, control or prevent infectious diseases in *animal*s;

b) avoid using *antimicrobial agents* routinely to compensate for inadequate *animal* husbandry practices;

c) take into consideration the OIE List of Antimicrobial Agent*s* of Veterinary Importance and follow science-based species or sector-specific antimicrobial use guidelines for responsible and prudent use when available and follow the principles of antimicrobial stewardship;

~~b~~d) make an appropriate choice of *antimicrobial agent* based on clinical experience and available diagnostic laboratory information (pathogenic agent isolation, identification and ~~antibiogram~~ antimicrobial susceptibility testing) ~~where possible~~;

~~c~~e) provide a detailed treatment protocol, including precautions and withdrawal period ~~times~~ (if applicable), especially when prescribing extra-label or off-label use~~.~~;

f) appropriate supportive therapy, which may, for example, include fluid therapy, segregation from other *animal*s, administration of anti-inflammatory or analgesic agents.

2. Choosing antimicrobial agents

~~a.~~ The effectiveness ~~expected efficacy~~ of the treatment is based on:

~~i~~a) the clinical experience of the *veterinarians*, their diagnostic insight and therapeutic judgement;

~~ii~~b) diagnostic laboratory information (pathogenic agent isolation, identification and ~~antibiogram~~ antimicrobial susceptibility testing);

~~iii~~c) pharmacodynamic~~s~~ properties of the selected antimicrobial agent, including the activity towards the pathogenic agents involved;

~~iv~~d) the appropriate dosage regimen and route of administration;

~~v~~e) pharmacokinetics and tissue distribution to ensure that the selected therapeutic agent is effective at the site of *infection*;

~~vi~~f) the epidemiological history relevant to ~~of~~ the *animal* or *animals* being treated ~~rearing unit~~, particularly in relation to the antimicrobial resistance profiles of the pathogens ~~pathogenic agents~~ involved.

Should a first-line antimicrobial treatment fail or should the disease recur, an investigation ~~a second line treatment~~ should be undertaken ~~based on the results of diagnostic tests. In the absence of such results, an appropriate~~[*~~antimicrobial agent~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique)~~belonging to a different class or sub-class should be used~~ to reassess the circumstances including reviewing the diagnosis and then formulate and implement a new treatment plan, which may or may not include another *antimicrobial agent*.

~~In emergencies~~In particular situations, a *veterinarian* may treat *animals* empirically,before ~~without recourse to~~ an accurate diagnosis and antimicrobial susceptibility testing results are available, to prevent the development of clinical disease and for reasons of *animal welfare*.

~~b.~~  ~~Use of combinations of~~ *~~antimicrobial agents~~* ~~should be scientifically supported.~~ Combinations of *antimicrobial agents* may be used ~~for their synergistic effect~~ to increase therapeutic effectiveness ~~efficacy or to broaden the spectrum of activity~~, but only when scientifically supported.

3. Appropriate use of the selected ~~VMP~~ veterinary medicinal product containing antimicrobial agents ~~chosen~~

The ~~A~~ prescription of a ~~for VMP~~ *veterinary medicinal product* containing *antimicrobial agents* should indicate ~~precisely~~ the dosage regimen, the withdrawal period where applicable, and when considering group treatments, the total amount of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* to be provided, which will depend ~~depending~~ on the dosage, duration of treatment, and the number of *animals* to be treated**.**

When prescribing, dispensing or administering a *veterinary medicinal product* containing *antimicrobial agents* intended for veterinary medical use to an individual or a group of *animal*s to treat, control or prevent infectious disease as defined in Chapter 6.9, the *veterinarian* should give specific consideration to their categorisation in the OIE List of Antimicrobial Agents of Veterinary Importance as well as to the WHO List of Critically Important Antimicrobials. Preference should be given to the least important *antimicrobial agent* as categorised by WHO that is appropriate for use.

The *veterinarian* should ensure that instructions for the administration of the product are clearly explained and understood by the food *animal* breeder, owner or keeper.

The extra-label or off-label use of a ~~VMP~~ *veterinary medicinal product* containing *antimicrobial agents* may be permitted in certain appropriate circumstances and should be in agreement with the national legislation in force including the withdrawal period~~s to be used~~, as applicable. It is the *veterinarian*'s responsibility to define the conditions of responsible and prudent use in such a case including the dosage regimen, the route of administration and the withdrawal period.

The use of compounded ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* and extra-label or off-label use of registered ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* should be limited to circumstances where an appropriate registered product is not available and should take into account recommendations provided in the OIE List of Antimicrobial Agents of Veterinary Importance.

4. Recording of data

Records of~~n~~ ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* should be kept in conformity with the national legislation. ~~Information r~~Records should include the following, as appropriate:

a) name of the *veterinary medicinal products*;

~~a~~b) quantities ~~of VMP~~ used ~~per~~ *~~animal~~* ~~species~~ in *animals* or supplied to each *establishment* or *animal* breeder, owner or keeper;

~~b)~~ ~~a list of all VMP supplied to each food-producing animal holding;~~

c)route of administration;

d) *animal* species;

e) number of *animal*s treated;

f) clinical condition treated;

~~c~~g) treatment schedules including *animal* identification and withdrawal period;

~~d~~h) antimicrobial susceptibility data;

~~e~~i) comments concerning the response of *animals* to treatment;

~~f~~j) the investigation of adverse reactions associated with ~~to~~ antimicrobial treatment, including lack of response due to possible antimicrobial resistance. Suspected adverse reactions should be reported to the appropriate *Competent Authority*~~regulatory authorities~~.

*Veterinarians* should also periodically review farm records on the use of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* to ensure compliance with their directions or prescriptions and use these records to evaluate the effectiveness ~~efficacy~~ of treatments.

5. Labelling

All ~~VMP~~ *veterinary medicinal products* supplied by a *veterinarian* should be labelled in accordance with the national legislation.

6. Training and continued professional development

Veterinary professional and paraprofessional organisations should participate in the training programmes as defined in point 13~~1~~) of Article 6.10.3. It is recommended that veterinary professional and paraprofessional organisations develop for their members species-specific clinical practice recommendations on the responsible and prudent use of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents*.

# Article 6.10.~~8~~7.

### Responsibilities of animal feed manufacturers

**1. The manufacturing and supply of medicated *feed* containing *antimicrobial agents* to farmers keeping food-**producing *animal*s by *animal* *feed* manufacturers should be allowed only on the prescription of a *veterinarian*. Alternatively, such medicated *feed* may be prescribed by other suitably trained persons authorised to prescribe ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* in accordance with the national legislation ~~and under the supervision of a veterinarian~~. *Animal* *feed* manufacturers preparing medicated *feed* should do so following rules put in place by the *Competent Authority* in accordance with the national legislation. All medicated *feed* and medicated premixes should be appropriately labelled.

2. Keep detailed records for medicated feed and premixes for a suitable period of time according to national legislation.

~~2.~~  ~~The regulations and recommendations on the responsible and prudent use of VMP containing~~[*~~antimicrobial agents~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_antibiotique)~~should be reinforced by~~ *~~animal~~*[*~~feed~~*](https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/index.php?id=169&L=1&htmfile=glossaire.htm#terme_aliment)~~manufacturers who should keep detailed records.~~

3. Use only approved sources of pharmaceutical products ~~medications~~: *Animal* *feed* manufacturers preparing medicated *feed* should ensure that only approved sources of medications are added to *feed* at a level, and for a species and purpose as permitted by the medicated ~~drug~~ premix label or a veterinary prescription.

4. Ensure appropriate labelling with product identification, direction for use and withdrawal time: *animal* feed manufacturers preparing medicated feed should ensure that medicated *animal* feed are labelled with the appropriate information (e.g., level of medication, approved claim, target ~~intended~~ species, directions for use, warning, cautions) ~~so as~~ to ensure effective and safe use by the producer.

5. Implement appropriate production practices to prevent contamination of other *feed*: *animal* *feed* manufacturers preparing medicated *feed* should implement *good manufacturing* ~~appropriate production~~ *practices* to avoid unnecessary carry over and unsafe cross contamination of unmedicated *feed*.

6. Feed manufacturers should participate in training programmes as defined in point 13 of Article 6.10.3.

# Article 6.10.~~7~~8.

### Responsibilities of food animal ~~producers~~ breeders, owners and keepers

1. Food *animal* ~~producers~~ breeders, owners and keepers, with the assistance and guidance of a *veterinarian*, are responsible for implementing *animal* health and *animal welfare* programmes, including *biosecurity* and good husbandry practices on their farms in order to reduce the need for the use of *antimicrobial agents* in *animal*s, and to promote *animal* health and food safety.

2. Food *animal* ~~producers~~ breeders, owners and keepers should:

a) draw up a health plan with the attending *veterinarian* that outlines preventive measures (e.g., feedlot health plans, mastitis control plans, endo- and ectoparasite control, *vaccination* programmes and other *biosecurity* measures);

b) address on-farm *biosecurity* measures and take hygiene precautions as appropriate;

~~d~~c) isolate sick *animals*, when appropriate, to avoid the transfer of pathogenic agents;

d) dispose of dead or dying *animal*s promptly under conditions approved by the relevant authorities;

~~e)~~ ~~address on-farm biosecurity measures and take basic hygiene precautions as appropriate;~~

~~b~~e) use *veterinary medicinal products* ~~VMP~~ containing *antimicrobial agents* only on the prescription and under the supervision of a *veterinarian, veterinary paraprofessional* or other suitably trained person ~~authorised to prescribe~~ *~~VMP~~* ~~containing~~ *~~antimicrobial agents~~* in accordance with the national legislation ~~and under the supervision of a~~ *~~veterinarian~~*;

~~c~~f) use *veterinary medicinal products* ~~VMP~~ containing *antimicrobial agents* in accordance with product label instructions, including storage conditions, and ~~or~~ the instructions of the ~~attending~~ prescribing *veterinarian*;

~~f~~g) comply with ~~and record~~ the recommended withdrawal periods to ensure that residue levels in *animal*-derived food do not present a *risk* for the consumer;

~~g~~h) use ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* within the expiry date and dispose of unused and expired surplus ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* under conditions safe for the environment according to the SPC or equivalent, or relevant national legislation;

i) ensure that only medicated premixes containing *antimicrobial agents* from authorised sources are added to feed at a dose and duration appropriate for the target *animal* species and purpose of use as permitted by the medicated premix label or a veterinary prescription when preparing medicated *feed* on-farm;

~~h~~j) maintain all the laboratory records of bacteriological and susceptibility tests; these data should be made available to the *veterinarian* responsible for treating the *animals*;

~~i~~k) keep adequate records of all ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents* used, including the following:

i) name of the product and active substance, batch number and expiry date;

ii) name of prescriber and the supplier;

iii) date of administration;

iv) identification of the *animal* or group of *animals*, and the number of *animals* to which the *antimicrobial agent* was administered;

v) clinical conditions treated;

vi) ~~dosage~~dose regimen;

vii) withdrawal periods including the end-date of the withdrawal periods;

viii) results of laboratory tests;

ix) effectiveness of therapy;

x) suspected adverse events;

~~j~~l) inform the responsible *veterinarian* of recurrent disease problems.

3. Training

Food *animal* ~~producers~~ breeders, owners and keepers should participate in the training programmes as defined in in point 13~~1~~ of Article 6.10.3.

It is recommended that food *animal* ~~producer~~ organisations work in cooperation with the veterinary professional organisations to implement existing guidelines for the responsible and prudent use of ~~VMP~~ *veterinary medicinal products* containing *antimicrobial agents*.

# Article 6.10.9.

### Responsibilities of breeders, owners and keepers of non-food producing animals

*Animal* breeders, owners and keepers, with the assistance and guidance of a *veterinarian*, are responsible for the health and welfare of their *animal*s and should:

1) implement the wellness plans and preventative health plans recommended by their *veterinarian*;

2) strictly follow their *veterinarian*’s recommendations and ensure that if any, the administration of *veterinary medicinal products* containing *antimicrobial agents* follows the veterinary prescription;

3) avoid administering over the counter, leftover and expired human and *animal* *antimicrobials agents* to their *animal*s;

4) inform their *veterinarian* or *veterinary paraprofessional* of the administration of any additional medicinal products than those prescribed by the *veterinarian* during the consultation;

5) inform their *veterinarian* of any observed lack of response or other adverse effect.

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