Antimicrobial resistance: responsible and prudent use of antimicrobial agents in veterinary medicine

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This report, prepared by the OIE Ad hoc Group of experts on antimicrobial resistance, has not yet received the approval of the International Committee of the OIE

Summary
A guideline on the responsible and prudent use of antimicrobials in animal husbandry has been developed by the Ad hoc Group of experts on antimicrobial resistance, created by the Office International des Epizooties. The objectives of responsible use are to maintain antibiotic efficacy, to avoid the dissemination of resistant bacteria or resistance determinants and to avoid the exposure of humans to resistance through food. The guideline attributes a central role to the competent authorities responsible for granting marketing authorisations for antimicrobial substances. Requirements before and after granting of marketing authorisations are defined. Important aspects include the control of the pharmaceutical product quality and the therapeutic efficacy, the assessment of the selection pressure, the protection of the environment, specific and non-specific antimicrobial resistance surveillance. The guideline is also addressed to the veterinary pharmaceutical industry, veterinary practitioners, dispensing pharmacists and farmers. The respective roles and responsibilities of these groups are defined.

Keywords
Introduction

This document provides guidance for the responsible and prudent use of antimicrobials in veterinary medicine, with the aim of protecting both animal and human health. The authors define the respective responsibilities of authorities and groups involved in the registration, production, control, distribution and use of veterinary antimicrobials, such as national competent authorities, the veterinary pharmaceutical industry, veterinarians, pharmacists and livestock producers.

Prudent use is principally determined by the outcome of the marketing authorisation procedure and by the implementation of specifications when antimicrobials are administered to animals.

A number of codes of practice, relating to the use of antimicrobials and the conditions thereof have been developed by different organisations. These codes were taken into consideration and some elements were included in the preparation of this guideline.

Aims and objectives

It is imperative that all who are involved in the authorisation, manufacture, sale and supply, prescription and use of antimicrobials in livestock act legally, responsibly and with the utmost care, in order to limit the spread of resistant bacteria among animals and to protect the health of consumers.

Antimicrobial agents: powerful tools for treating and preventing/controlling bacterial diseases in animals

Guidelines for the responsible use of antimicrobial agents in veterinary medicine include a set of practical measures and recommendations intended to prevent and/or reduce the selection of antimicrobial resistant bacteria in animals, with the following aims:

a) to maintain the efficacy of antimicrobial agents and to ensure the rational use of antimicrobials in animals with the purpose of optimising both their efficacy and safety in animals

b) to comply with the ethical obligation and economic need to keep animals in good health

c) to prevent, or reduce as far as possible, the transfer of bacteria (with their resistance determinants) within animal populations, to maintain the efficacy of antimicrobial agents used in livestock

d) to prevent or reduce the transfer of resistant bacteria or resistance determinants from animals to humans, to maintain the efficacy of antimicrobial agents used in human medicine

e) to prevent the contamination of animal-derived food with antimicrobial residues which exceed the established maximum residue limit (MRL)

f) to protect consumer health by ensuring the safety of food of animal origin intended for human consumption.

The responsible use of antimicrobials in veterinary medicine

The Ad hoc Group described responsible use as follows:

a) represents the scientific and technically directed use of these compounds that are the responsibility of professionals with the required expertise

b) is part of good veterinary and animal husbandry practice and takes into consideration disease prevention practices such as the use of vaccination and improvements in husbandry conditions when disease problems become evident

c) aims to reduce the use of antimicrobial agents to their approved and intended uses

d) takes into consideration on-farm sampling and testing of isolates from food-producing animals during their production (where appropriate), and makes adjustments to therapy when problems become evident

e) should be based on the results of resistance surveillance and monitoring (bacterial cultures and antimicrobial sensitivity testing)

f) is aimed at all the relevant professionals, including the following:

– administrative and scientific authorities

– the veterinary pharmaceutical industry

– distributors and others handling antimicrobials

– veterinarians, pharmacists and livestock producers.

Responsibilities of the regulatory authorities

The national regulatory authorities, which are responsible for granting the marketing authorisation, have a significant role in specifying the terms of this authorisation and in providing the appropriate information to the veterinarian through product labelling in support of the prudent use of antimicrobials in veterinary medicine.

It is the responsibility of the pharmaceutical industry to submit the data requested for the granting of the marketing authorisation.

The use of an antimicrobial agent in veterinary medicine requires a marketing authorisation, which is granted by the competent authorities only if the criteria of safety, quality and efficacy are met. The examination of applications for drug authorisation must include an assessment of the risks to both the animal and the consumer resulting from the use of
antimicrobial agents in food-producing animals. The evaluation should focus on each individual antimicrobial product and not be generalised to the class of antimicrobials to which the particular active principle belongs. The safety evaluation should include consideration of the potential impact on human health of the proposed use in food-producing animals. If dose ranges or different durations of treatment are suggested, the national authorities should give guidance on the approved product labelling regarding the conditions that will minimise the development of resistance.

Regulatory authorities should, where possible, expedite the market approval process of new antimicrobial molecule formulation, which is considered to have the potential to help the control of resistance. The preparation of internationally accepted guidelines would assist in this regard.

Countries lacking the necessary resources to implement an efficient registration procedure for veterinary medicinal products and whose supply of veterinary medicinal products principally depends on imports from foreign countries must undertake the following measures:

– check the efficacy of administrative controls on the import of these veterinary medicinal products
– check the validity of the registration procedures of the exporting country
– develop the necessary technical co-operation with experienced authorities to check the quality of imported veterinary medicinal products as well as the validity of the recommended conditions of use.

Regulatory authorities of importing countries could request the pharmaceutical industry to provide quality certificates prepared by the competent authority of the exporting country.

All countries should make every effort to actively combat the trade, distribution and use of illegal and counterfeit products.

**Quality control of antimicrobial agents**

Quality controls should be performed as follows:

– in compliance with the provisions of good manufacturing practices
– to ensure that analysis specifications of antimicrobial agents used as active ingredients comply with the provisions of approved monographs
– to ensure that the quality and concentration (stability) of antimicrobial agents in the marketed dosage form(s) is maintained until the expiry date, established under the recommended storage conditions
– to ensure the stability of antimicrobials when mixed with feed or drinking water
– to ensure that all antimicrobials are manufactured to the appropriate quality and purity in order to guarantee safety and efficacy

**Control of the therapeutic efficacy**

**Preclinical trials**

Preclinical trials should be undertaken, with the following aims:

– to assess the ability of the antimicrobial agent to select for resistant bacteria *in vitro* and *in vivo*. The design of *in vivo* studies is currently under development. In certain cases, preclinical trials should evaluate not only the bacteria of the target animals for resistance, but also the impact of the antimicrobial use on food-borne and/or commensal bacteria

– to establish an appropriate dosage regimen necessary to ensure the therapeutic efficacy of the antimicrobial agent and limit the selection of antimicrobial resistant bacteria.

**Pharmacodynamics and the establishment of the activity of antimicrobial agents towards the targeted bacteria**

The following criteria should be taken into account:

– mode of action
– minimum inhibitory and bactericidal concentrations
– time- or concentration-dependent activity
– activity at the site of infection.

**Pharmacokinetics and the establishment of the dosage regimens allowing maintenance of effective antimicrobial levels**

The following criteria should be taken into account:

– bio-availability according to the route of administration
– concentration of the antimicrobial at the site of infection and its distribution in the treated animal
– metabolism which may lead to the inactivation of antimicrobials
– excretion routes.

The use of combinations of antimicrobial agents should be justified, taking into account the following:

– pharmacodynamics (additive or synergistic effects towards the target bacteria)
– pharmacokinetics (maintenance of the levels of associated antibiotics responsible for additive or synergistic effects at the site of infection throughout the treatment period).

**Clinical trials**

Clinical trials 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 the protocols of clinical trials with good clinical practice
– eligibility of the studied clinical cases, based on appropriate criteria of clinical and bacteriological diagnoses
– parameters for qualitatively and quantitatively assessing the efficacy of the treatment.

**Assessment of the potential of antimicrobials to select for resistant bacteria**

Studies may be appropriate and requested in support of the assessment of the potential of antimicrobials to select for resistant bacteria.

However, it should be noted that the results from these in vivo studies may be very different from the resistance that develops under normal conditions. Therefore, the interpretation should be undertaken with great caution.

The party applying for market authorisation for antimicrobials for veterinary use should, where possible, supply data derived from the testing of antimicrobials for the development of antimicrobial resistance in target animal species under the intended conditions of use.

To reduce the potential selection of resistance, preclinical and clinical trials should, in certain cases, evaluate not only pathogenic bacteria of target animals for resistance, but also the impact of the antimicrobial use on food-borne and/or commensal (indicator) bacteria.

In these cases, considerations may include the following:
– the concentration of active compound in the gut of the animal (where the majority of potential food-borne pathogens reside) at the defined dosage level
– the level of human exposure to food-borne or other resistant bacteria
– the degree of cross-resistance within the class of antimicrobials and between classes of antimicrobials
– the pre-existing level of resistance in the pathogens of human health concern (baseline determination).

**Establishment of acceptable daily intake, maximum residue limit and withdrawal periods for antimicrobial compounds**

a) When setting the acceptable daily intake (ADI) and MRL for an antimicrobial substance, the safety evaluation should, for this class of substances, also include the potential biological effects on the intestinal flora of humans. Using in vitro and/or in vivo tests and/or data originating from human medicine, an assessment should be undertaken regarding the capability of antimicrobial residues, ingested by the consumer, to disturb the intestinal flora of humans by selecting resistant bacteria and/or weakening the barrier effect against the colonisation of pathogenic bacteria.

b) The establishment of an ADI for each antimicrobial agent, and an MRL for each animal-derived food, should be undertaken. An MRL is necessary in order that officially approved control laboratories can verify that all foods comply with the safety standards.

c) For each veterinary medicinal product containing antimicrobial agents, withdrawal periods should be established which make it possible to produce safe food in compliance with the MRL.

Withdrawal periods should be established for each veterinary medicinal product by taking into account the following:
– the MRL established for the antimicrobial agent under consideration
– the pharmaceutical form
– the target animal species
– the dosage regimen and the duration of treatment
– the route of administration.

The applicant should provide methods for regulatory testing of residues in food.

**Protection of the environment**

An assessment of the impact of the proposed antimicrobial use on the environment should be conducted. Efforts should be made to ensure that environmental contamination with antimicrobials is restricted to a minimum.

**Establishment of a summary of product characteristics for each veterinary medicinal product**

The summary of product characteristics contains the information necessary for the appropriate use of veterinary medicinal products containing antimicrobial agents. It constitutes, for each veterinary medicinal product, the official reference of the content of its labelling and package insert. This summary contains the following items:
– pharmacological properties
– target animal species
– therapeutic indications
– target bacteria
– dosage and administration route
– withdrawal periods
– incompatibilities
– expiry date
– operator safety
– particular precautions before use
– particular precautions for the proper disposal of un-used products.

The conditions of prudent use of an antimicrobial agent in veterinary medicine should be based on a safety evaluation, which takes into particular consideration the importance of the drug, or other antimicrobial agents belonging to the same therapeutic class, in human and/or veterinary medicine. Antimicrobials which are considered important in treating critical diseases in humans should only be used in animals when alternatives are either unavailable or inappropriate. Consideration should be given to providing such guidance to the veterinarian by means of the product label.

The oral route, which enhances the access of antimicrobial agents to the complex intestinal flora, and hence the possibility of the selection and the transfer of resistance genes, should be used with caution. For certain antimicrobial classes, other administration routes may also cause similar selection of resistance. Specific mention should be made on the product label.

Post-marketing antimicrobial surveillance

A structured approach is required to the investigation and reporting of the incidence and prevalence of resistance.

Regulatory authorities should have implemented a pharmacovigilance programme for the monitoring, recording and reporting of adverse reactions to antimicrobials, including the lack of efficacy related to antimicrobial resistance. The information collected through the pharmacovigilance programme should form part of the comprehensive strategy to minimise antimicrobial resistance.

A surveillance programme

A specific surveillance programme to assess the impact of the use of an authorised antimicrobial agent on the selection of antimicrobial resistant bacteria in food-producing animals may be implemented after the granting of the marketing authorisation. In certain cases, the surveillance programme should evaluate not only resistance development in target animal pathogens, but also in food-borne pathogens and/or commensals. This protocol of surveillance should be implemented if justified by the safety evaluation performed during the registration process.

Specific surveillance

The surveillance of animal bacteria resistant to antimicrobial agents is essential. The relevant authorities should implement a programme, established from the results of a risk analysis, which allows the ranking of priorities regarding antimicrobials and animal bacteria, whether or not they are pathogenic for animals and humans. For reasons of efficiency, the methods used to establish such programmes (laboratory techniques, sampling, choice of antimicrobial agents and bacteria, etc.) should be harmonised as much as possible at the international level (see Antimicrobial resistance: standardisation and harmonisation of laboratory methodologies for the detection and quantification of antimicrobial resistance and Antimicrobial resistance: harmonisation of national antimicrobial resistance monitoring and surveillance programmes in animals and in animal-derived food, later in this volume).

This epidemiological surveillance of antimicrobial resistance should be accompanied by a continuous survey on the amounts of antimicrobial agents used by veterinarians and other authorised users, in order to encourage the most appropriate prescription of these medicinal products.

If justified by the results of this post-registration surveillance of antimicrobial resistance, whether specific or not, the conditions of use of the antimicrobial agents in veterinary medicine should be modified.

Distribution of the antimicrobial agents used in veterinary medicine

The relevant authorities should, where possible, ensure that all the antimicrobial agents used in food animals fulfil the following criteria:

– are prescribed by a veterinarian or other suitably trained and authorised person
– are delivered by an authorised animal health professional
– are supplied only through licensed/authorised distribution systems
– are administered to animals by a veterinarian or under the supervision of a veterinarian or by his/her agent.

Control of advertising

All advertising of antimicrobials should be controlled by a code of advertising standards, and the relevant authorities must ensure that the advertising of antimicrobial products fulfils the following criteria:

– compliance with the marketing authorisation granted, in particular regarding the content of the summary of product characteristics
– restriction to authorised professionals, according to national legislation in each country.

Training of antibiotic users

Training of antibiotic users, involving all the relevant professional organisations, including regulatory authorities, the
pharmaceutical industry, veterinary schools, research institutes and professional associations, should focus on the following:

– information on disease prevention and management strategies to reduce the need to prescribe antimicrobials

– the ability of antimicrobials to select for resistant bacteria in food-producing animals, which may cause animal and/or human health problems

– the need to observe responsible use recommendations and the use of antimicrobial agents in animal husbandry in agreement with the provisions of the marketing authorisations, and veterinary advice, in order to assure the safety to the consumer of animal-derived food, and therefore the protection of public health

– relevant pharmacokinetic and pharmacodynamic information to enable the veterinarian to use antimicrobials prudently.

Development of research

The relevant authorities should encourage public and private research with the following aims:

– to improve knowledge regarding the mechanisms of action of antimicrobials, to optimise the dosage regimens and the therapeutic activity of these medicinal products

– to improve knowledge about the mechanisms of selection, emergence and dissemination of bacterial genes encoding resistance against antimicrobial agents

– to develop practical models for applying the concept of risk analysis to assess the public health concern precipitated by the development of resistant bacteria

– to further develop protocols to predict, during the registration process, the impact of the proposed use of the antimicrobials on the rate and extent of resistance development

– to develop alternative methods to control bacterial diseases (vaccines, changes in husbandry practices, etc.).

Responsibilities of the veterinary pharmaceutical industry

Marketing authorisation of veterinary medicinal products

The veterinary pharmaceutical industry has responsibilities in the following areas:

– to supply all the information requested by the national regulatory authority in order to establish objectively the quality, safety and efficacy of veterinary medicinal products

– to guarantee the quality of this information on the basis of the implementation of procedures, tests and trials in compliance with the provisions of good manufacturing, laboratory and clinical practices.

The pharmaceutical industry should be encouraged to perform post-approval studies, as practised for human medicinal products, in order to seek an extension of the authorised indications in the light of practical experience. This would limit the need for off-label use.

Marketing and export of veterinary medicinal products

In regard to marketing and export of veterinary medicinal products, the following suggestions are presented:

– only officially licensed and approved veterinary medicinal products should be sold and supplied, and then only through licensed/authorised distribution systems

– only veterinary medicinal products which have been authorised in the (exporting) country in which the product(s) is approved for sale or the quality of which is certified by a regulatory authority should be exported

– the national regulatory authority should be provided with the information necessary to evaluate the amount of antimicrobial agents marketed.

Advertising

The following are the responsibilities of the veterinary pharmaceutical industry:

– to disseminate information in compliance with the provisions of the granted authorisation and to ensure that this dissemination reaches only those authorised professionals involved in the prescription and distribution of the products

– to ensure that the advertising of antimicrobials directly to the livestock producer is discouraged.

Training

The veterinary pharmaceutical industry is responsible for participation in training programmes as defined in the earlier section entitled ‘Training of antibiotic users’.

Research

It is the responsibility of the veterinary pharmaceutical industry to contribute to the research effort as defined in the earlier section entitled ‘Development of research’.

Responsibilities of pharmacists

Pharmacists distributing veterinary antimicrobials should only do so on the prescription of a veterinarian, and all products should be appropriately labelled (see later section entitled ‘Labelling’).
The guidelines on the responsible use of antimicrobials should be reinforced by pharmacists, who should keep detailed records of all antimicrobials supplied, including the following:

- date of supply
- name of prescribing veterinarian
- name of user
- name of product
- batch number
- quantity supplied.

Pharmacists should also be involved in training programmes on the responsible use of antimicrobials.

Responsibilities of veterinarians

The use of antimicrobials is no substitute for good management practices and the prime concern of the veterinarian is to encourage good farming practice in order to minimise the need for antimicrobial use in livestock.

In the frame of good management practice, the veterinarian is responsible for identifying recurrent disease problems and developing alternative strategies to prevent or control disease. These may include changes in husbandry conditions and vaccination programmes where vaccines are available.

Veterinarians should only prescribe antimicrobials for animals under their care, which means that:

- the veterinarian must have been assigned responsibility for the health of the animal or the herd/flock by the producer or an agent of the producer
- that responsibility must be real and not merely nominal
- that the animal(s) or herd/flock must have been examined immediately before the prescription and supply or sufficiently recently or frequently for the veterinarian to have personal knowledge of the condition of the animal(s) or current health status of the herd or flock to make a diagnosis and prescribe
- the veterinarian should maintain clinical records of the animal(s)/herd/flock.

It is recommended that veterinary professional organisations develop for their members, species-specific clinical practice guidelines on the responsible use of antimicrobials, with particular reference to the choice of product, disease prevention strategies and treatment protocols.

The responsibilities of veterinarians in this area are described below.

Use of antimicrobial agents when necessary

The appropriate use of antimicrobials in practice is a critical decision which, where possible, should be based on the following:

- the experience and local expertise of the prescribing veterinarian
- an accurate diagnosis, based on adequate diagnostic procedures.

On certain occasions, a group of animals which may have been exposed to pathogenic bacteria may need to be treated without recourse to an accurate diagnosis and antimicrobial susceptibility testing, to prevent the development of clinical disease and for reasons of animal welfare.

Determination of the choice of an antimicrobial

The expected efficacy of the treatment

The expected efficacy of the treatment is based on the following:

- the clinical experience of the veterinarian
- the activity towards the pathogenic bacteria involved
- the epidemiological history of the rearing unit, particularly in relation to the antimicrobial resistance profiles of the pathogenic bacteria involved. Ideally, the antibiotic profiles should be established before the commencement of treatment. Should a first line antibiotic treatment fail or should the disease recur, the use of a second line antimicrobial agent should be based on the results of the microbiological tests
- the appropriate route of administration
- results of initial treatment
- known pharmacokinetics/tissue distribution to ensure that the selected therapeutic agent is active at the site of infection
- prognosis.

To minimise the likelihood of antimicrobial resistance developing, it is recommended that antimicrobials be targeted to bacteria likely to be the cause of infection.

Absence of selection or limited selection of antimicrobial resistant bacteria

The absence of selection or limited selection of antimicrobial resistant bacteria is influenced by the following:

- the choice of the activity spectrum of the antimicrobial
- the targeting of specific bacteria
- known or predictable susceptibilities using antimicrobial susceptibility testing
- the correct dosing regimens
- the use of combinations of antimicrobial agents
– the importance of the drug to human and/or veterinary medicine. Antimicrobials which are considered important to treat critical diseases in humans and/or animals, should be used only when other therapies are unavailable or inappropriate
– the route of administration.

**Combinations of antimicrobials**

Combinations of antimicrobials are used for their synergistic effect to increase therapeutic efficacy or to broaden the spectrum of activity.

Furthermore, the use of combinations of antimicrobials can be protective against the selection of resistance in cases in which bacteria exhibit a high mutation rate against a given antimicrobial.

However, a bad choice of a combination of antimicrobials may, in certain cases, lead to an increase of the selection of resistance.

If the use of a combination of antimicrobials is justified, the veterinarian should ensure that there is no antagonism between the chosen antimicrobials and should check the ability of these antibiotics to reach the infection site under similar time and concentration conditions, to maintain effective therapeutic concentrations as long as required.

**Appropriate use of the antimicrobial agent chosen**

A prescription for antimicrobial agents must precisely indicate the treatment regime, the dose, the dosage intervals, the duration of the treatment, the withdrawal period and the amount of drug to be delivered, depending on the dosage and the number of animals to be treated.

All medicinal products should be prescribed and used according to the conditions of the marketing authorisation, which are reflected in the summary of product characteristics provided by the manufacturer.

If the label conditions allow for some flexibility, the veterinarian should consider a therapeutic regimen that is sufficiently long to allow the effective recovery of the animal, but sufficiently short to limit the selection of resistance in food-borne and/or commensal bacteria.

‘Off label use’ (extra-label use) of veterinary medicinal products

Although all medicinal products should be prescribed and used in accordance with the specifications of the marketing authorisation, the prescribing veterinarian should have the discretion to adapt these in exceptional circumstances.

The ‘off label use’ of an antimicrobial agent may be permitted in appropriate circumstances and should be in agreement with the national legislation in force. The veterinarian has the responsibility to define the conditions of responsible use in such a case, including the therapeutic regimen, the route of administration and the duration of the treatment.

**Recording**

All available information should be consolidated into one form or database, such that this information should:
– allow monitoring of the quantities of medication used
– contain a list of all medicines supplied to each livestock holding
– contain a list of medicine withdrawal periods and a system for allowing information to be updated
– contain a record of antimicrobial susceptibilities
– provide comments concerning the response of animals to medication
– allow the investigation of adverse reactions to antimicrobial treatment, including lack of response due to antimicrobial resistance. Suspected adverse reactions should be reported to the appropriate regulatory authorities.

**Labelling**

All medicines supplied by a veterinarian should be adequately labelled with the following minimum information:
– the name of the owner/keeper or person who has control of the animal(s)
– the address of the premises where the animal(s) is kept
– the name and address of the prescribing veterinarian
– the date of supply
– the indication ‘For animal treatment only’
– the warning ‘Keep out of the reach of children’
– the relevant withdrawal period, even if this is nil.

The label should not obscure the expiry date of the preparation or any important information supplied by the manufacturer.

**Training**

Veterinary professional organisations should participate in the training programmes as defined in the earlier section entitled ‘Training of antibiotic users’.

**Responsibilities of producers**

Producers are responsible for preventing outbreaks of disease and implementing health and welfare programmes on their farms. They may, as appropriate, call on the assistance of their veterinarian in undertaking these duties. All those involved...
with the livestock on the farm have an important role to play in ensuring the responsible use of antimicrobials.

Therapeutic antimicrobial products should be regarded as complementing good management, vaccination and farm hygiene.

Efforts should be made to ensure that environmental contamination both by antimicrobials and by resistant bacteria is kept to a minimum.

Livestock producers have the following responsibilities:

a) to draw up a health plan with the veterinarian in charge of the animals that outlines preventative measures (mastitis plan, worming and vaccination programmes, etc.)

b) to use antimicrobial agents only on veterinary prescription and according to the provisions of the prescription

c) to use antimicrobial agents in the species, for the uses and at the doses on the approved/registered labels and in accordance with product label instructions or the advice of a veterinarian familiar with the animals and the production site

d) to isolate sick animals, when appropriate, to avoid the transfer of resistant bacteria

e) to comply with the storage conditions of antimicrobials in the rearing unit, according to the provisions of the leaflet and package insert

f) to address hygienic conditions regarding contacts between people (veterinarians, breeders, owners, children) and the animals treated

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

h) to dispose of surplus antimicrobials under safe conditions for the environment. Partially-used medicines should only be used within the expiry date, for the condition for which they were prescribed and, if possible, in consultation with the prescribing veterinarian

i) to maintain all the laboratory records of bacteriological and susceptibility tests. These data should be made available to the veterinarian responsible for treating the animals to optimise the use of antimicrobials in that unit

j) to keep adequate records of all medicines used, including the following:

- name of the product/active substance and batch number
- date of administration
- identification of the animal or group of animals to which the antimicrobial agent was administered
- diagnosis/clinical conditions treated
- quantity of the antimicrobial agent administered
- withdrawal periods
- result of laboratory tests
- effectiveness of therapy

k) to inform the veterinarian responsible for the unit of recurrent disease problems.

**Conclusion**

Antimicrobial agents are very important tools for controlling a great number of bacterial diseases in both animals and humans. It is vital that all countries implement the appropriate systems to ensure that antimicrobials are manufactured, marketed, distributed, prescribed, supplied and used responsibly, and that these systems are adequately audited.

The OIE Ad hoc Group of experts on antimicrobial resistance is well aware of the difficulties that a number of countries may face in the immediate implementation of all elements of this guideline.

This document is designed to provide the framework which countries should implement in accordance with their capabilities and resources, but within a reasonable period of time. A step-by-step approach may be appropriate for a number of countries, to properly implement all of the elements. The continued availability of veterinary medicines, which are essential for animal welfare and health, and consequently for human health, will ultimately depend on the responsible use of these products by all those involved in the authorisation, production, control, distribution and use of antimicrobials in animals.
Antibiorésistance : utilisation responsable et prudente des antibiotiques en médecine vétérinaire

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Résumé
Le Groupe ad hoc d’experts sur l’antibiorésistance mis en place par l’Office international des épizooties a mis au point une ligne directrice sur l’utilisation prudente et responsable des antibiotiques dans la production animale. L’utilisation responsable a pour objectif de perpétuer l’activité des antibiotiques, d’éviter la dissémination de bactéries résistantes ou des facteurs favorisant la résistance ainsi que l’exposition de l’homme à celle-ci au travers des aliments. La ligne directrice attribue un rôle majeur aux autorités compétentes chargées de la délivrance des autorisations de mise sur le marché (AMM) des substances antimicrobiennes. Les auteurs définissent les conditions préalables et consécutives à la délivrance de ces AMM. L’accent est mis sur le contrôle de la qualité et de l’efficacité thérapeutique des produits pharmaceutiques, sur l’évaluation de la pression sélective, sur la protection de l’environnement ainsi que sur la surveillance de l’antibiorésistance, spécifique et non spécifique. La ligne directrice s’adresse également à l’industrie des médicaments vétérinaires, aux praticiens, aux pharmaciens et aux éleveurs. Les rôles et responsabilités respectifs de ces groupes sont également définis.

Mots-clés

Resistencia a los antimicrobianos: uso prudente y responsable de productos antimicrobianos en medicina veterinaria

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Resumen
El Grupo Ad hoc de expertos sobre la resistencia de las bacterias a los productos antimicrobianos, creado por la Oficina Internacional de Epizootias, ha elaborado una directriz sobre el uso prudente y responsable de productos antimicrobianos en producción animal. El uso responsable ha de servir para: mantener la eficacia antibiótica de los productos; evitar la diseminación de bacterias resistentes o de determinantes de resistencia; y evitar que el ser humano se vea expuesto por vía
alimentaria a organismos resistentes. Esta directriz asigna un papel básico a las autoridades responsables de conceder las licencias de comercialización de sustancias antimicrobianas y define los requisitos que éstas deben cumplir (antes y después de la autorización de comercialización). Entre los aspectos más importantes cabe destacar: el control de la calidad y eficacia terapéutica de los productos farmacéuticos; la evaluación del grado de presión selectiva; la necesidad de proteger el medio ambiente; y la vigilancia de la aparición de resistencias específicas e inespecíficas a los antimicrobianos. La directriz establece también las respectivas funciones y responsabilidades de la industria farmacéutica veterinaria, los veterinarios, los farmacéuticos y los productores agropecuarios.

**Palabras clave**