

# Responsibilities of regulatory agencies in the marketing of antimicrobials

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## Summary

The regulatory agencies' main responsibility regarding the marketing of veterinary medicinal products is to ensure that the products have a marketing authorisation with specific conditions of use adequate to ensure the quality, safety and efficacy of the product under consideration. In addition, control and surveillance systems are necessary to allow monitoring of the product after it has been authorised. In respect to antimicrobials, specific consideration must be given to minimising resistance development and retaining the effectiveness of these drugs for the treatment of humans and animals. Surveillance programmes should be in place to follow trends in resistance development, as well as in the consumption of veterinary antimicrobials, in order to provide for science-based policy recommendations regarding public and animal health.

## Keywords

Antimicrobial agent – Antimicrobial resistance – Antimicrobial – Marketing authorisation – Prudent use – Registration – Responsible use – Surveillance.

## Introduction

Many countries have established legislation and a regulatory system for the authorisation, use, control and surveillance, such as inspections, residue control or pharmacovigilance, of veterinary medicinal products. As a general principle, any veterinary medicinal product (also called 'veterinary drug') has to be authorised (the terms 'registered' or 'licensed' are also used) before it is allowed to be marketed or used.

The processes and timelines involved in obtaining a marketing authorisation vary to some extent in different countries and regions depending on the structure of the authorisation system, the bodies responsible for review and the specificity of the legislative systems and laws. In addition, there can be systems requiring the submission of a complete marketing authorisation application dossier, including all parts and studies in one package (e.g. in the

European Union [EU]) or others allowing a phased submission of the dossier, with subsequent separate submission of the different parts (e.g. in the United States [USA]). What they have in common is that any questions arising or outstanding issues identified as a result of an initial assessment are brought to the attention of the applicant (also called 'sponsor') and time is allowed to address these issues. Once answers are received the responsible authority evaluates all data available and decides on the marketing authorisation based on a benefit–risk assessment of the product.

Systems should be in place for the control and surveillance of the authorised product, with mechanisms that allow review of whether the benefit–risk balance remains positive under actual conditions of use.

Feed additives given to animals on a daily basis also require authorisation. They are regulated in some countries under the same legislation as veterinary medicinal products

(e.g. Australia and the USA) while elsewhere they fall under separate legislation (e.g. the EU and Japan) and may be assessed by different responsible authorities.

This article provides an overview of the principles of marketing authorisations for veterinary medicinal products issued by regulatory authorities (data requirements, data assessment and the establishment of appropriate conditions of product use), as well as surveillance schemes established by authorities, focusing on the specificities regarding antimicrobials. It concentrates on countries with established regulatory schemes which are part of the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH). Links to the websites of the authorities or agencies responsible for the authorisation of veterinary medicines in VICH countries/regions have been included in the Appendix, where details of the specific procedures in the country/region can be found. In some cases, details are provided and used as examples of the responsibilities of the regulatory authorities in the EU.

This article also provides information and references on guidelines and standards available at the international level, intended to complement the work of the national/regional regulatory authorities in their efforts to minimise the development of antimicrobial resistance from the use of veterinary medicinal products.

## General principles of a marketing authorisation

A marketing authorisation specifies the product authorised, i.e. the name of the product, the active ingredient and other constituents, its strength and pharmaceutical form, target species, indications and possible contra-indications. It also describes the conditions for the use of the product, e.g. the dosage regimen (concentration/dose, administration route, dosing interval, duration of treatment, etc.), instructions for use, precautions for administration, withdrawal period for products for food-producing animals, storage conditions and shelf life.

For a given marketing authorisation of a veterinary medicinal product an extension can be granted (e.g. to include further animal species or other pharmaceutical forms) or an amendment (variation) can be made to take account of new developments. Amendments usually relate to changes to manufacturing processes that may have an impact on the quality evaluation, but various other amendments are also possible, e.g. administrative particulars can be updated or product literature can be revised to include new indications. Also, when new

information, in particular on safety, becomes available that alters the benefit–risk assessment of the product, the authority may decide to change the marketing authorisation to bring the description of the product and advice on its safe and effective use in line with the new information. Where necessary, the authorisation may be suspended or revoked.

To obtain a marketing authorisation it is necessary to prove the quality, safety and efficacy of the veterinary medicinal product to the agency/authority responsible for granting the authorisation by providing an application with the required data on quality, safety and efficacy.

Data describing the quality of the product are necessary to allow an assessment of whether the product contains the claimed ingredients to the necessary purity and quality standards and whether it is stable from production to end of shelf life and during use to ensure safety and efficacy throughout its lifespan.

Safety data are necessary to allow assessment of the safety of the target animal, the person administering the product (e.g. the veterinarian, the farmer or the animal owner) or other people that come into contact with the medicine or the treated animal, and the environment. For food-producing animals the safety of consumers of food originating from treated animals also needs to be addressed and appropriate data regarding residues provided.

Efficacy data are necessary to establish which indications the veterinary medicinal product is capable of treating and, together with target animal safety data, to determine appropriate dosage regimens (dose, duration of treatment and administration route).

For marketing authorisations for generic veterinary medicinal products, usually no new safety and efficacy data are required, provided that the generic medicine is the bioequivalent of the already authorised product for which safety and efficacy have been proven. However, residue data to establish specific withdrawal periods for the generic may be required.

The main data required for a marketing authorisation regarding quality, safety and efficacy have been harmonised at the international level within VICH, which was established in 1996 under the auspices of the World Organisation for Animal Health (OIE), with the EU, Japan and the USA as members and Australia, Canada and New Zealand joining as observers. The main objective of VICH is to establish internationally harmonised data requirements for marketing authorisations for veterinary medicinal products by developing guidelines describing the requirements for the different parts of a marketing authorisation dossier and requirements for pharmacovigilance in a consultative process. Following

adoption, the harmonised guidelines replace existing guidelines and regulations in the VICH countries.

In total, 47 VICH guidelines have been agreed to date: 13 on quality, 16 on safety, 9 on efficacy, 4 on immunologicals, 1 on good clinical practice and 4 on pharmacovigilance (13).

For veterinary medicinal products for food-producing animals the safety of food of animal origin for the consumer needs to be evaluated as well, and maximum residue limits (MRLs) for the pharmacologically active substance contained in the medicine must be established before a marketing authorisation is issued.

In order to evaluate the consumer safety of veterinary medicinal products and to establish MRLs, pharmacology studies, in particular a set of toxicity studies and residue studies, are required. The toxicity studies include repeat dose toxicity, reproductive toxicity (including developmental toxicity), genotoxicity, carcinogenicity or other specific studies dependant on the veterinary drug under consideration, e.g. neurotoxicity and studies to evaluate the microbiological risk of the substance to the human gut flora. VICH guidelines (GL) regarding toxicity studies and microbiological safety are available (VICH GLs 22, 23, 28, 31, 32, 33, 36, 37). Based on the results of the studies – and using uncertainty factors – a toxicological acceptable daily intake (ADI) is established and, where appropriate, a microbiological ADI and/or pharmacological ADI are also determined. (The ADI is an estimate of the substance and/or its residues, expressed in terms of µg/kg or mg/kg body weight, that can be ingested daily over a lifetime without any appreciable health risk to exposed individuals.) The lowest ADI is the overall ADI on which, subsequently, MRLs are based. For substances with antimicrobial activity, the ADI is normally set on the basis of microbiological data if these indicate a lower ADI than that indicated by toxicological and pharmacological data.

The evaluation principles are widely consistent and apply the principles used by the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (14). As another example, the guidance for safety assessment in the EU is given in the *Notice to Applicants and Guideline on the Establishment of Maximum Residue Limits for Residues of Veterinary Medicinal Products in Foodstuffs of Animal Origin* (8).

The evaluation of the safety of residues and establishment of MRLs can be carried out as a separate procedure prior to the application for the marketing authorisation, e.g. in the EU, or within the same process, e.g. in the USA. Countries may also choose to adopt MRLs already established elsewhere, in particular the MRLs established by Codex Alimentarius, or choose those established by other countries, e.g. if no Codex MRL is available for the active

substance. In any case, a withdrawal period(s), which is the time after which the animal can be slaughtered and its meat safely consumed, or the time after which milk or eggs can be taken from the treated animal, following administration of the medicine, will have to be established for the specific medicinal product. This is a separate step from the establishment of MRLs for the active substance(s), as the excipients used in the product may have an impact on the residue depletion. Thus, the withdrawal period is product specific. The withdrawal period is defined as the time when the residues have declined to levels below the MRL value for the food concerned (e.g. in the EU and Japan) or below the ADI (e.g. in the USA).

The safety assessment also includes environmental risk assessment. Internationally agreed guidelines on the data required and the approach to assessing the environmental impact of veterinary medicinal products have been developed in the context of VICH GL6 (Phase I) and GL38 (Phase II) (13). The approach follows the principle of considering, in the first instance, the potential exposure of the veterinary medicinal product to the environment. For products that have very restricted exposure, thus not representing a concern for the environment, no specific studies are required. For products expected to have higher exposure, i.e. for food-producing animals, the predicted environmental concentrations are derived, and the details of assessment and data required will depend on the expected environmental concentration.

The detail of a user-safety assessment, and whether specific studies are required, depends on the potential exposure of users to the medicine or persons coming into contact with it. If a detailed assessment is required, normally the toxicity studies available are used. Often acute toxicity results are relevant.

To establish safety to the target animal, available laboratory animal studies and field trials to assess efficacy in the target animals are used (13). Post-authorisation surveillance schemes allowing reviews of the safety of the product are in place, in particular pharmacovigilance and, for products for food-producing animals, residue control systems. With respect to antimicrobial resistance, schemes for resistance surveillance and monitoring of sales or use of antimicrobials are in place in many countries.

## Specific principles for marketing authorisations for antimicrobials

For a veterinary medicinal product containing an antimicrobial, additional data are required, in particular for

medicines for food-producing animals, and specific risk mitigation measures may be necessary to minimise resistance development and ensure that these antimicrobials retain their effectiveness for treating microbial infections in human beings.

The guideline on studies to evaluate the safety of residues of veterinary drugs in human food – ‘General approach to establish a microbiological ADI’ (VICH GL36) – applies to the establishment of MRLs. It addresses two endpoints: disruption of the colonisation barrier; and increase in the population of resistant bacteria in the human colon (12).

Specific data to evaluate the potential for antimicrobial resistance development are primarily required for food-producing animals. Recommendations on the data that should be provided for a marketing authorisation for an antimicrobial veterinary medicinal product are described in VICH GL27: ‘Pre-approval information for registration of new veterinary medicinal products for food-producing animals with respect to antimicrobial resistance’ (11). These are data from tests to establish the minimum inhibitory concentration (MIC) against a wide variety of microorganisms, information on the resistance mechanism(s) and the molecular genetic basis of resistance to the antimicrobial agent, and information on the occurrence, or absence, of transfer and rate of transfer of resistance genes. The aim of the data and information is to characterise potential resistance development as it might occur in the food-producing animal.

Preferably, the assessment of the potential for resistance development and risk management considerations should take into account the potential for cross- and co-selection for resistance.

In some countries, specific guidance is also available on the assessment of the resistance potential for antimicrobials in respect of a marketing authorisation, e.g. the risk assessment guidance by the Food and Drug Administration in the USA (16). The qualitative risk assessment considers the release assessment of the drug, as well as the exposure assessment and consequence assessment, based on whether the drug under consideration is ‘critically important’, ‘highly important’ or ‘important’, in terms of its importance to human medical therapy. Based on the risk assessment, the risk rating is determined. This rating is taken into account when establishing the conditions under which the drug can be used and when deciding whether or not to issue a marketing authorisation.

Guidance has also been developed by both the OIE and Codex Alimentarius on a risk analysis methodology for antimicrobials in respect of the potential for resistance to develop as a result of their use in animals (3, 18). The Codex Alimentarius guidelines for risk analysis of foodborne antimicrobial resistance also considers risk management options (3).

A key consideration in the authorisation of antimicrobials is to establish for which microorganisms and strains the product will be efficacious and to determine the appropriate dosage regimen. For this, data to establish the MIC and data on the pharmacokinetics and pharmacodynamics (PK/PD studies) of the antimicrobial substance will be required. The reference to the guideline used in the EU on the data required to establish efficacy of antimicrobials is given as an example (4).

Newer data indicate that resistance transfer from companion animals to humans is possible, and consideration may need to be given to this issue in the assessment of marketing authorisations of veterinary medicinal products for companion animals, depending in particular on the type or class of antimicrobial under consideration.

## How does the evaluation translate into specific conditions of marketing authorisations for antimicrobials?

When approving an application for a veterinary medicinal product containing an antimicrobial as the active substance, particular consideration needs to be given to the effectiveness of the drug by addressing the following: the proposed claims, in particular the bacteria against which the drug is intended to be effective; the intended aim of the product (treatment *versus* prevention *versus* growth promotion); and the appropriateness of the advice for use and dosage regimen. It is also important that the marketing authorisation conditions and information provided to the veterinary surgeon and other users contain the necessary information to allow the antimicrobial veterinary medicinal product to be used effectively and safely, while at the same time minimising the risk of development of antimicrobial resistance.

The indication for the approved medicine should identify the bacteria against which the drug is effective. These should be listed in the approved product literature for each target animal species and indication for use.

The product literature should contain the advice that, whenever possible, laboratory diagnosis and susceptibility testing should be carried out by the veterinary surgeon before prescribing the antimicrobial. Criteria for the decision on whether it is appropriate to use the medicine and how it should be used can be included in the product literature.

The conditions of use contained in the marketing authorisation must take into account the principles of prudent and responsible use. These principles need to be clearly communicated to the veterinary surgeon prescribing the veterinary medicine or other users of the product.

It is particularly important that the dosage regimen is determined based on the efficacy and safety data for the product. All deviations from approved dosing and treatment duration of the antimicrobial product should be minimised. Underdosing of antimicrobials is thought to increase the possibility of selection for antimicrobial resistance in bacteria. Too short a treatment duration can reduce the efficacy of the antimicrobial. However, an unnecessarily long treatment duration can be a factor in promoting selection for resistance to antimicrobials. The user of the product should comply with the posology as recommended, meaning that the correct quantity of the active substance or product is administered and that treatment is carried out for the entire period of time indicated. It is important that the advice on the dose and duration of treatment is clearly communicated in the product literature (5).

Advice on prudent use should be given in the product literature. The recommendations for products indicated for food-producing animals may be different from those indicated for companion animals. In food animals the main focus is on the higher pressure for selection of resistance, e.g. by treatment of animal groups or flocks and the potential spread of foodborne pathogens.

Examples of such prudent use phrases as applied in the EU include (5):

‘The <name of antimicrobial> should be used for treatment of severe infections only.’

‘The <name of antimicrobial> should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials.’

Examples of obligatory prudent use phrases in the EU for veterinary medicines containing fluoroquinolones include:

‘Fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials.’

‘Whenever possible, fluoroquinolones should only be used based on susceptibility testing.’

‘Use of the product deviating from the instructions given in the SPC [summary of product characteristics] may increase

the prevalence of bacteria resistant to the fluoroquinolones and may decrease the effectiveness of treatment with other quinolones due to the potential for cross resistance.’

## Use of antimicrobials in animals

The use of antimicrobials as growth promoters or feed additives in subclinical doses on a daily basis, usually *via* feed, is controversial among scientists and regulators, as this use has a higher potential for the selection of resistant strains. In some countries the use of growth promoters is restricted or has been phased out. In the EU the authorisations of antimicrobials in feed additives (which are defined as substances, microorganisms or preparations, other than feed material and premixtures, that are intentionally added to feed or water in order to perform particular functions) were withdrawn as of 1 January 2006. To date, in the EU, only coccidiostats of antibiotic origin are still allowed to be used as feed additives but with stricter rules for the authorisation being applied. Their phasing out is also planned for the future.

Antimicrobials used as veterinary medicinal products usually have a claim for the treatment of an indication, and often also one for prevention. The latter is not to be misunderstood as a claim that the product can be used as a growth promoter or as a feed additive. An attempt has been made recently in the EU to define the meaning of the term ‘treatment’ as opposed to ‘prevention’ (7). According to the Committee for Medicinal Products for Veterinary Use (CVMP), the term ‘treatment’ refers to the treatment of an individual animal, or a group of animals, showing clinical signs of an infectious disease. The term ‘prevention’ refers to the administration of the product at the same time to other in-contact animals to prevent them from developing clinical signs and to prevent further spread of the disease. The presence of the disease in the group/flock must be established before the product is used (7).

## Off-label use

As a general rule, veterinary medicinal products should be used only for the approved indications and species, and in accordance with the approved instructions for use, as indicated in the product literature, i.e. the label, package leaflet and detailed description, which is called in the EU ‘summary of product characteristics (SPC)’.

For situations in which no veterinary medicine has been authorised for a specific condition and/or species, the legal framework can allow the off-label use of authorised products in order to allow treatment of diseased animals. The exact conditions under which such off-label use is allowed vary between countries and regions. Common

principles are that clear restrictions and specifications for off-label use are in place to ensure public health, e.g. in which situations off-label use is allowed, scientifically established or minimum withdrawal periods to ensure the safety of the consumer of animal-derived food, and the record-keeping required of off-label use. Particular care should be taken by the prescribing veterinary surgeon when considering off-label use of antimicrobials and deciding on the appropriate veterinary medicine and dosage regimen and determining the adequate withdrawal period to avoid an increased risk of resistance development.

## Prudent and responsible use of antimicrobials

Antimicrobials should be used in a prudent way to retain their efficacy and to minimise resistance development. This principle has been emphasised by international organisations, e.g. WHO, OIE, FAO and Codex Alimentarius, and is also embraced at regional and national levels by regulatory authorities, e.g. of the European Commission and EU Member States, and other organisations, such as international, regional and national veterinary associations (e.g. the World Veterinary Association), agricultural organisations (e.g. the International Federation of Agricultural Producers) or animal health industry federations (e.g. the International Federation for Animal Health).

On an international level, guidance documents that provide advice on the responsible and prudent use of antimicrobials to minimise and contain antimicrobial resistance have been developed by the OIE and Codex Alimentarius (2, 18). It is important that regulatory authorities apply these principles for the use of antimicrobials in their country, and also for setting up national guidelines on the prudent and responsible use of antimicrobials.

An essential element for the success of responsible and prudent use advice is good communication with veterinarians, farmers and others who administer the veterinary medicines to animals. These professionals should receive advice on the use of antimicrobials and be given an explanation for the rationale for the measures. Governments should, where possible, collaborate with veterinary professional associations, farmer associations and appropriate federations of the food-producing industry to prepare and disseminate guidance documents on prudent use of antimicrobials at the national level in their local language(s), through which training could also be provided. Such guidance should be concise and in clear language.

It is also important that risk assessment and prudent/responsible use of antimicrobials is part of the training programme at schools of veterinary medicine.

Finally, as explained before, the conditions of use contained in a marketing authorisation for an antimicrobial should reflect the outcome of the risk assessment in respect of the potential for resistance development and include appropriate advice to the veterinary surgeon prescribing the medicine to ensure the correct therapeutic choice and promote prudent and responsible use.

## Surveillance and monitoring of antimicrobial resistance

Many countries have established programmes for surveillance and monitoring of antimicrobial resistance. Such data are necessary in order to follow trends in antimicrobial resistance development and detect the emergence of new resistance mechanisms. These data provide the necessary information for risk analysis and act as the basis for policy recommendations for animal and public health and for information on prescribing practices and prudent use. Usually, the monitoring and surveillance programmes include sampling bacteria from animals at farms, slaughterhouses and markets, as well as bacteria isolated from faecal samples. The surveillance usually includes zoonotic and commensal bacteria, in particular *Salmonella* spp., *Campylobacter* spp., *Escherichia coli* and enterococci. It is recommended that surveys be carried out to allow statistical analysis. Also, coordination of surveillance and harmonisation of sampling and analysis is recommended as well as publication of results to allow full use of the data.

The OIE has developed a guideline for the harmonisation of national antimicrobial resistance monitoring and surveillance programmes. It provides guidance on the criteria for the development of national antimicrobial resistance surveillance and monitoring programmes and harmonisation of existing programmes (18).

As examples, references to resistance surveillance schemes/reports are given for the EU (9), Japan (Japanese Veterinary Antimicrobial Resistance Monitoring System) (15) and the United States (National Antimicrobial Resistance Monitoring System) (1).

Post-marketing surveillance of veterinary medicinal products through pharmacovigilance, which has been established in many countries, e.g. the VICH countries, and for which harmonised guidelines have been established by VICH (13), collects reports on adverse reactions following use of veterinary medicines. These

reports may also be used to establish whether lack of efficacy is observed as a result of resistance development, which is a criterion in the EU for an adverse reaction that should be reported.

## Collection of data on use of antimicrobials

Several countries have established programmes to monitor consumption of veterinary antimicrobials to allow for the evaluation of antimicrobial exposure and risk analysis. Such data can be helpful in interpreting resistance surveillance data and can assist in evaluating the effectiveness of efforts to ensure prudent use and mitigation strategies.

The OIE has developed standards for monitoring the quantities of antimicrobials used in animal husbandry (18). These standards give guidance on the data to be collected to allow evaluation of the usage patterns, by animal species, antimicrobial class, dosage and type of use, in order to evaluate antimicrobial exposure.

Furthermore, the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project has developed a detailed protocol to obtain standardised data on the overall national sales of antimicrobial veterinary medicinal products in EU Member States (10). The ESVAC protocol describes, among other things, which antimicrobial classes are to be included in the surveillance and which variables are to be collected for each product.

Finally, WHO recently published detailed guidance for the surveillance of overall sales of antimicrobial agents (17); this guidance is similar to the ESVAC data collection protocol.

## Future developments

There is continuing research by countries and organisations at national and international levels on antimicrobial resistance that aims to improve the risk assessment methodology and the effectiveness of risk management tools. In particular, the data on sales and resistance that will become available from the surveillance programmes described above will improve the precision of risk assessment for antimicrobials used in veterinary medicine and will allow better and more targeted risk management decisions.

Given the increasing problem of resistance to antibiotics (including extended-spectrum beta-lactamases and meticillin-resistant *Staphylococcus aureus*) in the treatment

of infections in humans, restrictions on the use in veterinary medicine of certain antimicrobials that are of critical importance for human medicines are possible in the future. Any such restrictions are most likely to occur for new antibiotics developed for human use or antibiotics retained for use in the 'last resort'. Also, more pressure to reduce unnecessary use in animals is likely.

So far, consideration of the potential for resistance development has focused on medicines for food-producing animals. However, as a result of more recent findings indicating that antibiotic use in companion animals has an impact on resistance development in humans, it is possible that more attention will be paid to the use of antimicrobials in veterinary medicine for companion animals in the future.

In order for pharmaceutical companies to be able to make the necessary investment, a stable and predictable regulatory environment is necessary for the development of the products that are needed to treat sick animals and alleviate their suffering. In this context, bodies such as the CVMP have indicated that the availability of different formulations of narrow-spectrum antimicrobials is of special importance as these are essential to allow targeted treatment and provide a practical alternative to broad-spectrum antimicrobials (6).

It is hoped that changes to husbandry practices and further development of vaccines will result in a decrease in the use of antimicrobials in veterinary medicine, as has been seen in some food-producing sectors in the past, e.g. in aquaculture in Scandinavian countries.

The work at international level, in particular by the OIE and Codex Alimentarius, on providing guidance on risk assessment and risk management is expected to continue, and adherence to up-to-date advice and risk management recommendations will be important.

## Conclusions

In order to minimise antimicrobial resistance development and to retain the effectiveness of antimicrobials for treatment of humans and animals, marketing authorisations for veterinary antimicrobials should provide clear advice on the indications, the target species, the bacteria and strains for which the product is effective, and the appropriate dosage regimen and withdrawal period, based on scientific evaluation. The product information should also include clear responsible-use advice to the veterinary surgeon or other person administering the product. Antimicrobials should be prescription-only medicines, for which the prescription is based, wherever

possible, on susceptibility testing. Before the off-label use of an antimicrobial, its need should be very carefully considered and, if necessary, particular attention be given by the prescribing veterinary surgeon to the dosage regimen/withdrawal period.

Developments in the future may limit the use of certain medicines that are of critical importance as human

medicines. Improved risk assessment methodologies and risk management recommendations are expected to become available following new scientific knowledge and further discussions at the international level. ■

## Les responsabilités des autorités réglementaires dans la mise sur le marché des antibiotiques

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### Résumé

La principale responsabilité des autorités réglementaires dans le domaine de la commercialisation des produits pharmaceutiques vétérinaires consiste à s'assurer que ces produits font l'objet d'une autorisation de mise sur le marché assortie de conditions d'utilisation spécifiques, afin de garantir la qualité, l'innocuité et l'efficacité de ces produits. En outre, des systèmes de contrôle et de surveillance doivent être en place pour assurer le suivi du produit après l'autorisation de mise sur le marché. En ce qui concerne les antibiotiques, une attention particulière doit être réservée à l'atténuation du risque de développement de résistances et à la sauvegarde de l'efficacité thérapeutique des antibiotiques aussi bien pour l'homme que pour les animaux. Des programmes de surveillance doivent être en place afin de suivre les tendances du développement des résistances ainsi que celles de la consommation des antimicrobiens à usage vétérinaire, de sorte à étayer d'arguments scientifiques les recommandations sur les politiques à mener en matière de santé publique et de santé animale.

### Mots-clés

Agent antimicrobien – Antimicrobien – Autorisation de mise sur le marché – Enregistrement – Résistance aux antimicrobiens – Surveillance – Utilisation prudente – Utilisation responsable. ■

## Responsabilidades de las autoridades de reglamentación en la comercialización de antimicrobianos

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### Resumen

En todo lo referente a la comercialización de medicamentos veterinarios, la principal responsabilidad de las autoridades de reglamentación consiste en velar por que dichos productos dispongan de autorización de comercialización, con las condiciones específicas de uso que proceda para asegurar la calidad, inocuidad y eficacia del producto en cuestión. Además, se requieren sistemas

de control y vigilancia para hacer posible un seguimiento del producto una vez autorizado. En todo lo relativo a los antimicrobianos, conviene tener presente, específicamente, el doble objetivo de reducir al mínimo la aparición de resistencias y de conservar su eficacia terapéutica en personas y animales. Es necesario tener instituidos programas de vigilancia para seguir de cerca tanto las tendencias en la aparición de resistencias como el consumo de antimicrobianos de uso veterinario, con objeto de fundamentar recomendaciones normativas de salud pública y sanidad animal que reposen en datos científicos.

#### **Palabras clave**

Agente antimicrobiano – Antimicrobiano – Autorización de comercialización – Registro – Resistencia a los antimicrobianos – Uso prudente – Uso responsable – Vigilancia.



## Appendix

### **Links to web pages of regulatory authorities and agencies of VICH Member Countries and regions**

#### **Australia**

Australian Pesticides and Veterinary Medicines Authority: [www.apvma.gov.au](http://www.apvma.gov.au)

#### **Canada**

Veterinary Drugs Directorate Health Canada: [www.hc-sc.gc.ca/dhp-mps/vet/index-eng.php](http://www.hc-sc.gc.ca/dhp-mps/vet/index-eng.php)

Canadian Centre for Veterinary Biologics, Canadian Food Inspection Agency: [www.inspection.gc.ca/english/anima/vetbio/vbpbve.shtml](http://www.inspection.gc.ca/english/anima/vetbio/vbpbve.shtml)

#### **European Union**

European Medicines Agency, Veterinary Medicines: [www.ema.europa.eu/index/indexv1.htm](http://www.ema.europa.eu/index/indexv1.htm)

Link to web page addresses for regulatory authorities for veterinary medicines in Member States of the European Union: [www.hma.eu/](http://www.hma.eu/)

#### **Japan**

Animal Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries: [www.maff.go.jp/j/syouan/tikusui/yakuzi/index.html](http://www.maff.go.jp/j/syouan/tikusui/yakuzi/index.html)

National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries: [www.maff.go.jp/nval/english/](http://www.maff.go.jp/nval/english/)

#### **New Zealand**

New Zealand Food Safety Authority: [www.nzfsa.govt.nz/](http://www.nzfsa.govt.nz/)

#### **United States of America**

Center for Veterinary Medicine/Food and Drug Administration: [www.fda.gov/](http://www.fda.gov/); [www.fda.gov/AnimalVeterinary/default.htm](http://www.fda.gov/AnimalVeterinary/default.htm)

Center for Veterinary Biologics: [www.aphis.usda.gov/animal\\_health/vet\\_biologics/](http://www.aphis.usda.gov/animal_health/vet_biologics/)

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