

Antimicrobial resistance: monitoring the quantities of antimicrobials used in animal husbandry

†T. Nicholls⁽¹⁾, J. Acar⁽²⁾, F. Anthony⁽³⁾, A. Franklin⁽⁴⁾, R. Gupta⁽⁵⁾,
Y. Tamura⁽⁶⁾, S. Thompson⁽⁷⁾, E.J. Threlfall⁽⁸⁾, D. Vose⁽⁹⁾, M. van Vuuren⁽¹⁰⁾,
D.G. White⁽¹¹⁾, H.C. Wegener⁽¹²⁾ & M.L. Costarrica⁽¹³⁾

(1) National Offices of Animal and Plant Health and Food Safety, Animal Health Science and Emergency Management Branch, Department of Agriculture, Fisheries and Forestry, P.O. Box 858, Canberra, ACT 2601, Australia

(2) Université Pierre et Marie Curie, Service de Microbiologie Médicale, Fondation Hôpital Saint-Joseph, 185 rue Raymond Losserand, 75674 Paris Cedex 14, France

(3) Fresh Acre Veterinary Surgery, Flaggoners Green, Bromyard, Herefordshire HR7 4QR, United Kingdom

(4) The National Veterinary Institute (SVA), Department of Antibiotics, SE 751 89 Uppsala, Sweden

(5) College of Veterinary Sciences, Veterinary Bacteriology, Department of Microbiology, G.B. Pant University of Agriculture and Technology, Pantnagar, 263 145 Uttar Pradesh, India

(6) National Veterinary Assay Laboratory, Ministry of Agriculture, Forestry and Fisheries, 1-51-1 Tolura, Kokubunji, Tokyo 185-8511, Japan

(7) Joint Institute for Food Safety Research, Department for Health and Human Services Liaison, 1400 Independence Avenue, SW, Mail Stop 2256, Washington, DC 20250-2256, United States of America

(8) Public Health Laboratory Service (PHLS), Central Public Health Laboratory, Laboratory of Enteric Pathogens, 61 Collindale Avenue, London NW9 5HT, United Kingdom

(9) David Vose Consulting, Le Bourg, 24400 Les Lèches, France

(10) University of Pretoria, Faculty of Veterinary Science, Department of Veterinary Tropical Diseases, Private Bag X04, Onderstepoort 0110, South Africa

(11) Centre for Veterinary Medicine, Food and Drug Administration, Office of Research, HFV-530, 8401 Muirkirk Road, Laurel, Maryland 20708, United States of America

(12) World Health Organization, Detached National Expert, Division of Emerging and Transmissible Diseases, Animal and Food-related Public Health Risks, 20 avenue Appia, 1211 Geneva, Switzerland

(13) Food and Agriculture Organization, Food Quality and Standards Service, Senior Officer, via delle Terme di Caracalla, 00100 Rome, Italy

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

This guideline, developed by the Office International des Epizooties for the monitoring of the quantities of antimicrobials used in animal husbandry, provides the methodology required to assess the amounts of antimicrobials used, to supply data to be used for risk analysis and to improve guidance on the appropriate use of antimicrobials. Information may be gathered from a number of sources, such as the competent authorities, industry and users. The usefulness of different types of information is discussed and recommendations are given on how to collect detailed information, each year, on the antimicrobial quantities used per class and active substance. Information should also be collected on the route of administration (oral and parenteral) and the animal species.

Keywords

Animal health – Antimicrobial resistance – Containment of resistance – Human medicine – Monitoring of antimicrobial use – Office International des Epizooties – Public health – Risk analysis – Standards – Veterinary medicine.

Introduction

There is world-wide concern about antimicrobial resistance in bacteria and about the use of antimicrobials in food-producing animals which may contribute to antimicrobial resistance problems in human and veterinary medicine. Data on antimicrobial use in food animals is essential to identify such problems at the national level and in subsequent risk analysis, planning and execution of programmes where this concern is further defined and addressed.

The purpose of this document is to describe an approach for the monitoring of quantities of antimicrobials used in animal husbandry. The objectives of such a monitoring system will be defined, as will indications for the use of the data. The sources and the types of data to be collected will be identified. Attention will be given to the collection of information that most accurately describes the use of antimicrobials in animals, and potential difficulties in the collection of that data.

Monitoring programmes will also be useful for local authorities dealing with specific, individual or regional antimicrobial resistance problems. The reporting of data and future directions to facilitate international harmonisation will be addressed.

The information presented in this chapter is not designed to be prescriptive for Office International des Epizooties (OIE) Member Countries where abilities to monitor the quantities of antimicrobials used in animal husbandry vary greatly. Rather, this chapter outlines a systematic approach that Member Countries can consider when addressing this aspect of antimicrobial resistance management.

Reasons for collecting information on the quantities of antimicrobials used in animal husbandry

The goal of any programme to monitor the quantities of antimicrobials used in animals is to have objective and quantitative information to evaluate usage patterns by animal species, antimicrobial class, potency and type of use in order to evaluate antimicrobial exposure. These data are essential for risk analyses and planning, can be helpful in interpreting resistance surveillance data and can assist in the ability to respond to problems of antimicrobial resistance in a precise and targeted way. The data may also assist in evaluating the effectiveness of efforts to ensure prudent use and mitigation strategies (for example, by identifying changes in prescribing practices for veterinarians) and to indicate where alteration of antimicrobial prescribing practices might be appropriate, or if

changes in prescription practice have altered the pattern of antimicrobial use.

The continued collection of this basic data will also help give an indication of trends in the use of animal antimicrobials over time and the role thereof in the development of antimicrobial resistance in animals. This information could be compared with medical, agricultural and other antimicrobial use data as part of any risk analysis necessary for the holistic and integrated approach of a Member Country to optimise antimicrobial use.

The level of information collected will depend on the perceived or actual concern of a Member Country with the issue of antimicrobial resistance, and the ability of that country to fund the necessary programmes. However, in the consideration of antimicrobial resistance by a Member Country, there will also be a need for data on the medical and agricultural use of the chemicals if meaningful evaluations are to be undertaken.

For all OIE Member Countries, the minimum basic information collected should include the total amount of active antimicrobial ingredient used per kilogram by class, or specific formula if there are differences in potency within a class. In addition, the type of use (therapeutic or growth promotion) and route of administration (parenteral or oral administration) should be recorded.

Member Countries could explore the possibility of establishing regional or local databases of antimicrobial usage/resistance patterns, since these may be of more practical use to the consulting veterinarian. Such use would require a classification of food animal antimicrobial use. Such classifications need to produce useful data. For example, a simple classification of in-feed and veterinary use would probably be misleading in risk analysis because both in-feed use and veterinary use of antimicrobials can be for the purpose of treatment and growth promotion.

The key to understanding the relationship between antimicrobial use in animals and the development of resistance in animal bacteria is likely to be related to the reasons for selection of particular antimicrobials as well as the rate of prescription and the dose and length of treatment regimens. This information is critical if feedback pathways to veterinarians prescribing antimicrobials are to be established so usage patterns can be defined and the development of antimicrobial resistance in animal bacteria can be analysed and acted on by regulatory and other authorities, where appropriate.

The total consumption of antimicrobials for human, medical, food animal and other uses is a key factor in any consideration of this issue. While this guideline will only consider animal antimicrobial use, Member Countries may wish to consider, for reasons of cost and administrative efficiency, collecting medical,

food animal, agricultural and other antimicrobial use data in a single programme. A consolidated programme would also facilitate comparisons of animal use with human use data for relative risk analysis.

Sources of antimicrobial use data

Basic sources

Sources of data will vary from country to country and depend on factors such as whether a Member Country manufactures antimicrobials, exports and/or imports antimicrobials, and whether or not there is any accessible and accurate source of this information from the national regulatory authorities. Such sources may include customs, import and export data, manufacturing and manufacturing sales data.

Direct sources

Most countries have a legislative infrastructure for the registration, distribution and control of animal antimicrobial use (see *Antimicrobial resistance: responsible and prudent use of antimicrobial agents in veterinary medicine*, earlier in this volume). Data from animal drug wholesalers, retailers, pharmacists, veterinarians, feed stores, feed mills and organised industry associations in these countries might be an efficient and practical source of data on antimicrobial use in animals. A possible mechanism for the collection of this information is that the provision of appropriate information by manufacturers to the regulatory authority is a requirement of antimicrobial registration, provided commercial confidentiality requirements can be met.

End-use sources (veterinarians and food animal producers)

Periodic audits and statistically based surveys of either direct sources or end-use sources of animal antimicrobials, rather than ongoing data collection programmes, may be a method of obtaining accurate and detailed information on animal antimicrobial use. This may be appropriate when basic or direct sources cannot be used for the routine collection of this information. Targeted surveys or audits could be used as an adjunct to this information, or when more accurate and locally specific information is required. In addition to assisting in quantifying the extent of use of antimicrobials, end-use (particularly of veterinarians and food animal producers) surveys may be used to identify patterns of antimicrobial, prophylactic, therapeutic and growth promoter use that may have implications in an epidemiological investigation of the development of antimicrobial resistance. Factors such as seasonality and disease conditions, species affected, agricultural systems (e.g. extensive range conditions and feedlots), dose

rate, duration and length of treatment with antimicrobials relative to the recommendations for the purpose of the antimicrobial, may be important factors. An issue may be the need to recruit sufficient numbers of veterinarians and farmers to allow robust analysis. Collection, storage and processing of data from end-use sources are likely to be inefficient and expensive processes unless carefully designed and well managed, but should have the advantage of producing accurate and targeted information.

Recommendation

In consideration of antimicrobial resistance management programmes, the sources of data available and options for the collection of data for individual OIE Member Countries need early and careful analysis as well as careful consideration to ensure the cost-effective use of resources to fund national programme objectives.

Categories of data

Minimal antibiotic use data requirements and data levels

It is the opinion of the OIE Ad hoc Group on antimicrobial resistance that, in OIE Member Countries, the minimal data collected should be the annual weight in kilograms of the active ingredient of the antimicrobial(s) used in food animal production.

If a Member Country has the infrastructure for capturing basic animal antimicrobial use data for a specific antimicrobial, then additional information can be considered to cascade from this in a series of subdivisions or levels of detail. The relevant authorities within the Member Country should decide on the level of detail required so that the data collected can contribute to the aspirations of the Member Country to limit the development of antimicrobial resistance. Such a cascade of levels could include the following:

- a) the absolute amount in kilograms of antimicrobial active used per antimicrobial family per year, or for a specific antimicrobial chemical entity when this information is required
- b) therapeutic and growth promotion use in kilograms of the specific antimicrobial active
- c) subdivision of antimicrobial use into therapeutic and growth promotion use by species
- d) subdivision of the data into the route of administration, specifically in-feed, in-water, injectable, oral, intramammary, intra-uterine and topical
- e) further subdivision of these figures by season and region by a Member Country may be useful (note: this may be especially helpful in countries with large variations in environmental/

management conditions, or where animals are moved from one locality to another during production)

f) further breakdown of data for analysis of antimicrobial use at the regional, local, herd and individual veterinarian level may be possible using veterinary practice computer management software as part of specific targeted surveys or audits. Analysis of this information within the local or regional context could be useful for individual practitioners and practices where specific antimicrobial resistance has been identified and feedback is required.

Registration and regulation

All OIE Member Countries should have appropriate veterinary chemical registration standards, either through a national veterinary medicinal product registration authority, or through requirements that imported products comply with the registration system of the exporting country or of another country. This is to ensure that safe, efficacious and quality veterinary products are used in food animals. Many Member Countries also have agriculture and veterinary chemical residue monitoring and surveillance programmes for measuring chemical residues in food.

These two activities can guide Member Countries regarding the level of detail of animal antimicrobial use information required. For example, monitoring the amount of registered antimicrobial residues in food animals at slaughter would be an elementary data collection activity. If the antimicrobial residue programme or other information indicated that non-registered antimicrobials were used in food animals, then provisions could be made to collect animal antimicrobial use information at the end-user level, using targeted surveys or specially designed monitoring programmes.

However, if these programmes are not in place, a good starting point for Member Countries may be to utilise customs permit data to quantify imported antimicrobials. The basic regulatory requirements of Member Countries recommended by this OIE Ad hoc Group are discussed in more detail in *Antimicrobial resistance: responsible and prudent use of antimicrobial agents in veterinary medicine*.

Classes of antimicrobials

Decisions need to be made on what classes of antimicrobials should be considered and what members of various antimicrobial classes should be included in the data collection programme. These decisions should be based on currently known mechanisms of antimicrobial activity of the particular antimicrobial and its relative potency. For example, individual members of the dichloroacetic acid group of antimicrobials (e.g. chloramphenicol and florfenicol) have different mechanisms of action. Other preparations, such as the tetracyclines, have different potency levels, for example, chlortetracycline is not as

potent as doxycycline on a mg/kg basis. Ideally, animal-use data should be collected for each individual member of the antimicrobial group registered for use. Where common mechanisms of action exist, this data can be aggregated at a later date, if required.

An internationally accepted method of comparing antimicrobials, taking these factors into account, would be useful, as would internationally accepted nomenclature for antimicrobial classes so that future comparison of use data could be facilitated. An international code for the specific identification of medical and veterinary antimicrobials is available in the *ATCvet Index* (2). It is recommended that this code be used in the identification of specific antimicrobials.

Species, production system, regional and seasonal data

Most countries register animal use antimicrobials for a specific food animal species (cattle, sheep, goats, pigs, poultry, horses and fish) and often for specific diseases. Frequently, antimicrobial product registration is for multiple species use, such as for cattle, sheep and goats, and this may create difficulties in determining use patterns. In order for a country to effectively analyse animal antimicrobial use patterns, including off-label use, a good understanding of the circumstances of food animal antimicrobial use is required. For example, cattle are raised in extensive range conditions, in feedlots or held in barns during the winter. An understanding of what antimicrobials are used in specific animal species and industries in different regions, as well as seasonal influences on disease prevalence are likely to be important information in the risk analysis of this issue. Such general information may, for example, identify a potential problem, such as possible inappropriate animal antimicrobial use. Further investigation could lead to confirmation and suggest corrective action, such as feedback of information to veterinarians and producers.

Other important information

If an OIE Member Country is considering animal antimicrobial use in food animals, a breakdown of the animal industries may be useful in any risk analysis or for comparison of animal antimicrobial use with human medical use within and between countries. For example, the total number of animals (meat, dairy and draught cattle, and meat, fibre and dairy sheep) in the country would be essential basic information. In addition, the total number of animals raised and their weight in kilograms for food production per year would be essential information in the assessment of animal antimicrobial use figures.

Breakdown of the type of production enterprises (for example, extensive versus intensive) would also be useful if accurate

industry enterprise antimicrobial use data was not available to give an indication of how animal antimicrobials were being used.

Future directions

Since the crude amount of antimicrobial (in kilograms) used yearly only indirectly represents antimicrobial exposure, and hence the selective pressure on bacterial populations, more sophisticated measures are needed. Such concepts have been developed in human medicine. Medical monitoring of antibiotic use in community and hospital medicine has led to the evolution of the concept of the defined daily dose (DDD) expressed as the DDDs/1,000 population/day. This approach takes into account the activity and potency of individual antimicrobials and the basic unit of comparison between individual antimicrobials becomes the DDD/1,000/ population/day applied to the particular environment. However, a direct comparison between medical and animal use of antimicrobials is difficult and perhaps pointless other than for medical and veterinary authorities to have a rational baseline measure of national antibiotic use for ongoing comparison over a period of years. The management of medical and veterinary antimicrobial registration and use in most OIE Member Countries are separate and independent exercises. In the future, the management of animal antibiotic use may be dependent on risk analysis findings of the contribution of animal antibiotic use to medical antimicrobial resistance problems.

Developing a DDD approach for antimicrobials in food animals would be difficult because of the wide range of animal weights (e.g. compare the weight of newly hatched chickens and newborn calves or meat chickens and cattle at slaughter). The reports of the Danish Zoonosis Centre (DANMAPs) use the concept of milligram of antimicrobial used per kilogram of meat produced (1). This concept could be useful in the monitoring and analysis of animal use of antibiotics overall, and within particular species, although it does not address dose rate and length of treatment regimens in specific animal husbandry circumstances.

However, by using milligram of antimicrobial active used per kg of meat produced as a measure of antimicrobial use in food animals it may be possible to undertake a comparison for specific antimicrobials, thus enabling evaluation of the relative

selection pressure of, for example, two antibiotics with different activity and potency such as tetracycline and fluoroquinolones. This approach does not take into account the different pharmacological activity of different antibiotics and potency may need to be standardised in some way. Such a system would be a better measure, over time, of the total selection pressure applied to the particular environment under study, and would provide a more accurate measure of the relative importance of the different potential of antimicrobials for generating bacterial resistance. It would also be of value, for example, in measuring the consequence of changes in use patterns, such as the replacement of tetracycline use with fluoroquinolones, or in analyses where lifetime exposures of animals to antimicrobials were important.

The development of concepts on the action of antimicrobials reflecting their relative activity through the consideration of potency, in conjunction with the kilograms of food animal product produced using these antimicrobials, is important. It would provide useful baseline information and assist in assessing the possible contribution of the animal use of antimicrobials in the production of antimicrobial resistance of medical and veterinary concern.

Conclusions

Data on the use of antimicrobials in animals is essential for risk analysis and the design and planning of antimicrobial resistance monitoring and surveillance programmes, as well as for the ongoing management of antimicrobial resistance on the individual farm, district, regional, national and international levels.



Antibiorésistance : contrôle des quantités d'antibiotiques utilisées en production animale

†T. Nicholls, J. Acar, F. Anthony, A. Franklin, R. Gupta, Y. Tamura, S. Thompson, E.J. Threlfall, D. Vose, M. van Vuuren, D.G. White, H.C. Wegener & M.L. Costarrica

Résumé

Cette ligne directrice, préparée par l'Office international des épizooties et applicable au contrôle des quantités d'antibiotiques utilisées en production animale, fixe la méthodologie requise pour évaluer les quantités de produits antimicrobiens utilisés, pour fournir les informations nécessaires à l'analyse du risque et pour améliorer les instructions relatives à l'utilisation appropriée des antibiotiques. Les informations peuvent émaner de plusieurs sources, telles que les autorités compétentes, les professionnels du secteur et les utilisateurs. L'utilité des différents types d'information fait l'objet de la discussion et des recommandations sont données sur la manière de recueillir une information détaillée, chaque année, sur les quantités d'antibiotiques utilisés, par catégorie et par substance active. Il convient également de recueillir des informations relatives aux modes d'administration (orale ou parentérale) et aux espèces animales concernées.

Mots-clés

Analyse du risque – Antibiorésistance – Gestion de l'utilisation des antibiotiques – Maîtrise de la résistance – Médecine humaine – Médecine vétérinaire – Normes – Office international des épizooties – Santé animale – Santé publique.



Resistencia a los antimicrobianos: seguimiento del volumen de antimicrobianos utilizados en producción animal

†T. Nicholls, J. Acar, F. Anthony, A. Franklin, R. Gupta, Y. Tamura, S. Thompson, E.J. Threlfall, D. Vose, M. van Vuuren, D.G. White, H.C. Wegener & M.L. Costarrica

Resumen

Esta directriz, elaborada por la Oficina Internacional de Epizootias para facilitar el seguimiento de los volúmenes de antimicrobianos utilizados en producción animal, define la metodología indicada para evaluar ese parámetro, obtener datos útiles para el análisis de riesgos y orientar mejor al usuario sobre el empleo adecuado de los antimicrobianos. La información puede proceder simultáneamente de varias fuentes, como las autoridades competentes, los industriales del ramo y los usuarios. Los autores valoran la utilidad de distintos

tipos de información y recomiendan métodos para recabar anualmente datos exactos sobre los volúmenes de productos antimicrobianos utilizados (desglosados por clase y principio activo). Conviene también obtener información sobre la vía de administración (oral o parenteral) y la especie animal de que se trate.

Palabras clave

Análisis de riesgos – Contención de las resistencias – Gestión del uso de antimicrobianos – Medicina humana – Medicina veterinaria – Normativa – Oficina Internacional de Epizootias – Resistencia a los productos antimicrobianos – Salud pública – Sanidad animal.



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