

**DRAFT WORKING DOCUMENT FOR THE RISK MANAGEMENT WORKING
GROUP OF
THE CODEX *AD HOC* INTERGOVERNMENTAL TASK FORCE
ON ANTIMICROBIAL RESISTANCE**

FOR CONSULTATION ONLY

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DRAFT

RISK MANAGEMENT GUIDANCE TO CONTAIN FOODBORNE ANTIMICROBIAL RESISTANT MICROORGANISMS

INTRODUCTION

The introduction in 1930 of antimicrobial agents in human clinical medicine and animal husbandry was a most important achievement. Unfortunately, in all known cases, the introduction of new antimicrobial compounds was followed by the emergence of antimicrobial resistance. Modern food animal production uses large amounts of antimicrobials for disease control. This provides favourable conditions for selection, spread and persistence of antimicrobial resistant bacteria capable of causing infections in animals and humans. During the last decade there has been an increase in awareness of the potential problems that selection of antimicrobial resistance among bacterial pathogens from food producing animals could have on human health. In addition, food animals and food of animal origin are traded worldwide. This has emphasised the need for global initiatives limiting the selective pressure and the establishment of standardized monitoring systems for determining the occurrence of antimicrobial resistance in all countries.

Antimicrobial resistance (AMR) is a threat to effective treatment of infectious diseases in humans and animals. AMR is therefore a cause for concern and effective control measures should be implemented to limit the emergence and spread of antimicrobial resistance. AMR is a global, multifactorial problem as use of antimicrobials in food-producing animals inevitably leads to emergence of AMR in food-borne pathogens (WHO 2000, 2001).

PURPOSE AND SCOPE

Risk management follows a structured approach including preliminary risk management activities, evaluation of risk management options, monitoring and review of the decision taken.

The purpose of this document is to develop appropriate risk management guidance for national/regional authorities that may be necessary following risk profiling and/or risk assessments in order to contain foodborne antimicrobial resistant microorganisms (Codex 2007). Consideration is also given to the monitoring and review of the effectiveness of the selected risk management options and to risk communication.

Although all efforts should be made to base risk management decisions on the results of risk assessment, the seriousness of the threat posed by antimicrobial resistant bacteria to human and animal health makes it imperative for national and regional authorities to take steps to protect their populations even in the absence of risk assessments. This threat has been recognised by the international community on several occasions during the past few years (WHO 1990, 2000, FAO/OIE/WHO 2003, 2004, Rosdahl and Pedersen 1998, EMEA 1999) and as a result, governments have been urged to put in place the mechanisms which would enable them to contain this threat to the extent possible with the available resources.

In recognition of this serious threat therefore, attempts have been made in the following to provide suggestions regarding possible options which national and regional authorities may implement even when risk assessments have not been carried out.

Although this document deals in general with antimicrobial resistance, the recommendations focus on resistance in foodborne bacteria.

1. IDENTIFICATION OF THE AVAILABLE OPTIONS

1.1 CONTROLLING THE USE OF ANTIMICROBIAL AGENTS

Risk management options shall be directed toward two main areas as an interconnected continuum; pre-harvest, such as responsible use guidelines and codes of practice documents specifically directed to antimicrobial agents and their use in food animals, and post-harvest, such as food hygiene practices which are specifically directed to foodborne contamination interventions.

As part of the pre-harvest activities, appropriate emphasis should be laid on evaluation prior to approval, taking due account of the resistance inducing properties of antimicrobials. Countries with limited resources should pay particular attention to the establishment of the necessary instruments for approval, registration and enforcement of regulations regarding usage.

With regard to post-harvest, the aim should be to monitor trends in antimicrobial resistance and usage and to apply targeted interventions aimed at resistance patterns or determinants of importance to human and animal health.

1.1.1 Approval and licensing of Antimicrobials used in Animals and Horticulture

Licensing authorities have responsibilities in the authorisation of veterinary medicinal products but also in the distribution and in setting the conditions of use of these products.

The Authorisation process should ensure the quality, safety and efficacy of the products authorised. It is of particular importance that an authorisation system is developed by National/Regional authorities.

The licensing of new veterinary antimicrobials should be based on human health risk assessment, including antimicrobial resistance risk assessment.

The outcome of such an assessment can be considered as risk management measures.

Different options are available:

- Not to authorise the product if risk assessment indicates unacceptable levels of risk as a result of proposed use(s) of the antimicrobial agents.
- restrict the use of the product ensuring that only “approved claims” are indicated on the labels of approved veterinary antimicrobial drugs. Claims which cannot be substantiated should be prohibited.
- In any case the Marketing authorisation should specify the intended use and necessary precautions connected with the use of the product.

As indicated in the Codex code of practice to minimize and contain antimicrobial resistance, countries without the necessary resources to implement an efficient authorisation procedure for veterinary antimicrobial drugs and whose supply of veterinary antimicrobial drugs mostly depends on imports from foreign countries should:

- ensure the efficacy of their administrative controls on the import of these veterinary antimicrobial drugs,
- seek information on authorizations valid in other countries, and

- develop the necessary technical cooperation with experienced authorities to check the quality of imported veterinary antimicrobial drugs as well as the validity of the recommended conditions of use. Alternatively, a national authority could delegate a competent institution to provide quality certification of veterinary antimicrobial drugs (Codex 2005).

1.1.2 Usage of antimicrobials

The National/Regional authorities are also responsible for the general policy regarding the use of antimicrobials on their territories.

Any use of antimicrobials will result in a selective pressure. This poses a threat for emerging or sustaining antimicrobial resistance, including cross-resistance and co-resistance, thereby threatening both food safety and human as well as animal health. No matter the reason for the selective pressure - emerging from overuse, misuse or underuse, incomplete or inadequate treatment - this AMR can lead to treatment failure in animals and humans, prolonged disease or death (EMEA 1999). Limiting the use in veterinary medicine of antimicrobials of particular importance for human treatment is becoming more and more imperative, as developments of new AM drugs are sparse whereas AMR is increasing. So maintaining the efficacy of the current available antimicrobials by using them prudently is imperative. Since many parties are involved in the production and use of antimicrobials. Therefore, optimizing AM usage in veterinary medicine should be carried out in a multi-party approach. The involved parties could be: veterinarians, farmers and stakeholders such as the pharmaceutical industry and the food-producing industry as well as policy makers and international and national authorities.

As the rapid increase of AMR all over the world is not matched by development of new antimicrobials, it would be most unwise to wait for science based risk assessments on AMR before taking action with multitasked risk management strategies optimizing AM usage.

Where permitted by legislations/regulations, national regulatory authorities may impose bans, revoke or restrict licenses on using specific veterinary antimicrobial agents if supported by evidence from risk assessment. However, when there is evidence that a risk to human health exists but scientific data are insufficient or incomplete, it may be appropriate for countries to select a provisional decision, while obtaining additional information that may inform and if necessary modify the provisional decision.

This approach supports accountable, evidence-based decision-making in the management of the use of veterinary antimicrobial drugs.

Where legislations/regulations permit, National/Regional regulatory authorities may prohibit or regulate the mass medication and/or prophylactic use and/or the extra-label use of specific classes of veterinary antimicrobial drugs, especially those that will be of the highest risk classification. Where risk assessments are not available, authorities may be guided by the proposals in international documents (FAO/WHO/OIE 2008).

Supply and distribution of antimicrobials

As indicated in the Codex code of practice to minimize and contain antimicrobial resistance, the relevant authorities should make sure that all antimicrobial agents used in food-producing animals are prescribed by a veterinarian or other suitable trained person authorized in accordance with national legislation or used under conditions stipulated in the national legislation.

Ideally, all AM used for food producing animals should be prescription only in order to ensure that their use is restricted to professionals. By the same token, AM for animals should only be supplied by authorized outlets such as pharmacies, veterinary practices or authorized

feed mills, in order to prevent illicitly manufactured or imported AM, counterfeit or mis-branded AM being taken into use.

National/Regional authorities can implement actions to reduce profits from sales of antimicrobials by veterinarians by separating veterinary drug prescribing from dispensing (FAO/OIE/WHO 2003). National legislation should ensure that veterinarians are only compensated for the amount of time used when dispensing medicine to farmers. Results from several European countries show that AM usage can be markedly reduced when profit from sale of medicine is terminated.

National/Regional authorities have also responsibilities in controlling the advertising, in training and research activities linked to the use of antimicrobials and antimicrobial resistance.

With regard to counterfeit drugs, Codex has recommended that all countries should make every effort to actively combat the manufacture, advertisement, trade, distribution and use of illegal and/or counterfeit bulk active pharmaceutical ingredients and products. Regulatory authorities of importing countries could request the pharmaceutical industry to provide quality certificates or, where feasible, certificates of Good Manufacturing Practices prepared by the exporting country's national regulatory authority (Codex 2005).

Extra-label use

The extra-label use should be restricted, especially in CIA for human treatment, however due care should be given to animal health and welfare aspects in the case where no other antimicrobial is available or has proven to be effective in a given target species. In practice, particular conditions can be implemented such as the need to perform a bacterial diagnosis and susceptibility testing prior to treatment. However, this should not preclude the veterinarian initiating treatment with a given antimicrobial based on clinical experience where an acute need exists and subsequently reverting to another antimicrobial following the results of susceptibility testing.

Growth promoters

National/Regional regulatory authorities should conduct antimicrobial resistance risk assessment of existing antimicrobial growth promoters (AGP) in the context of their human health implications. In accordance with the WHO Global principles for the containment of antimicrobial resistance, use of antimicrobial growth promoters that belong to classes of antimicrobial agents used (or submitted for approval) in humans and animals should be terminated or rapidly phased-out in the absence of risk-based evaluations. The termination or phasing-out should be accomplished preferably by voluntary programmes of food animal producers, but by legislation if necessary (WHO 2000).

Veterinary use of antimicrobials critically important for human treatment

The WHO has pursued the concept of critically important antimicrobials (CIA) since 2005 (WHO 2007). Both WHO and OIE have now worked with this concept and categorized antimicrobials according to their importance in the treatment of human and animal infections (FAO/OIE/WHO 2008). There is a general agreement that quinolones, 3rd and 4th generation cephalosporins and macrolides are the antimicrobials, which are both used in animals and humans, where risk management strategies are needed most urgently.

1.1.3 Prudent use of antimicrobials

National/regional authorities and animal health stakeholders including veterinarians, farmers and the pharmaceutical industry should have a proactive approach in order to promote prudent use of AM in food-producing animals as an element of a national and international strategy for the containment of AM resistance. Specific recommendations aimed at reducing the over-use and misuse of antimicrobials have been previously elaborated in several international documents (WHO 2000, Codex 2003, Codex 2005, OIE 2007). These recommendations should be implemented by all partners involved to the extent possible in different geographic regions.

Treatment guidelines

National and regional authorities should elaborate animal species-specific prudent use treatment guidelines in consultation with all stakeholders involved in the production, marketing, prescription and use of antimicrobials. Existing national regulations and international standards (Codex 1993) relating to appropriate use of veterinary drugs should be strictly enforced.

The aim of treatment guidelines should be to ensure food safety and the future treatment possibilities for humans without jeopardizing animal health and welfare, thereby ensuring the continued possibility for and efficacy of antimicrobial treatment for both animals and humans. Guidelines should aim at finding an appropriate balance between animal health needs and public health considerations.

Treatment guidelines should give advice on different drug choices based on therapeutic effect, control of AMR, resistance patterns, practical clinical experience, human health concerns and CIA for both human and animal use.

Recommendations should be given on different AM to be used, if several antimicrobials can be used.

The free prescription right of practitioners should not be affected, but the rationale for deviating from the treatment guidelines must be justifiable. Thus treatment guidelines are also an indispensable reference tool in the regular supervision of all veterinary practitioners by the regulatory authorities.

Antimicrobials may only be used if it can be proved, or if it is highly probable, that the animals or livestock are infected with a pathogen sensitive to the antimicrobial that is to be administered. Prophylactic use in healthy (non-infected) animals is to be avoided on principle.

The need to use an antimicrobial must always be demonstrated by means of suitable, objective and diagnostic measures. Antimicrobials may only be administered following an exact diagnosis based on a clinical examination and, if necessary, further diagnostic laboratory tests, the animals' immune status, epidemiological aspects and other experience and insights.

A microbiological diagnosis of the pathogen and an antibiogram following pathogen differentiation is required:

- When a new antimicrobial is chosen during the course of the therapy due to insufficient efficacy,
- Regularly in the case of repeated or long-term use in groups of animals,
- When antimicrobials are combined with other medications, for one indication,

- When the antimicrobial is used under other conditions than those which are allowed.

Antimicrobials are to be used in accordance with the applicable licensing conditions. Each deviation (dose, method of application, indication, animal) must be accounted for:

- The choice of dosage is to be sufficiently high (according to the instructions for use),
- Treatment intervals are to be sufficiently short in order to avoid subtherapeutic levels of the active ingredient,
- In the case of oral administration to an entire stock, exact dosage is to be guaranteed and monitored at suitable intervals with suitable methods,
- The livestock holder is to be informed of the dosages in writing.

The length of the therapy is to be kept to a minimum, although it must be sufficient to guarantee the infection will be controlled in each case.

Ideally, the guidelines should consist of a full list of all antimicrobials registered by the authorities for specific animal species and their most common diseases and related pathogen(s). One method is to categorize the drugs from different criteria, prioritize the drugs for the specific animal species, disease and pathogen and follow their performance in all five criteria.

The guidelines should be the result of collaboration between the national/regional regulatory authorities and their advisory bodies such as the medical, veterinary and food research institutes on the one hand and the veterinary pharmaceutical industry, wholesalers and retail distributors, the veterinarians and producers of food animals on the other.

Criteria for choosing a suitable antimicrobial

The animal species-specific treatment guidelines should use different criteria for categorizing antimicrobials for different diseases and their pathogens. Some of these criteria may be:

- Efficacy of treatment
- Spectrum of Activity and therapeutic range
- Pharmacokinetics
- Development of resistance in veterinary pathogens at the national level
- Significance of the antimicrobial in human treatments
- WHO's criteria for importance of an antimicrobial in human treatment
- OIE's criteria for importance of an antimicrobial in animal treatment

The guidelines should be evaluated and revised regularly, if new information or new drugs emerge.

In conclusion, a drug is prioritised based on its performance in all the national and international criteria. Preferably, a drug should have the highest possible performance in all criteria. But often this will not be the case and drugs with a lower performance on one or more criteria might also be recommended, if this is the sole effective drug for treatment of this disease and pathogen in an animal species.

Supervision of use

Veterinary practitioners should provide proof of the following:

- Diagnostic measures
- Justification for deviations from recommendations,
- Monitoring of the success of the treatment,
- Results of tests to ascertain the pathogen and resistance in the livestock,
- Notice given of decreasing sensitivity of pathogens to the national/regional regulatory authorities as part of the system of reporting undesired effects of medications.

Training of users and stakeholders

The education and training of all stakeholders is a vital factor in ensuring the effective application of prudent use guidelines. The OIE has described the scope and principles of such training (OIE 2007).

According to Codex 2005, training should involve all relevant professional persons engaged in manufacturing, dispensing or using AM, such as for instance the pharmaceutical industry, farmers, veterinarians and regulatory authorities. Training should be undertaken to assure food safety, future treatment possibilities for both humans and animals and animal welfare.

1.2 CONTROLLING THE SPREAD OF ANTIMICROBIAL RESISTANT BACTERIA MEASURES

1.2.1 Animal health and infection control programs

With reference to Codex 2005 the responsibilities of veterinarians and producers of food-producing animals, should be followed, including keeping animal health and treatment records, in order to ensure animal health.

Maintenance of animal health involves biosecurity, feed and water quality, optimal nutrition, and good hygienic practices.. Programs to reduce the incidence of disease in herds and flocks of animals (for example vaccination programs) should be implemented and maintained. Moreover, national treatment guidelines should be followed.

National authorities in collaboration with local and regional authorities should encourage stringent implementation of Good Agricultural Practices (GAP, Codex 1969) in livestock and aquaculture sectors in order to reduce the necessity for on-farm use of antimicrobial agents. Implementation of GAP is absolutely critical to the reduction of antimicrobial resistance attributes in food production

Measures to prevent the transmission of zoonotic bacteria from animals to humans should be implemented and, if possible, efforts should be directed towards establishing eradication programmes against the most important zoonotic agents within the territory. The regular monitoring and surveillance of the presence of zoonotic bacteria in food producing animals is a vital aspect of disease control and eradication measures.

Measures to restrict trade with live animals can also be implemented.

Guidelines for the implementation of various control and prevention measures have been reviewed (Forshell and Wierup 2006, Wagenaar et al. 2006).

1.2.2 General Principles of Food Hygiene

Codex has developed general principles of food hygiene that are applicable throughout the food chain, including primary production through to the consumer, to achieve the goal of en-

sure that food is safe and suitable for human consumption (Codex 1969). Good hygienic practices are critical to the control of pathogens in the food chain and will, by their nature, address the occurrence of both resistant and susceptible bacteria in food. Such measures will also impact on some non-pathogenic bacteria that may be a reservoir of resistance genes.

1.2.3 HACCP

Implementation of Hazard Analysis and Critical Control Point (HACCP) programs will contribute to addressing the risk of antimicrobial-resistant bacteria in food and guidelines for the application of HACCP have been elaborated (Codex 1969). HACCP can be applied throughout the food chain from primary production to final consumption and its implementation should be guided by scientific evidence of risks to human health. Implementation of good agricultural practices may reduce the problems of both resistant and susceptible pathogens/bacteria in the food chain. While the principles of HACCP can be applied with great effect in the primary production, it should be considered a supplement to “good agricultural practice” at farm level.

1.2.4 Other possible sources of contamination

Risk management measures to contain antimicrobial resistance should not be limited to the use of antimicrobials in animals and other possible sources of contamination should be taken into account.

Environmental considerations are important in containing the spread of antimicrobial Resistance and preventing contamination of foodstuffs intended for human or animal consumption. Human, animal and plant waste may contain antimicrobial-resistant bacteria and residues of active compounds that continue to select for resistant bacterial populations. Human and animal waste of faecal origin may be used to fertilise crops intended for human and animal consumption, potentially propagating resistant bacteria widely onto plant materials. Risk management options to address the issue of waste management will vary depending on the sanitary infrastructure existing in an individual country or region.

Depending on its microbiological quality, water may impact on contamination of food with antimicrobial-resistant bacteria throughout the food chain from primary production to consumption.

Effluents have been identified as sources of antimicrobial resistant human pathogens as well as antimicrobials (FAO/WHO/OIE 2008). This potential problem should be considered when identifying and selecting possible risk management options to address this issue. In particular, direct use of human and animal waste in animal production should be discontinued.

1.2.5 Control and enforcement

Control measures should be directed towards the identification of foodborne zoonotic bacteria and measures to prevent their transmission to humans through food. This involves surveillance of foodborne zoonotic bacteria and the implementation of eradication measures to the extent possible, taking due consideration of available resources.

There are currently no international microbiological criteria for the degree of contamination with antimicrobial resistant bacteria that is considered acceptable. However, principles for the establishment of microbiological criteria have been formulated by Codex (Codex 1997).

Targeted interventions using microbiological criteria have to be very specific in the use of criteria. For example the use of multiple resistance is not meaningful since this depends on the number of antimicrobial agents tested. A possibility is to only target interventions towards those bacteria that are resistant to antimicrobials that the authorities consider of critical importance to public and animal health in their territories. In addition, authorities should target food borne zoonotic bacteria.

National authorities may determine whether food of animal origin would pose a risk for the consumer, and if so, take appropriate steps to prevent the food reaching the consumer. Such steps may include withdrawal from the market for reprocessing or destruction. Parameters for determining whether the meat will pose a risk for the consumers may include numbers of infected samples, type of zoonotic bacteria and antimicrobial resistance profile.

2. SELECTION AND IMPLEMENTATION OF RISK MANAGEMENT MEASURES

Risk management options should be assessed in terms of the scope and purpose of the risk analysis and the level of consumer health protection they provide. Antimicrobial resistance risk management strategy should be goal-oriented and should be backed by mechanisms to evaluate success in terms of the achievement of stated public health objectives. In the case of antimicrobial resistance risk management, the goal is to contain and minimize antimicrobial resistance that may be transmitted through the food chain.

A mix of options at varying degrees of interventions is necessary to achieve successful outcomes.

This includes developing regulatory programs backed by the various stakeholders involved.

Proposed management options should be proportionate to the risk classification. However, it is recognized that general measures based on prudent use should be implemented in any case. Additional options could be used for antimicrobial products and foodborne antimicrobial resistant organism that will be of the highest risk classification.

Each national/regional authority, according to their particular situation, should select management measures taking into account the options' effectiveness, legality, fairness, economic implications, enforcement and compliance.

2.1. EVALUATION OF THE IDENTIFIED RISK MANAGEMENT OPTIONS

As outlined in the FAO Food and Nutrition Paper 87, "in the ideal situation, the following information should be available for evaluating individual or groups of possible risk management options:

- A "menu" of estimates of risk that would result from application of potential risk management measures (either singly or in combination), expressed either qualitatively or quantitatively.
- Estimates of the relative impact of different potential risk management measures (either singly or in combination) on risk estimates.
- Technical information on the feasibility and practicality of implementing different options.

- Cost-benefit analysis of different potential measures, including both magnitude and distribution (i.e. who benefits, who pays the costs).
- WTO SPS implications of different options in international trade situations.”

However, the absence of one or all of these items of information should not limit the possibilities of individual countries to implement precautionary measures where there is evidence of a risk to human or animal health.

Because antimicrobials play a major role in animal health, animal health should be considered when evaluating risk management options.

Evaluation of the identified Risk management options should be performed at National/Regional level as feasibility and practicability of the implementation will depend on local/regional situations.

2.2. SELECTION OF RISK MANAGEMENT OPTIONS

2.2.1 Identifying a desired level of consumer health protection

Risk management decisions on appropriate options should be achieved by considering and integrating all evaluation information obtained from preliminary risk management activities and the risk assessment.

The level of consumer health protection provided by a decision on risk management measures is often called the “Appropriate Level of Protection” (ALOP).

ALOP is defined in the SPS Agreement as “the level of protection deemed appropriate by the Member establishing a sanitary or phytosanitary measure to protect human, animal or plant life or health within its territory”.

ALOPs may range from general to specific depending upon the level of information available with regards to the source of hazards and risks and will depend on the public health goals.

Public health goals for microbiological risk assessment may be complemented by more specific public health goals related to antimicrobial resistance risk.

Examples of appropriate level of protection that can be used for selecting risk management options are given hereafter. These approaches can be taken alone or in combination.

Benefit-risk approach:

Because antimicrobials play a major role in animal health, animal health should be considered when evaluating risk management options, but this must be considered secondary to protecting consumers. When evaluating restrictions on the use of antimicrobial products it is necessary to consider substitutes or alternative practices that would reduce the need for the product. Substitutes could be other less important antimicrobials, non-antimicrobial products, or changes in livestock husbandry that promote animal health. The impact of reduced antimicrobial resistance on animal health should also be considered when evaluating restrictions on antimicrobial use.

Threshold approach:

Given the geographic variations in the levels of resistance and the increasing emergence of resistance, it may be necessary to explore the need to develop resistance thresholds for specific antimicrobial-species-pathogen combinations, above which any of a range of risk management options may be triggered. However, this approach needs to be carefully assessed as it should be put in perspective with the current use of antimicrobials and the current level of resistance.

Precautionary approach:

When there is evidence that a risk to human health exists but scientific data are insufficient or incomplete, it may be appropriate for countries to select a provisional decision, while obtaining additional information that may inform and if necessary modify the provisional decision. In those instances, the nature of the provisional decision should be communicated to all interested parties and the timeframe or circumstances under which the provisional decision will be reconsidered (e.g. reconsideration after completion of a risk assessment) should be articulated when the decision is communicated initially.

2.2.2 Reaching a decision on the preferred risk management options

Risk management strategies should be based on Risk assessment and risk profiling where these are available.

As a matter of risk management principle, prudent use guidelines, monitoring of antimicrobial usage and general food hygiene principles should as a minimum be implemented.

Proportional measures to the identified risk should be developed to manage the risk attributable to the use of each category of antimicrobial agents in food-producing animals. Cross-resistance, co-resistance issues should be considered in making risk management decisions.

Restrictions may be placed on the use of specific antimicrobial agent in some species or some route of administration or even specific industries. Restriction of use should be explicitly specified on antimicrobial veterinary drug labels/package inserts for this category of antimicrobials, and where appropriate, supported by legislations/regulations.

For those antimicrobials that will be in the highest risk classification, (matched with specific associated antimicrobial resistant bacteria of human health concern), the following additional options should be considered for priority implementation by the national authorities:

- Regulatory review of currently approved antimicrobials by national risk assessments;
- Ongoing (longitudinal) Resistance monitoring and usage monitoring (specifics to be determined)
- Specific Responsible use guidelines including consideration of alternative treatments or conditions of use
- Restriction to the use of antimicrobials to reduce the selective pressure (no use, limited use in group of animals, use in individual animal, no off-label use, etc.)
- Reduction of the transmission of resistance in the food chain (recall associated foods, restriction of movement of infected or colonized animals, processing that guarantees removal of all resistant bacteria, destruction of food items or groups of animals infected or colonized).

2.3 IMPLEMENTATION OF RISK MANAGEMENT OPTIONS

Implementation involves giving effect to the selected risk management option(s) and verifying compliance, i.e. assuring that the risk management option(s) is/are implemented as in-

tended. Implementation may involve different interested parties, including competent authorities, industry and consumers.

The implementation strategy will depend on the risk management option(s) selected and should be developed within a consultative process with interested parties. Implementation can occur at different points in the food/feed chain and may involve more than one segment of the industry and consumers.

It is recommended that selected antimicrobial resistance risk management strategy should be goal-oriented. As a consequence of this, monitoring and surveillance of both antimicrobial usage and antimicrobial resistance are essential.

Once a risk management option is selected, risk managers should develop an implementation plan that describes how the option will be implemented, by whom, and when. In some situations, a stepwise phase-in implementation strategy could be considered, e.g. different sized establishments or different sectors, in part based on risk and/or capability. Guidance and support may need to be provided in particular for small and less developed businesses.

To ensure transparency, risk managers should communicate decisions on risk management options to all interested parties, including the rationale, and how those affected will be expected to implement. To the extent imports will be affected, other governments should be informed of the decision(s) and rationale in order to ensure their own risk management strategies to achieve equivalence.

If the risk management options selected are provisional, the rationale and the expected timeframe for finalising the decision should be communicated.

Governments should ensure an appropriate regulatory framework and infrastructure, including adequately trained personnel and inspection staff, in order to enforce regulations and verify compliance. Inspection and targeted sampling plans may be applied at different steps of the food chain. The competent authorities should ensure that industry applies the appropriate good practices and, within the application of the HACCP system, does effectively monitor CCPs and implement corrective actions and verification steps.

Governments should define an evaluation process to assess whether the risk management options have been properly implemented. This process should allow for adjustment of the implementation plan or of the risk management options, if the options selected are not successful in achieving the required level of control over the hazard. This is intended to provide short-term evaluation to allow modification, particularly for provisional risk management options, versus longer-term monitoring and review.

To enable implementation of risk management options, it is proposed that resource-limited regional/national authorities work cooperatively with nations/organisations/companies that have programs in place. Support for the following capacity building efforts should be enhanced.

Capacity building has been previously discussed (FAO/WHO/OIE 2005 and FAO/OIE/WHO 2006).

As an example, risk management options, consistent with the resource constraints that the various national authorities experience, could consist of a sequence of risk management options as described below. It should be emphasized that the risk management options should not be different food safety standards, rather they should be different approaches to imple-

mentation of the risk management options selected to have the greatest effect to minimize and contain antimicrobial resistant micro-organisms and that maximize available resources. Ideally, prudent use guidelines, monitoring of antimicrobial usage and general food hygiene principles should be implemented as a minimum.

Minimal resources available for national authorities:

Ensure adequate veterinarian (or equivalent animal health professionals) coverage for the country, veterinarian training in judicious/appropriate/responsible antimicrobial use and animal production practices, and appropriate involvement in food production and food safety processes.

Ensure adequate infrastructure for food production/food hygiene with respect to existing Codex standards and guidelines.

National authorities should capitalize upon regulatory precedents and expertise of “peer” authorities in the region when capabilities are limited.

Communicate to the public the necessity of proper food preparation and hygiene.

Moderate resources available for national authorities:

Implement responsible use guidelines via professional veterinary organizations.

Ensure reliable national food safety authority oversight of food safety activities consistent with Codex food hygiene guidance.

Implement adequate infrastructure and enforcement capacity to ensure compliance with quality product availability and veterinary involvement in antimicrobial usage.

Implement local/regional surveillance programs for foodborne disease.

High level of resources available for national authorities:

Implement national surveillance programs for foodborne disease.

Implement national resistance monitoring program, and where possible, usage monitoring.

Implement regulatory review of new antimicrobial agents prior to product approval.

Work in collaboration with food producing companies to maintain vigilance for implementation of food hygiene practices (i.e. HACCP) that safeguard against food contamination.

Work with professional associations (e.g. veterinary profession, species specific groups, etc.) to ensure compliance with responsible use guidelines by all members.

Implement research programs to develop new research to fill data gaps that will improve antimicrobial use practices, or minimize the need for antimicrobial use by preventing disease, etc.

Encourage animal health companies to develop products that will avoid resistance selection of currently used human use antibiotic classes.

3. MONITORING AND REVIEW

3.1 Monitoring and surveillance of the use of antimicrobials in animals and horticulture

An essential part of the risk management process is the on-going gathering, analysing, and interpreting of data related to the effect of the risk management actions. Monitoring is essential to establish a baseline for comparing the effectiveness of new risk management activities. It can also provide information which the manager may use to determine what steps may be

taken to achieve further improvements in the extent or efficiency of risk mitigation and public health.

Monitoring is essential for effectively implementing targeted interventions and for the continuous evaluation of the effects of risk management interventions, although monitoring does not by itself change the use of antimicrobial agents or the occurrence of antimicrobial resistance. Monitoring and surveillance must therefore be supported by effective regulation and the enforcement of control measures.

For the purposes of monitoring and evaluation, the single most important monitoring strategy is surveillance of antimicrobial resistance and antimicrobial use.

Principles for the monitoring and surveillance of the use of drugs in food animals have been previously described (WHO 2000, OIE 2007).

Monitoring and surveillance of AM usage can be done at different levels according to the abilities of National/Regional authorities ranging from state of the art veterinary medicine databases to regular information on wholesale and import of different antimicrobial drug groups within a country. However, a minimum level of monitoring has to be established in order to measure usage and risk management effects and to be able to compare between countries.

Ideally, monitoring should include all antimicrobials sold for veterinary purposes i.e. through manufacture, import, retail (including over the counter sale), feed mills, wholesale, or through veterinary prescription. Also, a common standard of measuring usage should be enforced in all countries. Preferably, monitoring of usage should be on the animal species level and if possible also on age-group level.

Monitoring should where possible be based on existing surveillance systems. There are major differences between countries in laboratory capacity, technical skills and available infrastructure. Resource-limited national/regional authorities should cooperate with nations/organisations that have programs in place.

Ideally, a monitoring and surveillance system involving both AM usage and antimicrobial resistance should be established, monitoring antimicrobial resistance in food-producing animals, in food of animal origin and in humans and should focus on human and animal pathogens as well as zoonotic and indicator bacteria.

To this end, national/regional authorities should preferably institutionalize the collection, analysis and dissemination of antimicrobial resistance data and antimicrobial use data across the food chain through the development of an integrated surveillance system.

Levels of resistance should be regularly compared with baseline levels to monitor trends in antimicrobial resistance in food-borne bacterial species. It is essential to have a proper integration of surveillance data from humans and from animal-derived food products to explore possible human exposures. To the extent possible, antimicrobial resistance data should be analyzed with antimicrobial use data to assess possible causal relationships.

The results of monitoring the effectiveness and adequacy of risk management actions should be shared between national/regional authorities.

When establishing a monitoring scheme several issues need to be addressed such as determining the study population, bacterial species to be included, sampling strategies, isolation procedures, number of samples tested, susceptibility testing methods, and data recording, computing and reporting, as well as internal and external quality control. Guidelines for the harmonisation of antimicrobial resistance monitoring and surveillance programmes exist (OIE 2007)

The European Food Safety Authority has established working groups with the purpose of implementing standardized monitoring of antimicrobial resistance in all EU member states. Detailed protocols for monitoring of Salmonella and Campylobacter are available and monitoring protocols for E. coli and enterococci are under development (EFSA 2007, Franklin et al. 2001, McEwan et al. 2006 and White et al. 2001).

In order to monitor the potential effects of risk management measures, possible endpoints may include:

- a. Nature and extent of antimicrobial resistance.
- b. Nature and extent of antimicrobial resistance in animal-derived food products at retail level.
- c. Prevalence of antimicrobial-resistant bacteria on farm level.
- d. Prevalence of antimicrobial-resistant bacteria in animal-derived food products at retail level.
- e. Prevalence of antimicrobial-resistant bacteria or resistant genes in human clinical isolates of food-borne diseases.
- f. Development of new bacterial resistance patterns.
- g. Prevalence of foodborne pathogens on farms.
- h. Prevalence of food-borne pathogens in food.
- i. Prevalence of food borne disease in humans.
- j. Number of deaths attributable to food-borne antimicrobial-resistant bacteria.
- k. Number of treatment failures attributable to food-borne antimicrobial-resistant bacteria.
- l. Frequency of human infections attributable to food-borne antimicrobial-resistant bacteria.
- m. Frequency of adverse human health effects attributable to food-borne antimicrobial-resistant bacteria.
- n. Mortality due to food-borne antimicrobial-resistant bacterial infections in “vulnerable populations”.
- o. Level of awareness of antimicrobial resistance risk (producers, consumers, industry and others).
- p. Level of compliance with specific drug use restriction or compliance with prudent use guidelines.
- q. Trends in usage of antimicrobials in food-producing animals.
- r. Trends in usage of CIA in food-producing animals.

The effectiveness and appropriateness of the risk management activities selected, and of the implementation thereof, need to be continuously reviewed and evaluated. Review is an integral part of the management process and ideally should take place at a predetermined moment in time or whenever new relevant information becomes available. The criteria for review should be established as part of the implementation plan. Thus, it should as part of the implementation be decided when a review should be performed, or what type of new information

that might initiate an earlier review process as well as the measurements that should be included in the review. Review may lead to a change in the risk management activities.

Planning periodic review of management activities is the best way to assess whether or not the expected consumer health protection is delivered. On the basis of a review of the information collected through the various appropriate monitoring activities or changes in trade habits, production forms etc., a decision may be taken to amend the risk management activities implemented or to substitute the option for another one.

Management activities should be reviewed when new activities or new information (e.g., emerging hazard, virulence of a pathogen, prevalence and concentration in foods, sensitivity of sub-populations, changes in dietary intake patterns) become available.

Evaluation of the success of risk management activities in industry may include reviewing the effectiveness of the food safety control system and its pre-requisite programs, results of product testing, the incidence and nature of product withdrawals/recalls and consumer complaints.

The results of review and the associated actions that risk managers are considering taking, as a consequence of the review, should be made public and communicated to all interested parties.

4. RISK COMMUNICATION

Risk communication is a two-way process and includes developing an understanding of the needs of stakeholders, addressing their concerns, and providing information, consulting and educating.

As already noted under implementation, risk managers should communicate decisions on risk management options to all interested parties, including other governments in cases where imports are affected.

Effective risk communication is crucial to achieving the objectives of antimicrobial resistance risk management giving the complexity of the issue and the variety of stakeholder needs/concerns. Thus, to be effective, risk communication on antimicrobial resistance strategy should be guided by the following principles:

- s. The need to focus our scientific understanding of the nature as well as the magnitude of the antimicrobial resistance risks. Determine scientific facts and identify the unknowns
- t. Understanding stakeholders current thinking, goals and choices and developing strategies that are sensitive to stakeholders' perspectives
- u. Ensuring that both the substance and the process of risk management decisions are understood by and acceptable to a broad range of affected and interested stakeholders
- v. Pre-testing of strategies, plans and messages

- w. Implementation of strategies while ensuring consistency of messages
- x. Evaluation of risk communication process and outcomes.

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