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White Paper: Bridging the gap between surveillance data and antimicrobial stewardship in the animal sector—practical guidance from the JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks

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Background: The JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks have joined efforts to formulate a set of target actions to link the surveillance of antimicrobial usage (AMU) and antimicrobial resistance (AMR) with antimicrobial stewardship (AMS) activities in four different settings. This White Paper focuses on the veterinary setting and embraces the One Health approach.

Methods: A review of the literature was carried out addressing research questions in three areas: AMS leadership and accountability; AMU surveillance and AMS; and AMR surveillance and AMS. Consensus on target actions was reached through a RAND-modified Delphi process involving over 40 experts in infectious diseases, clinical microbiology, AMS, veterinary medicine and public health, from 18 countries.

Results/discussion: Forty-six target actions were developed and qualified as essential or desirable. Essential actions included the setup of AMS teams in all veterinary settings, building government-supported AMS programmes and following specific requirements on the production, collection and communication of AMU and AMR data. Activities of AMS teams should be tailored to the local situation and capacities, and be linked to local or national surveillance systems and infection control programmes. Several research priorities were also identified, such as the need to develop more clinical breakpoints in veterinary medicine.

Conclusions: This White Paper offers a practical tool to veterinary practitioners and policy makers to improve AMS in the One Health approach, thanks to surveillance data generated in the veterinary setting. This work may also be useful to medical doctors wishing to better understand the specificities of the veterinary setting and facilitate cross-sectoral collaborations.

Introduction

Veterinary and human medicine share the responsibility of preserving the efficacy of antibiotics and preventing the spread of antimicrobial resistance (AMR). To a large extent, the antimicrobial drugs (or classes) that are used in animals are the same as those in human settings[1–3] and resistant bacteria can be transferred between animals, the environment and humans through different routes of transmission.[1–4] This renders AMR a One Health issue requiring multi-sectoral collaborations.[4–6]

To prevent the spread of AMR, antimicrobial stewardship (AMS) should be developed collectively in all settings where antimicrobials are used as 'a coherent set of actions which promote using antimicrobials responsibly'.[7] Indeed, AMS interventions in one setting can have a positive impact in another,[5] and this is particularly the case for the animal sector, where interventions are commonly carried out with a public health perspective.[1,8,9] However, the specificities of each setting should always be carefully taken into account when devising an AMS programme.[10–14]

The veterinary sector is highly heterogeneous. Veterinarians can work as independent private practitioners (acting alone) or be organized in veterinary clinics or hospitals with multiple staff, that can be owned by individuals or by national or multinational veterinary healthcare enterprises. Veterinarians deal with different animal species that include companion animals, food-producing animals and, although less commonly, wild animals. Veterinarians can prescribe and dispense antimicrobials for various purposes, i.e. treatment, metaphylaxis (administration of a drug to a group of clinically healthy animals in contact with diseased animals),[15] prevention and growth promotion (where allowed) for individual animals or groups of animals.[15–17] Access to antimicrobials also differs greatly between countries[18–20] and is sometimes readily available without any prescription to farmers or pet owners,[21–23] leading to further difficulties in controlling antimicrobial usage (AMU).

Monitoring AMU is important to quantitatively assess the performance of a National Action Plan (NAP) in reducing the overall use of antimicrobials, to target interventions in animal species to prevent using unjustified amounts of antimicrobials and to check that the veterinary use of antimicrobials critically important for human health is minimized.[24–26] When carried out at the level of prescription, it can become a benchmarking tool where prescribers, sellers or farmers can compare their antimicrobial usage against a regional average or a particular food-production sector.[27–30] Although such systems may require specific legislation, they can be useful to reduce AMU, especially when linked with incentives for lower usage or targeted interventions to high antimicrobial users.[31] It is noteworthy that NAPs on AMR, although recommended by the World Health Organization (WHO) and WHO Member States, are not legally binding. This limits the power of NAPs as a governance tool.[32]

In addition, it is key to monitor AMR in animal bacterial pathogens[33–35] to help veterinarians and farmers use antimicrobials more prudently, follow AMR trends and advise action at national or more local levels. Moreover, showing AMS teams and other actors in animal health that their efforts succeed not only in decreasing AMU but also AMR is necessary to maintain their commitment. In the One Health approach it is also paramount to monitor AMR in zoonotic and commensal bacteria[36,37] from healthy animals to assess the risk of transmission to humans through the food chain (or by direct contact), as this can lead to better risk management interventions.[38] Of note, commensal bacteria are a useful indicator for the comparison of AMR rates over time and between different animal species, countries or farms.

Despite a general call to develop monitoring systems that are able to provide relevant, accurate and complete data to drive AMS programmes in all settings, including the animal sector, many gaps still remain, along with many harmonization challenges. For example, only fragmentary data on AMU and AMR are available for companion and aquatic animals.[39–42] Regarding AMR data, most of the available information comes from healthy terrestrial food-producing animals and relatively few multi-annual programmes are in place for the monitoring of AMR in animal pathogens.[43–45]

The complexity of the veterinary setting (including its interconnections with the human sector, the varying purposes of surveillance systems[26,46,47] and the non-homogeneous availability of surveillance data and resources around the world[48,49]) make many activities difficult to standardize. Thus, practical details are not available for many AMS activities, and indications on how surveillance data should intertwine with AMS interventions are lacking.

The JPIAMR ARCH[50] and COMBACTE-MAGNET EPI-Net[51] networks have come together for the shared goal of implementing a framework of actions to facilitate antibiotic policy interventions and foster use of surveillance data on AMR and consumption and implementation of AMS activities in human and animal health.

In this regard, the ARCH and COMBACTE-MAGNET EPI-Net international expert panel is focusing on four settings: hospital, outpatient, long-term care facility, and veterinary. The efforts involve three areas: (i) AMS leadership and accountability; (ii) AMU and AMS; and (iii) AMR and AMS, all considering the feasibility of the actions and the One Health approach.

This White Paper focuses on the veterinary sector and targets veterinarians, policymakers and other actors in animal and human health who are involved in AMS activities. The proposed guidance is intended as a practical tool regarding the production and use of AMU and AMR data to plan and implement AMS programmes in line with the One Health approach and applicable in different veterinary contexts, including resource-limited countries. Dissemination to the intended audience will be ensured by the networks involved in the JPIAMR ARCH project as listed in Table 1 of the first paper in this series.[52] Checklist formats of the target actions are downloadable from the ARCH website.[50] These checklists can be used by health professionals and policymakers to establish and/or monitor stewardship activities.

Methods

Adopting a One Health approach, the present project was planned to develop expert consensus considering the literature and guidance on AMS and surveillance. A first draft of targets and a RAND-modified Delphi process were used for validation of targets (protocol on ARCH website).[50] The process involved development of key research questions arising from a systematic review on surveillance reporting of AMR that was previously developed (EPI-Net COACH project)[53] and adapted to a veterinary setting (Table 1); a narrative review of the available evidence was performed, and a first draft of targets was provided to the experts in a web-based survey. Agreement was expressed on a nine-point Likert scale. A 2 day face-to-face meeting took place at the end of October 2019. A literature search of relevant publications in English, published in the last 10 years, was carried out using MEDLINE (National Library of Medicine, Bethesda, MD, USA) using a combination of the following terms: antimicrobial*, consumption, animal*, veterinary, antimicrobial drug resistance, surveillance. More details are available in the first paper in this series.[52]

During the meeting, the experts were presented with a summary of the available evidence and the results of the online survey. The entire set of targets was reviewed and discussed. Following the meeting, a core team (M.C., E.M., R.M., R.S.) of the veterinary working group performed a further revision and fine-tuning of the list of targets, which was then approved by the entire panel in an additional consultation. To cover all different veterinary features and related interconnections with human health, different

Table 1. Key questions for the veterinary setting

1. Leadership commitment, accountability and antimicrobial stewardship team
- Participants in the antimicrobial stewardship team
- Targets of antimicrobial stewardship (e.g. is antimicrobial stewardship targeted to diseased animals?)
- Institutional support for organization and management of antimicrobial stewardship programmes: legal framework
- Institutional support for organization and management of antimicrobial stewardship programmes: staffing personnel
2. Antimicrobial usage and antimicrobial stewardship
- Which antibiotics should be monitored?
- Which metrics should be employed for monitoring antimicrobial usage?
- Should the surveillance specify the purpose of antimicrobial usage?
- Which criteria for reporting and time interval should be used?
- Who should be the end user of the report?
- Should a restrictive policy be adopted?
- Should a ranking for antibiotic use be adopted?
3. Antimicrobial resistance and antimicrobial stewardship
- Which criteria are needed to target resistant pathogens?
- How should resistance be monitored?
- Which prevalence data and selective monitoring screening should be considered?
- Which criteria for reporting and time interval should be used?
- Which criteria should be applied to stratify the results?
- Who should be the end user of the report?
- Should the report set specific thresholds for establishing empirical therapy and surgical prophylaxis?
- Which criteria should be used to drive selective reporting of antibiograms?

settings (farms, veterinary clinics, etc.) and animal populations (companion and food-producing animals, including aquatic animals) were considered. Recommendations, state of the art, and original approaches were evaluated by focusing on feasibility and adaptability to different economic and veterinary contexts to compile a list of 'essential' and 'desirable' targets. Targets were recognized as 'essential' when widely practicable if not already broadly accomplished, and 'desirable' in the case of limited feasibility or having a resource-intensive nature. Topics for which more evidence was required in order to draw up recommendations were added as priority topics for further research.

Over 40 experts from 18 countries and representing 30 networks developed the protocol, contributed to reaching a consensus and approved the final list of indications (see first paper in this series).[52]

Results

A total of 49 guidance documents (23 international and 26 national documents) and 45 articles including systematic reviews, studies and expert opinions were included for the full evidence appraisal.[1,3,4,8–17,19,20,22,24,27,28,31,33,34,36–38,40,41,46–48,54–117] International and national guidelines, practical guides or tools, surveillance reports and systematic reviews provided most of the evidence. The majority of the documents (71/94, 76%) were from high-income countries (Europe, North America, Australia and New Zealand).

For two research questions ('Should the report set specific thresholds for establishing empirical therapy and surgical prophylaxis?' and 'Which criteria should be used to drive selective reporting of antibiograms?'), the information did not allow drafting of specific targets, and thus these topics were addressed as future research areas.

An initial set of 65 targets was developed based on retrieved documents and assessed by eight experts in the field of human and veterinary medicine through the online survey. Consensus was reached on 54 targets, and additional comments were provided for most of them.

Eleven targets, where the agreement was not reached after first consultation, were discussed in the meeting. Main topics of discussion revolved around: (i) the organization of AMS considering participants and roles of the AMS team and institutional support; (ii) bacterial species to monitor considering human and animal health; and (iii) how to deal with the lack of clinical breakpoints to implement AMS activities. Nine targets were deleted during the meeting. All other targets were reconsidered and proposed for rephrasing (some were merged or split) or additional evaluation following the suggestions of the panel.

After the meeting, a list of 46 revised targets (25 essential and 21 desirable) was drafted by the core group and approved by the entire expert panel. Tables 2–4, respectively, list the recommended targets for AMS leadership and accountability, AMU and AMS, and AMR and AMS. Tables 5–8 refer to the statements of Tables 2–4.

Discussion

Interestingly, AMS leadership and accountability in the animal sector was one of the main topics of discussion during the meeting. This may reveal that more efforts have been made to develop AMR and AMU surveillance systems in comparison with efforts for structuring and guiding AMS activities in veterinary practices. Although preliminary agreement was reached for all proposed targets but one within the online survey, comments and suggestions were provided during the consultations that required further evaluation. This is likely due to the broad heterogeneity of the veterinary sector considering animal species, animal populations (food-producing animals including aquaculture and companion animals) and the various contexts where animal healthcare is provided (farms, small veterinary clinics, large hospitals, etc.).

The expert group is aware that the desirable composition of the AMS team described is often not feasible, but the action point aims to define the best options when establishing an AMS team. Very often, the team may be composed of only a farmer and his/her veterinarian, working together to rationalize AMU. However, for large clinics and farming industries that have their own pharmacies and laboratories, the composition of the AMS team could come close to what is recommended.[10,12,54,99,100]

Debates also arose regarding the role of animal owners. Although pet owners are responsible for the administration of antimicrobial treatments to their animals, it is not realistic to include them in AMS teams. On the other hand, farmers (and also breeders of horses or companion animals), who are professional animal keepers, do bear responsibility for the prudent use of antibiotics[11,55,56] and have a major role to play in AMS.[4,19,90] Still, pet owners should be targeted by educational activities to foster the

Table 2. Leadership commitment, accountability and antimicrobial stewardship team

Antimicrobial stewardship programme and team
1.1. Essential Antimicrobial stewardship programmes should be in place in every setting where antimicrobials are used to treat food-producing or companion animals, with targets and interventions tailored to the local situation and linked to local and national surveillance systems and infection control programmes.
1.2. Essential Antimicrobial stewardship programmes should be defined, planned, implemented and evaluated by a dedicated and competent team. This team should be tailored, depending on the animal species and production type, to the local context and availability of resources and personnel.
1.3. Desirable The team should include a veterinarian competent in antimicrobial stewardship and representatives of all professionals involved in animal care (para-veterinarians, veterinary nurses, farmers, veterinary pharmacists, microbiologists from diagnostic laboratories, etc.) in a collaborative approach, under the leadership of the veterinarian. This team should seek professional advice from additional experts when needed to adequately fulfil their antimicrobial stewardship activities.
Institutional support for organization and management of antimicrobial stewardship programmes
1.4. Essential Antimicrobial stewardship programmes should be supported at the governmental level through frameworks such as the National Action Plan in line with relevant international standards. The National Action Plan should include regulatory decisions to restrict the usage of antimicrobials in food-producing and companion animals, set specific reduction targets for antimicrobial usage and establish monitoring systems for antimicrobial usage and antimicrobial resistance.
1.5. Desirable Surveillance data on antimicrobial usage and antimicrobial resistance should be made freely available to local antimicrobial stewardship teams, as well as to all other professionals working in animal, human or environmental health.
1.6. Desirable Voluntary approaches to improve antimicrobial stewardship and surveillance in the animal sector should be encouraged, e.g. when the farming industry adopts its own measures to increase biosecurity, infection control and reduce antimicrobial usage.

appropriate use of antimicrobials, along with veterinarians, farmers and other actors in animal health.[13,58,101,118]

AMS should be implemented from the local to the global level, spanning human health, animal health and the environment.[2,12,58,119] Therefore, even in the veterinary setting, AMS should be devised and supported at a higher level, especially by governments and industry[57,59,60,110] in the form of NAPs and good practice charters. These should recommend measures to reduce AMR and provide guidance to AMS teams in the field. Setting targets for reduction,[61,62] as well as restricting AMU in animals,[9,41,63,104] has been shown to be very effective in several countries.[120] To foster AMS, governments should support AMU and AMR monitoring systems.[39,58,59,113] More broadly, institutional support is crucial in terms of communication and progress reporting, and to ensure transparency of information on both AMU and AMR.

There must also be support for any voluntary approaches, provided they are in line with government policy.[60] For example, industry initiatives to restrict the use of some antimicrobial classes have been shown to be efficient at reducing resistance rates[120,121] and should be encouraged. The development of quality policies in veterinary clinics with a dedicated component on AMS activities should also be promoted.

The design of AMU or AMR monitoring systems should depend on their objectives, existing contexts and capacities, and be consistent with national guidelines, if any.[14,48] However, existing policies on access and use of antimicrobials may differ substantially among countries.[19,21,22,42,56] A veterinary prescription may or may not be compulsory, impairing the availability of herd-level benchmarking. Additionally, the lack of national legislations/regulations still permits some countries to use antimicrobials as growth promoters,[17,18,122] although this practice is strongly discouraged by international organizations, including the WHO,[1] the World Organisation for Animal Health (OIE),[123] and European legislation.[15] To help in their design, rankings of antimicrobials from international organizations can be used (WHO, OIE, EMA), in particular categorizations that consider the risk that animal usage of antimicrobials may pose to public health in the One Health approach.[9]

The consensus between experts regarding AMU statements was easily achieved, likely due to the numerous efforts that have already been established in this field, namely in the framework of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC). If usage of all antimicrobials cannot be monitored, as would be desirable,[64] targeting specific animal species and antimicrobial classes is preferred. A major issue is that AMU data can be collected in different ways.[26,28,40,92] When possible, prescriptions and, even better, animal administration data should be collected from veterinarians and farmers as these provide the most accurate data on AMU (when properly recorded) and allow benchmarking.[27,36,62,112] If this is not possible, sales data may be collected from pharmaceutical companies.[26,65,66]

Table 3. Antimicrobial usage and antimicrobial stewardship

Which types of antimicrobial usage, animal species and antimicrobials should be monitored?	
2.1. Essential	Antimicrobial usage should be monitored whatever the purpose of antimicrobial administration. This includes growth promotion, a practice that should be discouraged.
2.2. Essential	Antimicrobial usage should be monitored in food-producing (including aquatic) and companion animals.
2.3. Desirable	Antimicrobial usage should be monitored for all animals for which antimicrobials are authorized in a country.
2.4. Essential	If national monitoring of antimicrobial usage including all antimicrobials is not feasible, a risk-based approach should be promoted to target monitoring to the most relevant antibiotics for animal and/or human health and only within the most important animal species in a country or region.
2.5. Essential	The choice of antimicrobials to be monitored should be guided by the World Health Organization (WHO) ranking of critically important antimicrobials, by the World Organisation for Animal Health (OIE) list of antimicrobial agents of veterinary importance and by specific rankings of risk to public health from antimicrobial resistance due to the use of antimicrobials in veterinary medicine (example in Table 5).
Which metrics should be employed?	
2.6. Essential	Antimicrobial usage should be monitored at least at the country level, for all or selected combinations of animal species and antimicrobials.
2.7. Desirable	Antimicrobial usage should be monitored at the level of each prescription, sale or animal administration, such as veterinary clinics, pharmacies and farms, for all or selected combinations of animal species and antimicrobials.
2.8. Essential	Sales data are the minimum that should be provided for all or selected combinations of animal species and antimicrobials, in kilograms of active ingredient for all animals and in milligrams per population correction unit (PCU) for food-producing animals.
2.9. Desirable	When data are available on prescriptions, sales and animal administration, the amount of overall usage should be standardized according to animal production and antimicrobial daily doses or antimicrobial treatment course.
Which data and stratification criteria should be adopted?	
2.10. Desirable	Additional data should be collected as part of an antimicrobial usage monitoring such as age, production type, route of administration or treatment type (therapy, metaphylaxis, prophylaxis or growth promotion). The data analysis should be stratified according to these additional data.
Which criteria for time interval and reporting should be used?	
2.11. Essential	Antimicrobial usage data should be reported annually.
2.12. Essential	Surveillance data on antimicrobial usage should be reported at the national level.
2.13. Desirable	Surveillance data on antimicrobial usage should be reported at the local level.
2.14. Essential	All methods used to provide antimicrobial usage data should be clearly described.
2.15. Desirable	Antimicrobial usage and antimicrobial resistance data in the animal sector should be analysed, interpreted and reported in the same report. In the One Health approach, this report should also include data on antimicrobial usage and antimicrobial resistance from the human sector.
2.16. Desirable	The report should include an English version to foster easier sharing of information between countries.
Who should be the end user of the report?	
2.17. Essential	The end users of reports on antimicrobial usage should be antimicrobial stewardship teams and all other stakeholders in animal, human and environmental health at the local, institutional or industry level.
2.18. Desirable	The report should be freely available online to anyone and include a summary that is understandable for the general public.

Table 4. Antimicrobial resistance and antimicrobial stewardship

Which animal species and resistant bacteria should be targeted?
3.1. Essential Antimicrobial resistance should be monitored in food-producing (including aquatic) and companion animals.
3.2. Essential The target resistant bacteria should be animal pathogens, but also zoonotic pathogens and commensals in the One Health approach.
3.3. Essential OIE criteria should be followed for the choice of animal pathogenic bacteria to monitor (Table 6). Examples from OIE in terrestrial food-producing animals are provided in Table 7.
3.4. Desirable In companion animals, target pathogenic bacteria may include methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus pseudintermedius* from skin samples and *Escherichia coli* from urine samples, considering their importance for animal health and the zoonotic potential of MRSA.
3.5. Essential Selection criteria for the foodborne zoonotic and commensal bacteria to include in an antimicrobial resistance integrated surveillance programme should depend on public health priorities, antimicrobial use practices and the estimates of the burden of foodborne illnesses, as stated by WHO (Table 8).
3.6. Essential The choice of antimicrobials to monitor should be guided by the WHO ranking of critically important antimicrobials, by the OIE list of antimicrobial agents of veterinary importance and by specific rankings of risk to public health from antimicrobial resistance due to the use of antimicrobials in veterinary medicine (example in Table 5).
How should resistance be monitored?
3.7. Essential For animal pathogenic bacteria, samples should originate from diseased or dead animals.
3.8. Essential For indicator and zoonotic bacteria from food-producing animals, samples should be taken from healthy animals of defined age.
3.9. Essential Standardized and internationally recognized antimicrobial susceptibility testing methods should be used.
3.10. Desirable To support field antimicrobial stewardship teams and provide recommendations for antimicrobial therapy in veterinary settings, clinical breakpoints should be used to interpret antimicrobial susceptibility testing results. If not available, epidemiological cut-off values may be used. When the objective is to detect decreased susceptibility (i.e. to display a microbiological resistance), epidemiological cut-offs should be used.
3.11. Desirable Quantitative data (MICs or inhibition zone diameters) should be collected rather than interpreted data (susceptible/intermediate/resistance or wild type/non-wild type).
3.12. Desirable Specific monitoring schemes may be performed in healthy animals and food thereof using selective media, e.g. to detect the presence ESBL/AmpC, carbapenemase-producing, colistin-resistant Enterobacterales, MRSA or vancomycin-resistant enterococci to assess public health risk.
3.13. Desirable Resistance mechanisms should be characterized at the molecular level, e.g. using the polymerase chain reaction, sequencing or whole-genome sequencing for colistin-resistant ESBL/AmpC- and carbapenemase-producing Enterobacterales.
Which data and stratification criteria should be adopted?
3.14. Desirable Additional data should be collected as part of antimicrobial resistance monitoring, such as age, production type and specimen, and if the antimicrobial susceptibility testing was requested due to a previous antimicrobial treatment failure. The analysis should be stratified according to these additional data.

Continued

Table 4. Continued

Which criteria for time interval and reporting should be used?
3.15. Essential The time interval for reporting resistance data should be annual, but emerging resistances should be reported in as timely a fashion as possible.
3.16. Essential Surveillance data on antimicrobial resistance should be reported at the national level.
3.17. Desirable Surveillance data on antimicrobial resistance should be reported at the local level.
3.18. Essential All standards and guidance documents used for bacterial isolation, bacterial identification and antimicrobial susceptibility testing should be clearly described.
3.19. Desirable Antimicrobial usage and antimicrobial resistance data in the animal sector should be analysed, interpreted and reported in the same report. In the One Health approach, this report should also include data on antimicrobial usage and antimicrobial resistance from the human sector.
3.20. Desirable The report should include an English version to foster easier sharing of information between countries.
Who should be the end users of the report?
3.21. Essential The end users of reports on antimicrobial resistance should be antimicrobial stewardship teams and all other stakeholders in animal, human and environmental health at the local, institutional or industry level.
3.22. Desirable The report should be freely available online to anyone and include a summary that is understandable for the general public.

However, such data have a number of limitations, such as lack of information on the animal species, categories (adult versus young animal) to be treated and scope of treatments.

Regarding the monitoring of AMR, the online survey highlighted several areas of only partial agreement, such as the bacteria to be monitored. This is likely due to the complexity of AMR monitoring in the animal sector, as both animal and public health need to be considered. The differences in design possibilities for AMU also apply to the monitoring of AMR,[34,35,46,67,124] especially since it should be done for animal bacterial pathogens to help in the development of empirical therapy recommendations in the veterinary setting,[10,34,47,49] and for zoonotic and commensal bacteria in the One Health approach.[35,36,55,68,97] This leads to very different sampling schemes: passive monitoring in diseased animals for animal pathogens and active monitoring in healthy animals for commensal and zoonotic bacteria. Monitoring systems may rely on phenotypic identification of resistance, but molecular identification of AMR determinants brings more accurate insights into the epidemiology of resistance genes,[36,48,58,69] especially between the animal and human sectors, and can generate better risk-management measures.

A specific challenge that applies to the translation of AMR surveillance data into AMS actions is the lack of clinical breakpoints to interpret antimicrobial susceptibility testing (AST) results for many combinations of animal species, bacterial species and clinical form. The large majority of existing breakpoints were produced by the CLSI.[125] In 2019, the Veterinary Committee on Antimicrobial Susceptibility Testing (VetCAST) of the EUCAST proposed its first clinical breakpoints.[126] However, developing clinical breakpoints is a long and difficult process, and it is unlikely that many of the missing ones will be determined in the short term. When no breakpoint is available, epidemiological cut-offs (ECOFFs) can be used as an alternative.[36,108,114] However, ECOFFs detect decreased susceptibilities and, as such, are not proper indicators of clinical resistance.[46,115] When using ECOFFs instead of clinical breakpoints, resistance rates can be overestimated, so one should be cautious when providing treatment recommendations based on them.[46] Indeed, using ECOFFs must not lead to wrongly recommending the prescription of critically important antimicrobials when older drugs remain clinically efficient. Because interpretative criteria, either clinical breakpoints or ECOFFs, can change over time, it is important to collect and report on quantitative data (inhibition diameters or MICs) to enable the recalculation of resistance rates in historical data and still be able to analyse trends.[33,36,46,69,115]

To ensure that AMR and AMU monitoring systems serve AMS in the One Health approach, it is key to report data jointly with those of AMU and AMR in other sectors, especially the human one.[36,48,60] This prevents the provision of a fragmented picture of the AMR situation and facilitates a reciprocal understanding between actors that need to collaborate to improve AMS. However, cross-sectoral data analysis of AMU and AMR data is complex and requires prudent interpretation. This is why experts should always seek to summarize the results in a format that is understandable by all stakeholders in animal, public and environmental health, as well as by the general public.[48]

Table 5. Categorization of antimicrobials considering the risk to public health from their usage in veterinary medicine due to antimicrobial resistance, by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) from the European Medicines Agency (EMA)[9]

Category	List of drugs
Category A 'Avoid'	• Aminopenicillins • Carbapenems • Other cephalosporins (other than 1st, 2nd, 3rd and 4th generation) and penems (ATC code J01DI), including combinations of 3rd-generation cephalosporins with β-lactamase inhibitors • Glycopeptides • Glycylcyclines • Ketolides • Lipopeptides • Monobactams • Oxazolidinones • Penicillins (carboxypenicillins and ureidopenicillins, including combinations with β-lactamase inhibitors) • Phosphonic acid derivatives • Pseudomonic acid • Rifamycins (except rifaximin) • Riminofenazines • Streptogramins • Sulfones • Drugs used solely to treat tuberculosis or other mycobacterial diseases • Substances newly authorized in human medicine following publication of the AMEG categorization
Category B 'Restrict'	• 3rd- and 4th-generation cephalosporins, except combinations with β-lactamase inhibitors • Polymyxins • Quinolones (fluoroquinolones and other quinolones)
Category C 'Caution'	• Aminoglycosides (except spectinomycin) • Aminopenicillins in combination with β-lactamase inhibitors • Amphenicols • 1st- and 2nd-generation cephalosporins and cephamycins • Macrolides (not including ketolides) • Lincosamides • Pleuromutilins • Rifamycins (rifaximin only)
Category D 'Prudent'	• Aminopenicillins without β-lactamase inhibitors • Cyclic polypeptides • Nitrofuran derivatives • Nitroimidazoles • Penicillins (antistaphylococcal penicillins and natural penicillins) • Aminoglycosides (spectinomycin only) • Steroid antibacterials • Sulphonamides, dihydrofolate reductase inhibitors and combinations • Tetracyclines

Further topics were explored and addressed as research areas during consultations. Although planning dedicated time and allocating specific measures for AMS teams are essential for AMS activities, detailed information on the minimum requirements for personnel according to the tasks of AMS programmes are lacking in the literature. Additionally, the lack of clinical breakpoints for many antimicrobials for many animal species remains an important limitation for the interpretation of AST and to guide prudent use of antimicrobials. This represents the main issue that must be addressed to improve AMS activities. Due to the lack of available documents retrieved for two key questions and following the numerous discussions among the panel, additional topics were considered as important future research areas that should be investigated and could complement the current checklist. The main research priorities are summarized in Table 9.

To our knowledge, this is the first time that a consensus from an international group of veterinary and medical experts has been reached in the veterinary setting regarding AMS leadership and accountability, as well as on the AMU and AMR information that monitoring systems should provide in the animal sector to support AMS

Table 6. OIE criteria to be considered in the choice of animal bacterial pathogens for inclusion in an AMR monitoring programme[a]

- Impact on animal health and welfare
- Implication of antimicrobial resistance of the animal bacterial pathogen on therapeutic options in veterinary practice
- Impact on food security and on production (economic importance of associated diseases)
- Bacterial diseases responsible for the majority of veterinary antimicrobial usage (stratified by usage of different classes or their importance)
- Existence of validated susceptibility testing methodologies for the bacterial pathogen
- Existence of quality assurance programmes or other pathogen-reduction options that are non-antimicrobial, such as vaccines and Good Agricultural Practices

[a]Adapted from Table 2 of reference 33.

Table 7. OIE example of bacterial pathogens in terrestrial food-producing animals to include in an AMR monitoring programme[a]

Species	Respiratory pathogens	Enteric pathogens	Other pathogens
Cattle	*Pasteurella multocida*, *Mannheimia haemolytica*	*Escherichia coli*, *Salmonella* spp.	Udder pathogens[b], such as *Staphylococcus aureus*, *Streptococcus* spp.
Pigs	*Actinobacillus pleuropneumoniae*	*Escherichia coli*, *Salmonella* spp.	*Streptococcus suis*
Poultry	–	*Salmonella* spp.	*Escherichia coli*

[a]Adapted from information in reference 33.
[b]Refers to pathogens causing mastitis (mammary gland infection).

Table 8. Foodborne and indicator bacteria to include in an AMR monitoring programme

- In terrestrial food-producing animals, zoonotic bacteria typically include *Salmonella* spp. and *Campylobacter* spp. from caecal samples
- In terrestrial food-producing animals, indicator bacteria (animal commensal bacteria as potential reservoir of drug resistance genes) typically include *Escherichia coli* and enterococci from caecal samples
- Other bacteria (e.g. methicillin-resistant *Staphylococcus aureus, Clostridioides* spp. and *Listeria monocytogenes* from terrestrial food-producing animals or *Vibrio parahaemolyticus* and *Salmonella* spp. from aquaculture production) may be included according to the epidemiology of foodborne diseases in the area

activities in the One Health approach. The initial step of the literature review was useful in guiding group discussions and finding agreement. However, the subjective nature of the experts' opinions and the small number of participants remain limitations of the approach.

A major strength of this document is that it provides practical and concise indications for AMS teams in the field, but also for institutions wishing to support AMS from a higher level, especially when it relates to the production of AMR and AMU data that are relevant for prescribers, sellers and users of antimicrobials in animals. These indications are also useful for medical doctors wishing to better understand the specificities of the veterinary sector in terms of surveillance and AMS, especially as some activities are designed with a public health perspective. This work also enabled the identification of several important future research areas to facilitate the development of AMS programmes and the translation of AMR surveillance data into prudent use of antimicrobials in the veterinary setting. However, due to the diversity and complexity of the veterinary sector, along with the fact that diverse economic contexts were considered, many targets of the checklist are rather generic and need to be adapted to each specific context. In this scenario, the indications given herein represent a first step to better structure AMS activities in the animal sector.

Conclusions

A list of essential and desirable targets was produced following development of consensus between experts from both medical and

Table 9. Research priorities

- **Develop guidance on the specific tasks of AMS programmes, including staff requirement and time allocation per task, in different veterinary contexts.**

  Rationale
  Definition of roles and accountability is a prerequisite for any AMS programme. Compared with human medicine, the veterinary sector shows greater variability in animal species, animal populations (food-producing animals including aquaculture and companion animals) and the various contexts where animal healthcare is provided (farms, small veterinary clinics, large hospitals, etc.). Although planning dedicated time and allocating specific measures for AMS teams are essential for AMS activities, detailed information on the minimum requirements for personnel according to tasks of AMS programmes are not available in the literature. In this scenario, appropriate and detailed guidance on staff requirement and time to be allocated per specific task of AMS programmes, and tailored to the different veterinary contexts, represents a fundamental measure to foster AMS activities.

- **Produce missing veterinary clinical breakpoints.**

  Rationale
  A specific challenge that applies to the translation of AMR surveillance data into AMS activities in the veterinary setting is the lack of clinical breakpoints to interpret AST results for many combinations of animal species/bacterial species/clinical condition. When no breakpoint is available, epidemiological cut-offs (ECOFFs) can be used as an alternative. However, ECOFFs detect decreased susceptibilities and, as such, are not proper indicators of clinical resistance. When using ECOFFs instead of clinical breakpoints, resistance rates can be overestimated, so one should be cautious when providing treatment recommendations based on them.

- **Provide indications for the selective reporting of AST results to veterinarians.**

  Rationale
  The use of selective reporting is an important measure to optimize animal care and foster AMS. Reporting drugs that are typically effective against the pathogen and which are recommended for first-line regimens aids the veterinary clinicians in the appropriate use of antimicrobial agents, discouraging the unnecessary use of broad-spectrum agents. However, criteria for selective reporting in the animal sector have not been clearly defined.

- **Provide indications about resistance thresholds to translate AMR data into empirical therapy and surgical prophylaxis.**

  Rationale
  There are currently no indications regarding if and how resistance thresholds should be defined as part of AMS programmes to guide empirical therapy and prophylaxis. Studies forecasting reproducible models to support the determination of an antimicrobial-specific threshold (i.e. baseline resistance rate beyond which an antimicrobial must not be used) and exploring treatment outcomes of a threshold-driven switch in antimicrobial choices are fundamentally needed to ascertain and establish the role of resistance thresholds as criteria for decision support on choice of antimicrobials.

veterinary backgrounds. The proposed indications, which consider the connection with human medicine and the heterogeneity of the veterinary setting, aim to facilitate the development of AMS programmes linked to AMU and AMR surveillance data in the animal sector, but with benefits for both animal and human health. This White Paper, together with those produced in the hospital, outpatient and long-term care facility settings, provides the opportunity to compare practices and learn from other areas.

This series of White Papers represents a practical example of how the One Health approach can be useful in understanding priorities, capacities and needs among sectors. This overall initiative facilitates collaboration between all actors in animal and human health who are involved in AMS activities. This series also enabled the identification of relevant areas to engage for future research in order to facilitate the development of AMS programmes and the translation of surveillance data into prudent use of antimicrobials in the human and animal sectors.

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