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31 August 2021

Allen and Clarke Consulting

Melbourne, VIC 3000

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Dear consultants,

Re: Developing Options for a One Health Antimicrobial Resistance and Antimicrobial Usage Surveillance System

We are pleased to provide this submission on behalf of the members of Animal Medicines Australia (AMA). AMA is the peak body representing the leading animal health companies in Australia. Our member companies are the innovators, manufacturers, formulators and registrants of a broad range of veterinary medicine products that prevent, control and cure disease across the companion animal, livestock and equine sectors. AMA members represent more than 90% of sales of registered veterinary products in Australia.

Antibiotics are critically important medicines for animals and antibiotic resistance poses a grave threat to animal health and welfare, as it does to human health. It is vital that antibiotics remain available for a veterinarian to use when an animal is sick, or likely to become sick, from a bacterial infection.

We strongly support the responsible and judicious use of antimicrobials in animals to protect animal health and welfare, and in a way that minimises the development of antimicrobial resistance, to ensure that we are able to treat and control many debilitating animal diseases, now and in the future.

A true One Health surveillance system that appropriately represents both human and animal health will provide a critical evidence base to inform effective policy and appropriate response strategies that support animal health and welfare and preserve the effectiveness of these critically important medicines for the future. In doing so, such a system would protect public health, facilitate the sustainable production of safe food and fibre, and maintain Australia's global reputation for high quality agricultural products.

We hope that the following information will be of assistance. As noted during our earlier conversation, AMA has chosen to provide a written submission, as many key issues for our sector were not easily captured by the format and constraints of the survey form.

As requested, we have also attached a number of references on different metrics used to assess antibiotic use in animals.

If you have any questions or would like further information, please do not hesitate to contact us.

Yours Sincerely,

(unsigned for electronic submission)

Dr Charmian Bennett — Director Science and Policy

Dr Katie Asplin — Director Animal Health Stewardship

SUBMISSION ON

Developing Options for a One Health Antimicrobial Resistance (AMR) and Antimicrobial Usage (AU) Surveillance System

31 August 2021

Animal Medicines Australia

Introduction

Antimicrobial resistance (AMR) is a growing threat to both human and animal health worldwide. Resistance means that the usual antibiotic treatments for common infections become less effective, leaving healthcare and veterinary professionals with limited (or sometimes, no) treatment options.

Effective treatment of bacterial infections in animals facilitates a safe and nutritious food supply chain, protects public health, supports farm productivity and protects the sustainability of our critically important agricultural industries. AMR is also becoming an increasingly important trade factor for agricultural products.

Surveillance of commensal and pathogenic bacteria in both animals and humans is essential to understand the impact and importance of cross-species transmission of bacteria and resistance mechanisms. To date, the Australian government has invested more than $50 million to tackle this issue, with the vast majority of that funding being assigned to the Department of (Human) Health. Virtually nothing has been allocated directly to the animal health sector.

Further, any consideration of the animal sector has focussed on the role of animal health in determining human health outcomes; the impact of human health decisions on animal health outcomes (such as the removal of antibiotic classes from animal use when they are not used in human health) has not been considered.

The animal health sector is deeply concerned about AMR and its potential threats to animal health and welfare, and it has been proactive in its actions to respond to the challenges of AMR voluntarily and in the absence of government support. Significant reductions in use, antibiotic stewardship and accreditation programs, and evidence-based best practice prescribing guidelines to support the responsible and judicious use of all antibiotics are now widespread across the Australian livestock, equine and companion animal sectors.

Public health, animal health and environmental health are inextricably linked, which is explicitly recognised by the One Health framework. Understanding AMR in Australia's animal populations is essential to protect both human and animal health and to support the development of effective, evidence-based responses to AMR that support animal health and welfare, protect public health, facilitate the sustainable production of safe food and fibre, maintain our global reputation for high quality agricultural products, and preserve the effectiveness of these critically important medicines for the future.

Submission Structure

This submission addresses the following key questions:

- What are the key enablers of a One Health surveillance system?
- What are the biggest barriers to a One Health surveillance system?
- What other existing systems, activities or databases could be leveraged/adapted/incorporated to support a national One Health surveillance model in Australia?
- What components need attention to achieve a national One Health AMR surveillance system?
- What principles should influence which microbe, AMR or agents are included in a One Health surveillance system? What must be considered in prioritising antimicrobial resistance or use?
- What are the biggest barriers to a coordinated, multisectoral One Health approach and how could they be addressed?

What are the key enablers of a One Health surveillance system?

Antibiotics are critically important medicines for animals as well as people. AMR poses a grave threat to animal health and welfare, food safety and public health, as well as agricultural productivity and sustainability.

A key strategy to address AMR globally is the development of 'new' antibiotics to replace those where resistance has significantly reduced their efficacy. However, it is unlikely that animals will get access to any new antibiotics that may be developed in the future – they will most likely be reserved for human use only. This places significant pressure on the animal health sector to use the antibiotics currently available as responsibly as possible to ensure they remain effective in the future.

All major animal industries in Australia are already well advanced in (voluntarily) establishing and implementing antimicrobial surveillance and accreditation systems that are appropriate to their context. It is important that any national actions recognise and support these existing systems and structures, not disregard or undermine them, or seek to replicate them.

The veterinary diagnostic laboratories in Australia have also undertaken significant work in recent years to develop and align testing methods, equipment and standards to facilitate the collation and analysis of data across the animal health sector. Again, the work of these laboratories to collaborate and integrate their data for the greater good must be respected by any future national actions.

AMA wishes to emphasise that there is significant goodwill in the animal health sector and associated industries. The threats posed by AMR to Australia's $28 billion dollar livestock industry and $31 billion dollar pet industry are of major concern and the animal sector is committed to supporting efforts that reduce these risks. However, the animal sector has traditionally been regarded as a scapegoat for AMR issues arising in human health, with little consideration given to the context of antibiotic use in animals in Australia, nor the strict regulatory environment and controls on antibiotic use. The animal health sector is keen to participate and work collaboratively to address the challenges of AMR, but there is a pressing need for the sector to be included as genuine partners, where the specific contexts of antibiotic use in animals and the associated risks to animal health and welfare, are recognised and respected.

What are the biggest barriers to a One Health surveillance system?

Misunderstandings and misinformation are major barriers to the integration of the animal health sector into a One Health system. The use of antibiotics in animals is often inappropriately compared to use in human health settings, and the specific contexts of antibiotic use in animals are overlooked. For example, reporting often focuses on the gross quantity of antibiotics used in animals, which is measured in tonnes. However, that metric does not reflect the reality that dose rates for animals are incomparable to dose rates for people – a 700kg cow or horse will require a vastly different quantity of antibiotic to treat an infection compared to an 80kg human or a 5kg cat. Further, a focus on gross volumes provides minimal information on the necessity or appropriateness of antibiotic use, nor the risks (if any) of that use to human health.

There is significant concern in the animal health sector on misinformation in the public discourse that promotes fear and mistrust of animal-derived commodities. For example, one myth is that if an animal receives antibiotics during their lifetime, then the food produced from that animal will 'contain antibiotics.' Another is that residues and Maximum Residue Limits (MRLs) indicate health-related

targets (which they do not). Misinformation supports perceptions that any number other than zero is 'bad' and surveillance data can be easily misrepresented to promote this point of view.

Misunderstandings also arise from differences in the way antibiotics may be used in animals compared to how they are used in human medicine, such as being administered in feed or water to a group of animals. Livestock are usually raised in groups. Bacterial infections can spread extremely quickly between individuals and it may not be possible to identify and physically isolate individual animals before an infection spreads. This means that the most appropriate treatment for that animal must consider the welfare of the whole herd or flock in which it lives, including the species, age and condition, severity of illness, number of animals, type of housing, range of medicines registered for that use in that species and the formulations of the medicines that may be available (e.g.: tablet, feed additive, water soluble or injectable forms). The infection of an entire herd or flock of animals would be associated with substantial animal pain and suffering; treating the entire group of animals may therefore be necessary to prevent the spread of disease and protect the welfare of many animals.

The confidentiality and commercial sensitivity of data on antimicrobial use is of particular concern to the animal health sector, with significant risks of data being inappropriately used to target individuals (veterinarians, farmers) or businesses (manufacturers, researchers, veterinary practices). This has already occurred in the agricultural sector, where livestock farmers were identified and their properties invaded and vandalised by activists.

Another major barrier to implementing a coordinated surveillance system for antimicrobial use in the animal health sector is funding. The human health sector is well supported by the government to undertake a multitude of monitoring and surveillance activities. There is no equivalent support for the animal health sector. The achievements of the animal health sector in addressing AMR have been almost entirely self-funded. Sufficient and ongoing funding certainty is needed to establish the infrastructure to enable surveillance activities in the animal sector (such as databases and reporting systems), but also to support capacity-building within the veterinary sector and diagnostic laboratories to collect and analyse samples.

In addition, the animal health sector does not have access to a system similar to that of Medicare to reduce the cost of any sampling, testing, treatment or repeat consultations – the entire cost is, instead, borne by the animal owner. This leads to considerable differences in how a decision to seek more advanced testing and treatment for a sick animal is made, depending on the context. A household pet is more likely to be treated similarly to a human family member, with laboratory testing of samples, multiple veterinary consultations and treatment refinements, due to the emotional value and connection between owner and animal. In contrast, a livestock producer must prioritise other considerations such as the economic value of the animal, treatment costs, the need to observe withholding periods and their ability to isolate and/or handle an individual animal. Some production systems involve minimal direct human contact and the animals are unaccustomed to handling, so the need to capture and restrain an animal for testing or administering medication can be very stressful, as well as dangerous for those handling the animal.

What other existing systems, activities or databases could be leveraged/adapted/incorporated to support a national One Health surveillance model in Australia?

All major livestock industries in Australia have antimicrobial stewardship programs and systems in place that are appropriate to their industry and reflect their specific needs. It is important that these systems are respected and supported by any future national actions.

One Health surveillance has been the focus of considerable work internationally in recent years, especially in relation to AMR. There have been numerous attempts to integrate human health and animal health data, with varying degrees of success. AMA would strongly suggest that a comprehensive review of international actions should be undertaken to inform the development of surveillance in Australia. It would be especially useful to examine where these systems have failed and how those issues may be mitigated here.

It is important to note, however, that many overseas frameworks for monitoring antimicrobial use and resistance are targeted at ultimately reducing antibiotic use in animals to zero. This is unrealistic and undesirable, and would pose unacceptable risks to animal health and welfare, human health, food safety and agricultural sustainability. Whilst reductions in the use of some antimicrobials may be desirable, and possible, the goal (whether implicit or explicit) of any surveillance system must not be zero.

We have an ethical and moral responsibility to prevent illness when possible and treat sick animals when necessary; withholding appropriate treatment from a sick animal is unacceptable. Animal welfare always starts with good animal care and management practices that reduce the risk of injury and disease, and improve the animal's quality of life. However even with the highest possible standards of animal health and welfare, it is inevitable that some animals, at some point in their lifetime, may develop a bacterial infection and require antibiotic treatment to regain health. Bacteria are ubiquitous in the environment – it is impossible to prevent the exposure of animals, or humans, to all bacteria that could, potentially, cause an infection. It is essential that antibiotics remain available for veterinarians to treat infections in animals.

Australia already has a good surveillance framework in place through the AURA program. This appears to function well for human health. AMA would encourage the project team to focus on how aspects of the AURA system could be developed to incorporate relevant data on animal health in a meaningful and appropriate way.

What components need attention to achieve a national One Health surveillance system?

Clarity of Objectives

Clear and transparent objectives are critically important. The system must be capable of delivering answers to the questions being asked, not just collecting data for data's sake.

There are significant differences between monitoring usage and surveillance of resistance, which need to be measured in different ways. Resistance is the factor of greatest concern with respect to human health outcomes, but there must be clarity around the type of resistance and its relative risks to human health outcomes. For example, surveillance can be targeted to measure resistance of a specific pathogen (to multiple antibiotics), resistance to a specific antibiotic (by a range of pathogens), or carriage of a specific resistance mechanism. Further distinctions can be made between active and passive surveillance systems. Passive surveillance involves using lists of reportable diseases or resistances, with mandated reporting of such cases by providers. In contrast, active surveillance involves data collection on a routine basis (e.g.: at slaughter) or in response to a specific disease detection. Active surveillance can provide more data but is more expensive to undertake and maintain. It is unrealistic to expect a surveillance system to monitor anything and everything; it is therefore necessary to clearly specify the questions that surveillance seeks to answer in order to identify the most effective and efficient use of resources.

Some pathogens are important to animal health but are not relevant to human health; some are important to human health and not to animal health; some infections can be spread between humans and animals – from humans to animals, and from animals to humans. Detection is just the first step. Advanced analysis techniques such as genomic sequencing are becoming increasingly important to determine the origin and direction of transmission of resistance. A surveillance system must include advanced analytics into its core structure and function to support targeted use of scarce resources and identify key points for intervention.

AMA would like to emphasise that the major animal industries in Australia are already well advanced in establishing surveillance that is appropriate and relevant for their industry. We believe that the most effective pathway forward for this project would be to engage directly with each industry to explore how they can be supported to expand and integrate their surveillance activities with those of other industries.

Infrastructure

There needs to be a centralised data repository for animal health data, like the AURA system. This will allow for the collation of data on zoonotic pathogens from both human and veterinary diagnostic laboratories and support the development of One Health reports. This central data repository needs to be digitally and securely connected to the diagnostic laboratories and use standardised data templates to facilitate accurate and efficient data transfer.

More advanced analyses may only be available at specific laboratories. For example, Lab A does culture and sensitivity testing and identifies a resistant isolate, which is then genomically analysed at Lab B. Reliable systems need to be established to ensure efficient transport of isolates and communication of findings between laboratories.

Diagnostic equivalency must be established between human and animal health laboratories. Methods, testing regimes, susceptibility cut-offs etc. need to be aligned to ensure comparability of data across sectors. Multiple laboratory accreditation standards must also be considered.

The capacity of existing veterinary diagnostic laboratories to process increasing numbers of samples or undertake additional testing must also be prioritised. This will likely include new staff recruitment, up-skilling of existing staff, new equipment, larger facilities, accreditation costs, increasing consumables costs and associated administration requirements.

Funding

There are currently several business models in place for existing veterinary diagnostic laboratories. Some are independent, some are government-affiliated (Commonwealth and/or state/territory level) and some are integrated into a university structure that may or may not include some external contract work. These different business and funding models will affect the ability of each laboratory to participate in any national surveillance systems.

The cost of diagnostic testing is currently borne entirely by animal owners. Diagnostic testing is an added expense for animal owners that is often portrayed as optional. Subsidising the cost to animal owners would be a significant incentive to encourage behaviour change and increase testing rates. Vets also need to be supported in encouraging animal owners to agree to diagnostic testing.

Logistics

It is imperative that laboratories and veterinarians are closely engaged in the development of a surveillance system. The success or failure of any system will depend on the ability of these key stakeholders to use it. The new system must be efficient and easy to use. Veterinarians are already under extreme pressure. If a new system is too difficult or time-consuming to engage with, it will not be used.

There is no single system in use for the collection of veterinary prescribing data at practitioner-level and some vet practices continue to use paper records. A surveillance system will need to incorporate multiple data sources and formats.

Logistical concerns are especially important for major livestock industries and vets in remote areas. It can be extremely difficult to physically get samples from a farm to a diagnostic laboratory in a timely manner. There is a need to consider how these issues could be addressed.

What principles should influence which microbe, AMR or agents are included in a One Health surveillance system? Other considerations in prioritising antimicrobial resistance or use?

Clear and transparent objectives are critically important – what is the question that surveillance is intended to answer? There must be clarity on what is being monitored, how and *why*. Surveillance activities could be directed at specific antimicrobials, antimicrobial classes, diseases (human-only, animal-only and/or zoonotic infections), resistance to specific antibiotics, resistance in specific pathogens, mechanisms of resistance and transmission pathways… resources are scarce, so priority must be given to allocating effort where it is most needed and can generate the greatest benefits.

AMA would strongly suggest that the initial focus is on zoonotic bacterial pathogens and antibiotic resistance. Viral and fungal resistance are important, but do not account for a major disease burden and can be incorporated into the system in future when resources permit.

For the animal sector, there is some key baseline work that needs to be completed in advance of any surveillance activities. Most notably, a list of priority pathogens needs to be established, similar to what exists for human health. This will allow effort to be targeted at the pathogens of greatest concern. AMA would suggest that initial surveillance is focussed on establishing surveillance for 4 or 5 key zoonotic pathogens. Surveillance scope can then be incrementally expanded as resources allow.

AMA notes that the use of APVMA sales data on antimicrobials is frequently discussed as a proxy for assessing antibiotic use. It is not possible to estimate use from sales data in a meaningful way. To do so would involve making many significant assumptions that would invalidate any conclusions. As discussed, AMA and MLA have already tried, on multiple occasions, to derive reliable information on use from sales data without success. We would be happy to discuss the specifics of these efforts (in confidence) at any time.

What are the biggest barriers to a coordinated, multisectoral One Health approach and how could they be addressed?

System focus

At present, One Health is heavily focussed on human health outcomes, and includes animal and/or environmental health as contributors to those human health outcomes. A true One Health approach

should also examine the role of human health in determining animal or environmental health outcomes. In particular, consideration of the impacts on animal health and welfare from decisions that prioritise human health and are made in the absence of appropriate risk assessment. For example, chicken meat production systems in North America which have removed the use of antibiotics that are *not* used in human health, have seen chicken mortality rates soar to 50-60% per flock. There is also strong scientific evidence that resistant infections and resistance genes frequently originate in humans and are subsequently transferred to animals in their care – both pets and livestock.

A true One Health approach in global activities is lacking. For example, the Codex Alimentarius Commission states that its forthcoming guidelines on monitoring and surveillance of foodborne antimicrobial resistance are 'One Health', yet the guideline fails to consider the role of humans in the food production chain. The guideline suggests sites for sampling throughout the production line, including equipment and the ground. However, whilst the greatest source of bacterial contamination in the food chain is likely to be from the people handling the food product, the guideline completely fails to include people in its sampling protocols.

It is vital that any surveillance system moves beyond detection and seeks to understand what the data actually means. In particular, understanding the origins of resistance and direction of transmission pathways, such as through genomic analysis of resistant isolates. This would support more efficient resource allocation through evidence-based, targeted interventions.

Funding

A major barrier to a coordinated multisectoral approach is funding. The Australian government has provided considerable funding to address AMR, but this has been directed to human health. All sectors that are expected to contribute to a One Health system should be centrally funded on an ongoing basis.

Further, there is an outstanding need for some foundational work on animal health to be completed before an appropriate surveillance system can be developed and implemented. Most notably, the animal sector does not yet have a list of priority zoonotic and animal-specific pathogens, resistances and genes to inform any surveillance activities and support data collection that is useful and meaningful.

Confidentiality

Data confidentiality is a key concern for the animal health sector. Data on antimicrobial sales and use is commercially sensitive and subject to anti-competition laws and regulations. The risks to individuals, companies and industries from such data being inappropriately interpreted and misrepresented are considerable. Australian farmers have already experienced illegal farm invasions and vandalism by those who disagree with livestock production. Sensitive data on antimicrobial use could easily be used in a similar way to target those who legally and legitimately use antibiotics in their production system. Sufficient de-identification of data may be difficult in some industries, such as those with small numbers of producers, highly centralised production systems or companies with small product portfolios.

Understanding usage data

Data on veterinary antimicrobial usage is particularly complex and significant work is required to identify appropriate metrics and methods that are sector-appropriate and meaningful in a One Health context. Some antibiotics are used in both human and animal medicine (known as 'shared class' antibiotics); some antibiotics are only available for use in human medicine; and some antibiotics are only used in animals.

Many antibiotic products are registered for use in multiple animal species, which makes it difficult to know what proportion has been used in a particular species. Dose rates for the same antibiotic can vary according to the reason for use, by production system, by species and within species (where dose rates may be based on age, sex or body weight). Veterinarians also have the legal right to prescribe antibiotics at a rate different to that on the label in order to protect animal health and welfare, and record keeping requirements for off-label use vary by jurisdiction.

There are significant logistical issues associated with collecting data on antimicrobial use in animals. There are multiple commercial software systems in use in veterinary clinics, as well as bespoke systems and practices that still rely on paper records. The type and detail of veterinary records will vary depending on the context (for example, companion animal practices versus cattle feedlots or chicken meat farms). State and territory requirements for veterinary record keeping also vary.

The drivers of antibiotic use are also significantly different by sector. A household pet is more likely to be treated similarly to a human family member, where the cost of testing and treatment is considered against the emotional value of the pet. In comparison, a livestock farmer must balance the burden of morbidity and mortality against the cost of treatment, the economic value of the animal, logistical demands (such as needing to handle treated animals and observe withholding periods), and other production costs.

Data on veterinary use of antimicrobials is often inappropriately used as a driver towards zero usage. The complete removal of antibiotic use in all animals is unrealistic and undesirable; bacteria are ubiquitous in the environment and even with the best possible care, animals will continue to get bacterial infections, just as humans will. It is essential that antibiotics remain available for veterinary use to protect animal health and welfare.