Antimicrobial use governance in the Australian food animal sector

Prepared by FAI on behalf of World Animal Protection 2021

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About FAI

FAI is a multi-disciplinary international team of farmers, veterinarians, scientists, designers, copy writers and strategists with first-hand experience of food production and its challenges. Through strategic partnerships with leading food brands and organisations, we implement better farming practices, on land and at sea. Our 3Es framework of Economics, Environment and Ethics guide us toward a sustainable food system.

FAI have offices and agriculture R&D sites in the UK, Brazil, Norway and the USA. We work with farmers, suppliers and retailers to identify the most important problems and mobilise science, practical expertise and evidence to find the most effective solutions. Our strategic and evidence-based approach is focused on driving meaningful improvements across supply chains, to mitigate risks and realise long-term business benefits for our partners, by inspiring producers to meet and exceed key performance outcome measures, rather than telling farmers how to farm.

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Glossary

Antibiotics are naturally occurring, semi-synthetic or synthetic substances that kill or inhibit the growth of bacteria. Antibiotics are a specific sub-set of antimicrobials. These include ionophore antibiotics.

Antibiotic resistance is the ability of bacteria to grow or survive in the presence of an antibiotic agent. The effect of this phenomenon is to make an antibiotic ineffective at treating infection with these bacteria in an individual (animal, human or plant).

Antimicrobials and Antimicrobial Use (AMU): Antimicrobials are naturally occurring, semi-synthetic or synthetic substances that kill or inhibit the growth of microbes. These medicines can include antibiotics, antivirals, antifungals and antiparasitics – they are medicines used to prevent and treat infections in humans, animals and plants.

Antimicrobial resistance (AMR) is the ability of microbes to grow or survive in the presence of an antimicrobial agent. The effect of this phenomenon is to make an antimicrobial ineffective at treating infection with these microbes in an individual (animal, human or plant).

ASTAG Ratings: The ranking of antimicrobials based on their importance to human and animal health by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG), most recently in 2018.

Critically-important Antimicrobials (CIAs): The World Health Organisation's latest guidelines (2019) on classification of the critically-important antimicrobials for human health. The highest priority critically-important antimicrobials (HP-CIAs) defined in this list of relevance to the food animal sector are the fluoroquinolones, modern cephalosporins, macrolides and colistin.

Food-producing animals: Any animal that is fed, bred or kept for the production of food for human consumption, including animals that are not used for human consumption, but that belong to a species that is normally used for human consumption. These species include, but are not limited to, cattle, sheep, pigs, poultry and salmonids.

Growth promotion is the continuous use of antibiotics in-feed, often at sub-therapeutic dose rates, to increase growth rates and feed efficiency in food-producing animals.

Metaphylaxis (or metaphylactic treatment) is the treatment of a group of animals in which one or more of the animals, or previously 'in-contact' animals, are showing clinical signs of a disease.

Microbes are microscopic organisms, which can be further defined as 'living things not visible to the naked eye'. These include bacteria, viruses, fungi and protozoa.

Prophylaxis (or prophylactic treatment) is the treatment of a healthy animal or group of animals to prevent infection, before an expected disease challenge. Prophylactic antibiotic use is commonly administered in feed or water for food animals.

Treatment or therapy is the administration of a medicine to an individual animal, or a group of animals, showing clinical signs of a disease.

Withdrawal period is the time that must elapse between the last administration of a veterinary medicine to an animal and the slaughter or production of food from that animal, to ensure that the food does not contain levels of the medicine that exceed the maximum residue limit.

PREFACE

World Animal Protection is working to create a world free from cruel factory farming, where all farmed animals are given good lives. Factory farming and poor animal welfare practices can also lead to the excessive use of antibiotics, which creates a threat to both human and animal health. This report, commissioned by World Animal Protection and written by the team at FAI Farms, found that Australia is lagging behind other developed countries when it comes to the way in which antibiotics are used in animal agriculture in a number of critical areas. The report also demonstrates a worrying lack of transparency, showing that the Australian public is being kept in the dark on what antibiotics are being sold for animal agriculture and how they are being used. Existing research demonstrates that the overuse of antibiotics on factory farms can lead to the emergence of superbugs.[1] Superbugs can spread from farms, to workers, into the environment and on to the food chain, posing a real threat to human health.

Superbugs are bacteria resistant to antibiotics, which means the antibiotics are no longer effective at treating the bacteria that cause infections. Antibiotics are one of a group of medicines known as antimicrobials. Microbes are germs, bugs or viruses that can infect a human or animal host. Antimicrobial resistance (AMR) is one of the most significant health challenges of our time. Currently, it is estimated that AMR, or superbugs, are responsible for 700,000 human deaths each year. This is projected to rise to 10 million deaths a year by 2050. In a world without effective antibiotics, a number of lifesaving procedures could be lost. This includes procedures and treatments like chemotherapy, heart bypass surgery, hip and joint replacements, organ transplants, or caesarean delivery.[2]

In recognition of the serious threat posed by superbugs, countries around the world have taken action to curb irresponsible use of antibiotics in animal agriculture. Critically, 90 countries including the United Kingdom (UK) and those across the European Union (EU) have taken steps to ban the use of antibiotics for growth promotion. Using low dose, sub-therapeutic levels of antibiotics for an extended period of time can foster resistance, helping to create superbugs. Despite this, Australia continues to allow antibiotics to be given to farmed animals to promote faster growth and weight gain. Other countries first began phasing out the use of antibiotics to promote growth in the 1990s, and it is alarming to see that Australia is allowing this risky practice to continue, more than 20 years after concerns were first raised. The failure to introduce similar regulations could also have implications for trade between the European Union and Australia, given the EU regulations require similar standards be met for imported goods. With negotiations for a free trade agreement between Australia and the EU currently underway, it is worth considering what is at risk from a trade and economic perspective if the Government fails to ban the use of antibiotics for growth promotion.

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[1] See, e.g., Aarestrup, F. M., Kruse, H., Tast, E., Hammerum, A. M., & Jensen, L. B. (2000). Associations between the use of antimicrobial agents for growth promotion and the occurrence of resistance among Enterococcus faecium from broilers and pigs in Denmark, Finland, and Norway. *Microbial Drug Resistance*, *6*(1), 63

[2] See, e.g., World Health Organisation, 'Antimicrobial resistance' (webpage 2021) < https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>

Australia also permits antibiotics to be used preventatively; that is, before there are clinical signs of sickness in animals. Doses of antibiotics can be administered in feed and water supplies to entire herds or flocks of animals that are not sick. Commonly, routine group prophylactic use occurs in situations where animals are kept in low welfare conditions.[3] This may include situations where breeds with low welfare outcomes are used (such as fast-growing broilers), or where animals are fed poor diets high in grain or kept in overcrowded conditions.[4] Rather than addressing the root cause of these issues that may lead to sickness in groups of animals, there is evidence to suggest that antibiotics are being administered preventatively, to allow poor animal welfare standards to continue.

The Australian Government has not expressly prohibited the use of antibiotics for routine disease prevention. Industries including the chicken industry acknowledge that they are still currently using antibiotics in a preventative way – including limiting the risk and spread of diseases such as necrotic enteritis.[5] Studies have demonstrated that any conditions that increase stress for broiler chickens, including high stocking densities, can predispose them to developing necrotic enteritis.[6] While a lack of transparent public reporting from the agriculture industry means that we do not have a clear picture of usage patterns across different sectors, it appears clear that some level of antibiotics are being used on a routine preventative basis. Routine group prophylactic use can increase overall volumes of use and foster resistance to antibiotics and giving rise to superbugs. This is why the practice is being phased out in jurisdictions like the EU. The European Union has taken steps to phase out the routine use of preventative antibiotics for groups of animals; with a complete ban coming into effect from the end of January 2022.[7] Once again, if Australia fails to keep up with the new standards being introduced globally, our ability to maintain exports to countries including those in the EU may be impacted. While the Australian Government is to be commended on their decision not to allow certain antibiotics that are critical to human health to be used in animal agriculture, the continued use of other antibiotics for growth promotion and for administration to groups of animals with no diagnosed illness should not be permitted.

Finally, this report demonstrated a concerning lack of transparency in the reporting of antibiotic use in farmed animal agriculture here in Australia. The last publicly available data on sales of veterinary antibiotics used in agriculture is now more than 10 years out of date. The report, published in 2014,

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[3] World Animal Protection, Fuelling the Pandemic Crisis (Report 2020) 6.
[4] See, e.g., Compassion in World Farming, Dutch slower growing broilers require less antibiotics than fast growing chickens (Report 2019), summary available at https://www.ciwf.org.uk/media/7438137/dutch-slower-growing-broilers-require-less-antibiotics-than-fast-growing-chickens.pdf.
[5] Australian Chicken Meat Federation, Antimicrobial stewardship in the Australian chicken meat industry, page 7, available at https://www.chicken.org.au/wp-content/uploads/2021/05/ACMF_chicken-meat-AMS-report_Version2_FINAL.pdf
[6] Vasilios Tsiouris, 'Poultry management: a useful tool for the control of necrotic enteritis in poultry' (2016) PubMed 45(3)323.
[7] Regulation (EU) 2019/4 of the European Parliament and of the Council of 11 December 2018 on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC

covered sales of veterinary antibiotics from 2005-2010. The public are being kept in the dark about what antibiotics are being sold to the agriculture industry and how they are being used. Given the very real threat posed by the rise of superbugs, the public have a right to know what is being sold and how it's being used. Other countries including the UK and the United States have mandatory reporting every 12 months, and this information is made publicly available on a regular basis. This allows for clear oversight, so the agriculture industry and the Government can be held to account on whether their policies are ensuring responsible use of antibiotics. We have no such transparency and accountability in Australia.

The issues raised in this report should not be unfamiliar to the Australian Government. The Joint Expert Technical Advisory Committee on Antibiotic Resistance released a report in 1999 that contained 22 key recommendations for management of antibiotic use in food-producing animals. While the Government initially supported the recommendations, more than 20 years later, concrete actions to introduce the necessary reforms remain scarce. Various committees have been formed and then disbanded, leading to inaction. The Government cannot afford to delay actioning the recommendations of these committees any longer. The World Health Organisation has labelled antimicrobial resistance as one of the top 10 global public health threats facing humanity, outlining the implications for human health as well as the economy.[8] The time to act is now.

The Australian Government must act on the final recommendations from World Animal Protection put forward at the end of this report. The use of antibiotics for growth promotion must end immediately and the Government also needs to ban the routine use of antibiotics for prevention of disease in groups of animals. Better monitoring and mandatory public reporting of the sales and use data for veterinary antibiotics in animal agriculture must be introduced, including a national antimicrobial resistance monitoring scheme. We note that the second edition of the antimicrobial stewardship in Australian livestock industries report notes that Australia currently only has 'ad-hoc' systems in place to capture information on antimicrobial use, and antimicrobial resistance.[9] The Government needs to commit to improving this situation to ensure a comprehensive monitoring program is in place, that captures antimicrobial use in agriculture, as well as the incidence of antimicrobial resistance on farms, in the environment and in our food chain.

Irresponsible use of antibiotics increases the risk of superbugs. We need transparency and accountability to ensure that the welfare of animals, and the health and safety of our population, is not being put at risk.

Ben Pearson, Interim Country Director

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[8] World Health Organisation, Antimicrobial resistance (webpage 2021) < https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>

[9] Jo Coombe, Aantimicrobial stewardship in Australian livestock industries (Report 2021), 7, available at https://aiasrdestrategy.com.au/wp-content/uploads/2021/07/AMS-in-Livestock-Report-2021.pdf

Executive Summary

Antimicrobial resistance (AMR) is amongst the most significant and pressing health challenges facing human civilisation. It is responsible for an estimated 700,000 human deaths per year, which is projected to rise to 10 million by 2050, with a predicted cumulative cost to global economic output of 100 trillion USD[1]. These impacts are due to a decline in the efficacy of the antimicrobial compounds that have defined and supported modern medical systems.

Antimicrobial use in food animals is understood to contribute towards the global health burden of AMR affecting public health. Reducing use of antibiotic agents in all health spheres including in the food animal sector is therefore a public and animal health imperative, and ensuring responsible use of antibiotics in all animals must play an important role. Considering the importance and magnitude of the animal agriculture sector in Australia and the rising global threat of AMR, it is important to understand current practices and trends in antimicrobial use in the farming sector in the country.

This report was commission by World Animal Protection to FAI, with the aim of synthesising information and evidence around the governance of antimicrobial use and resistance in relation to the food animal sector in Australia. The results of this literature review highlight the strengths and weaknesses of Australia's antimicrobial stewardship programmes.

The strengths include Australia's progressive stance on the use of certain antimicrobials listed as 'highest priority critically-important' (HP-CIA) antimicrobials to human health by the World Health Organisation (WHO): specifically, the fluoroquinolones, colistin and fourth-generation cephalosporins are not approved for use in food animals, a position rarely seen in other jurisdictions. It is thought that this has led to relatively low prevalence of resistance to antimicrobials of importance to human health (as defined by Australia's ASTAG group) detected in food-borne pathogens from livestock sources. The weaknesses of Australia's antimicrobial stewardship programmes include the lack of regular public reporting of antimicrobial use and resistance data from the food animal sector. Two reports are available in the public domain, but the most recent report was published in 2014. In contrast, a number of other comparison member countries of The Organisation for Economic Co-operation and Development (OECD countries) have reported these data on an annual basis for over 10 years. In addition, antimicrobial growth promoters are still permitted in Australia. Although the antibiotics currently used for this purpose are not medically-important antimicrobials, other comparison OECD countries have either banned or are phasing out all growth promoter use.

Further details regarding the findings of this report are summarised below.

Antibiotic use in the food animal sector in Australia

- *Volumes of use*: Many countries collect and report data on volumes of antibiotics sold for use in food animals. Australia last reported their antimicrobial sales data in 2014, documenting sales of between 482 and 655 tonnes of veterinary antimicrobials for use in food animals annually, during the time period 2005 to 2010. The trend in sales suggest little significant change in volumes of usage over the reporting period. 98% by weight of all veterinary antimicrobials sold were intended for use in food animals. The 2014 report does not normalise antimicrobial sales data for the animal populations in Australia, therefore trends in usage in terms of mg/livestock unit or mg/kg biomass cannot be ascertained.

- *Antibiotic classifications*: Antibiotics have been classified according to their importance to human health by the WHO (the 'critically-important antimicrobials' classification and the AWaRE classification). The antimicrobials used in food animals in Australia are listed in a 2014 report

published by the Australian Government, and are categorised in terms of their approved uses (therapeutic, coccidiostat, growth promoter). Antibiotics from all WHO classifications are being used in food animals for various purposes in Australia. Of particular note are the macrolides – a class of antimicrobials listed as ‘highest priority critically-important’ (HP-CIA) for human health by the WHO, which are approved for use as growth promoters. However, the pharmaceutical industry voluntarily removed the growth promotion label claim from medically-important antibiotics in 2017. Secondly, sulphonamides and diaminopyramidine potentiators are classified as ‘highly-important’ for human health by the WHO, but are approved as coccidiostats for food animals.

Australia has adopted a progressive position with regards to the HP-CIAs fluoroquinolones, colistin and fourth-generation cephalosporins – these classes of antimicrobials are not approved for use in food animals, a position rarely seen in other jurisdictions. However, the issue of co-resistance/co-selection highlights the deep complexities in the field of antimicrobial resistance, and how removing individual classes of antibiotics from use cannot replace broader use reductions and stewardship of *all* classes of antimicrobials.

There is no publicly available information regarding ‘off-label’ use of veterinary antimicrobials in Australia.

- *Latest data*: The most recent official government report on antimicrobial usage (sales) was published in 2014. There has, however, been a number of recent studies documenting antimicrobial use practices in Australia. A small selection of these papers highlight the significant levels of use of ionophore growth promoters in the Australian beef feedlot sector, the varied and often inappropriate antibiotic dose rates prescribed by Australian veterinarians, often attributed to inappropriate drug labelling, and the antibiotic agents frequently used, and their reasons for use, in the pig sector.

- *Reasons for use*: In the 2014 government report, antibiotic sales by antimicrobial class are categorised into three reasons for use: therapy (includes both therapy and prophylaxis), growth promotion and coccidiostats. Coccidiostat use accounted for the majority (51%) of veterinary antimicrobial sales for food animals between 2005 and 2010, with therapy (therapy and prophylaxis combined) and growth promotion accounting for 43% and 6% of sales, respectively. Sales volumes for therapy and prophylaxis cannot be disaggregated, due to the limited information pharmaceutical companies hold regarding use of medicines, post-sale. In terms of route of administration, 76% of all antibiotic sales for food animals (2005-2010) were indicated for in-feed administration, which facilitates group therapy and prophylactic treatment. There is a general narrative of reduced support for antimicrobial growth promotion in Australia, and in 2017, the pharmaceutical industry voluntarily agreed to remove growth promotion label claims from antimicrobials of importance to human health. The use of macrolides as growth promoters became ‘off-label’ thereafter; however the use of other non-medically-important antimicrobials as growth promoters persists.

- *Trends in use*: According to the 2014 Australian Government report, overall sales of antimicrobials for use food animals decreased slightly between 2005 and 2010. Reductions in sales were most notable for growth promoters, although this was attributed to the decline in sales of non-medically-important antimicrobial growth promoters, while sales of macrolide growth promoters actually increased over this time period. However, significant fluctuations in sales volumes for different antimicrobial classes, species and reasons for use were observed, and in the absence of more recent sales data over longer time periods and normalised by animal population sizes, trends should be interpreted with caution.

- *Use in the human medical sector*: The Antimicrobial Use and Resistance in Australia (AURA) surveillance system provides integrated reporting on priority organisms and antimicrobial use in the human medical sector. The latest report indicates increased use of antibiotics in the Australian

medical sector, from 933 Defined Daily Doses (DDD) per Occupied Bed Days (OBDs) in 2016, to 957 DDDs/1000 OBDs in 2017. Different metrics for reporting antibiotic sales/use for the animal and human health sectors make direct comparisons challenging. However, one study extrapolated data from animal and human sources, and determined that for antimicrobials of importance to human health, an average of 182,138 kg were sold per year for animal use between 2005 and 2010; compared to 121,076 kg per year for use in humans. Animal antibiotic use therefore accounted for 60% of total sales by weight, over the period 2005-2010.

Comparative antibiotic use across OECD countries

- *Comparing Australia's antimicrobial sales for food animals with other OECD countries, by volume*: The Netherlands, the United Kingdom (UK) and the United States (USA) have reported antimicrobial sales annually for more than 10 years; Australia has provided two reports – for 1999-2002 and 2005-2010. These reports show that in the Netherlands, UK and USA, 461 tonnes, 456 tonnes and 13,287 tonnes of antimicrobials were sold for food animals in 2010, respectively. 644 tonnes were sold for food animals in the same year in Australia. However, as Australia's sales data are not corrected with animal population-based denominators, meaningful comparisons on a per-livestock unit basis between the different countries cannot be drawn. For the Netherlands, UK and USA, a decreasing trajectory of antimicrobial sales for food animals between 2010 and 2018 is documented, but in the absence of sales data for Australia beyond 2010, such sales trends cannot be determined.

- *Antibiotics used in Australia and prohibited in other countries*: The use of antimicrobial growth promoters is still permitted in Australia, but the practice has been banned in the EU since 1 January 2006 and is being phased out in the USA. According to the 2014 government report, growth promoters constituted 4-7% of the total volume of antimicrobials sold in Australia (2005-2010). On the other hand, WHO HP-CIAs fluoroquinolones, colistin and fourth-generation cephalosporins are not approved for use in food-producing animals in Australia, whilst permitted in most of the other OECD countries.

- *The ASTAG system*: Although the WHO's critically-important antimicrobials (CIA) list is the global standard for ranking important antimicrobials for human medicine, the application of this ranking system varies from country to country according to the local context. The Australia Strategic and Technical Advisory Group on AMR developed a separate ranking system - 'ASTAG' - for Australia. The ASTAG ratings, for some classes of antibiotics, are in agreement with the WHO's CIA list. For example, some antibiotics rated as WHO HP-CIAs are ranked as 'High' importance by ASTAG. However, there are some notable differences. For example, macrolides, moderate-spectrum penicillins and several aminoglycosides are ranked as 'Low' importance by ASTAG, but rated as critically-important antimicrobials according to the WHO. These differences may be due to lower levels of use of certain antibiotics and lower health burdens due to specific pathogens of interest in Australia.

  The European Union (EU) and the USA have also developed their own ranking systems for antimicrobials. The EU's rating system is largely in agreement with the WHO CIA list, with the notable exception of the macrolides, which are HP-CIAs according to the WHO, but assigned Category C ("Caution") by the European Medicines Agency (EMA), and therefore are not subject to any recommended use restrictions in food animals. In the USA, the Food and Drug Administration (FDA) have also developed an antibiotics importance rating, which differs significantly to the WHO CIA list. These examples demonstrate the importance of locally relevant antimicrobial stewardship strategies and the protection of certain antimicrobial classes for human health according to in-country usage and resistance patterns. However, it also highlights the challenges in international harmonisation of antibiotic use policies.

- *Regulations on antibiotics of medium and higher importance*: ‘High’ ASTAG ranking antimicrobials are generally not registered by the Australian Pesticides and Veterinary Medicines Authority (APVMA) for use in food-producing animals, and antibiotics with ‘Medium’ and ‘High’ ratings are used for therapeutic and prophylactic purposes only – they are not registered for use as growth promoters. Furthermore, certain ‘High’ importance antimicrobials including fluoroquinolones, fourth-generation cephalosporins and colistin are not registered for use in food animals in Australia.

- *Use of antibiotics for group prophylaxis:* Data concerning the volume or frequency of use of antibiotics for group prophylaxis in animals in Australia – and in many other countries – are not available. The difficulties for registrant companies to estimate the proportions of their products used for therapeutic or prophylactic purposes is acknowledged.

Current surveillance, monitoring and reporting requirements for antimicrobial use in the Australian food animal sector

- *Monitoring and reporting requirements:* There is currently a legal requirement for pharmaceutical companies to provide to the APVMA an annual return detailing the quantities of veterinary chemicals that were imported, manufactured or exported during that year. The Australian Government has collated this data relating to sales of antimicrobials intended for use in food animals, in two previous reports. There are also a number of published papers available highlighting aspects of antimicrobial use practices amongst farmers and veterinarians in Australia.

- *Compliance with the Government’s National Antimicrobial Stewardship plan:* The 2015 Strategy is the first national, cross-sectoral response to the AMR threat in Australia. The seven objectives addressed in this Strategy were translated into action via the Implementation Plan. The second National Antimicrobial Stewardship Plan was released in 2020. Multiple stakeholder activities in contribution to the strategic objectives have since been described; however, there is limited information available publicly regarding the progress made towards the objectives.

- *Implementation of the JETACAR recommendations:* The 1999 JETACAR report laid out 22 recommendations for management of antibiotic use in food-producing animals. The Australian government responded with strong support and intent to establish several committees. However, subsequent actions are unclear, and have been critiqued by the Senate (Finance and Public Administration References Committee).

- *Integrity of data on AMR and AMU in the Australian food sector:* There has been substantial work investigating AMR and AMU in the broiler and pig industries in Australia. Research has demonstrated relatively low levels of antimicrobial resistance in broiler chickens, and the relatively higher prevalence of resistant and multi-drug resistant strains in food-borne pathogens in pigs. In both species however, detected resistance was usually to antibiotics of lower significance to human health. Due to Australia’s progressive position on the use of fluoroquinolones, colistin and fourth-generation cephalosporins, where resistance to WHO HP-CIAs were detected, this was attributed to historical antibiotic use, possible off-label use, and an increasingly globalised food supply chain. Fewer studies are available for the aquaculture, beef and dairy sectors, and further research is warranted.

- *Evidence of AMR along the supply chain:* The government funded study ‘Pilot surveillance program for antimicrobial resistance in bacteria of animal origin’ reported evidence of AMR in the major food animals. Among the antibiotics with established resistance, all but one antibiotic was of low importance to human medicine (according to ASTAG). Relatively low levels of resistance to WHO HP-CIAs were detected in cattle and poultry, but more significant levels of resistance to CIAs were

found in pigs. It has been suggested that this finding may be due to the relatively higher level of antibiotic use in the pig sector.

- *Comparison with the OIE/WHO/FAO recommendations:* WHO's Global Action Plan on AMR, OIE's Terrestrial and Aquatic Animal Health Codes and FAO/WHO's Codex Alimentarius Code of Practice all proposed recommendations and strategies for establishing unified AMU and AMR surveillance systems in member states. The Australian Government adopted many principles into their national strategies, but is yet to adopt a surveillance programme for regularly collecting and publicly reporting AMU and AMR data relating to food animals and the food chain.

- *Comparison with other OECD countries:* The Netherlands, Denmark, UK, EU, Canada and the US have all established national/multinational monitoring and reporting programmes for AMU and AMR in food animals. Australia most recently published AMU data relating to food animals in 2014, and is yet to implement its own programme for more regular surveillance and reporting.

- *Funding allocation:* There are several notable surveillance programmes for AMR and AMU funded by different Australian government agencies. However, there is insufficient data to accurately calculate the percentage of GDP allocated to enhance surveillance, monitoring and reporting programmes for AMR and AMU in the Australian food animal sector.

- *Comparison of Australia's spending on AMR with other OECD countries:* There is insufficient data available in the public domain to accurately compare funding allocated to AMU/AMR across multiple OECD countries. However, as a broad indictor of capacity, the annual tripartite AMR country self-assessment survey found that 15 out of 49 high income countries, including the USA and the Netherlands, reported implementation and funding sources for their national AMR action plans. Australia, UK and Denmark reported that a National AMR action plan was approved by government, with a budgeted operational plan and monitoring arrangements in place.

Introduction

Antimicrobial resistance (AMR) is amongst the most significant and pressing health challenges facing human civilisation. It is responsible for an estimated 700,000 human deaths per year, which is projected to rise to 10 million by 2050, with a predicted cumulative cost to global economic output of 100 trillion USD[1]. These impacts are due to a decline in the efficacy of the antimicrobial compounds that have defined and supported modern medical systems.

The most significant risk factors for antimicrobial resistance in human patients are underlying disease, antibiotic use and invasive procedures in health-care settings[2]. However, there is a growing consensus that antimicrobial use (AMU) in food animal agriculture is a key driver of resistance pressure, with a growing, albeit complex, evidence base implicating antibiotic use in food animals as a risk factor for human disease caused by antimicrobial resistant infections[3,4]. In addition to presenting a nascent public health risk, antibiotic use in animals favours the emergence of AMR with animal health and welfare impacts[5]. Reducing use of antibiotic agents in all health spheres is therefore a public and animal health imperative, and ensuring responsible use of antibiotics in all animals must play an important role, with a particular focus on mitigating high level use in certain regions, species and husbandry systems[6].

Food animal agriculture is an important and growing sector in the Australian economy catering for the domestic and the international trade markets, the latter of which accounts for the majority of agricultural production[7]. Given the rising threat of AMR, it is important to understand current practices and trends in antimicrobial use in the farming sector in Australia. However, the Australian Government has not publicly reported antibiotic use or sales in the farm animal sector since 2014[8], and further investigation into usage levels and governance is warranted – issues that are explored in this report.

About this report

This report was commissioned by World Animal Protection to FAI. It consists of a non-systematic desk-based literature review including relevant peer-reviewed and grey literature and white papers, and is intended to address the research questions presented by World Animal Protection in the document Brief 0.1 (23/02/21). Only source materials accessible online in the public domain were utilised for this project, hence unpublished works or stakeholder insights were not included.

For clarity, a glossary is provided to define the various terminologies used in this report. However, with a focus on the problem of *antibiotic* resistance, and in line with the European Food Safety Authority (EFSA)[9], the terms ‘antimicrobial’ and ‘antibiotic’ will be used interchangeably in this review.

1. Antibiotic use in the food animal sector in Australia

In the first section of this report, we summarise the literature on antibiotic use in food animals in Australia, in terms of volumes, classifications and trends, as well as usage in the human medical sector.

a. Volumes of use

Data on antimicrobial usage in food-producing animals are universally scarce, due to a lack of surveillance systems to track antibiotic usage in the majority of countries globally. The collection of robust data on antimicrobial usage from farms is challenging – in many countries, paper medicine use records are still used, although electronic medicine books and software to record and monitor data in machine-readable formats are increasingly available. Usage records are usually based on actual use in animals, recorded by farmers and stockpersons, or veterinary sales or prescriptions, which are assumed to align closely with actual use.

More commonly however, countries collect and report sales data reported by pharmaceutical companies. Volume of antibiotics sold by Marketing Authorisation Holders (MAH) is a blunt metric for estimating antimicrobial use in animals, due to the following limitations: they do not account for wastage resulting from damage or expiry of products in transport and storage, they do not include drug imports or “off-label” use of human pharmaceuticals in the animal sector, and they are likely to include drugs purchased and exported for use in other countries. Additionally, in many reports, antimicrobial sales data are not normalised for the animal population, meaning they do not necessarily reflect changes in use on a per-animal or per-kilogram biomass basis. Finally, total sales figures do not account for differences in potency between the antimicrobial drug classes: changes in sales of a potent antimicrobial agent of greater concern to human health will be less significant in volume due to their usually lower dose rates, compared to changes in sales of less potent antibiotics with higher dose rates.

Notwithstanding these limitations, collecting sales data from MAHs is practically easier than collating farm usage or veterinary prescription data at national level, and allows the useful monitoring of macro-trends in populations. Many countries, including Australia, currently rely on the reporting of pharmaceutical sales data as an indicator of usage.

Antimicrobial sales in food animals in Australia were last reported in 2014, relating to sales between the years 2005 and 2010[8]. This report indicated that between 482 and 655 tonnes of veterinary antimicrobials were sold for use in food animal species annually in the years 2005-2010, accounting for 98% by weight of all veterinary antimicrobials (see **Figures 1 and 2; Table 1**). Over the five-year monitoring period, usage in the various species fluctuates (**Table 1**), with the low level of reported sales in 2008-2009 thought to be attributed to under-reporting. Therefore, the trends in use are variable and suggest little change over the reporting period, although it should be noted that these data are not normalised for changes in animal populations and should be interpreted accordingly.

A more detailed breakdown of usage by species (for example, disaggregating cattle and sheep, types of poultry, and including aquaculture), and data relating to more recent usage levels, are currently unavailable in the public domain and therefore more recent trends in use cannot be ascertained.

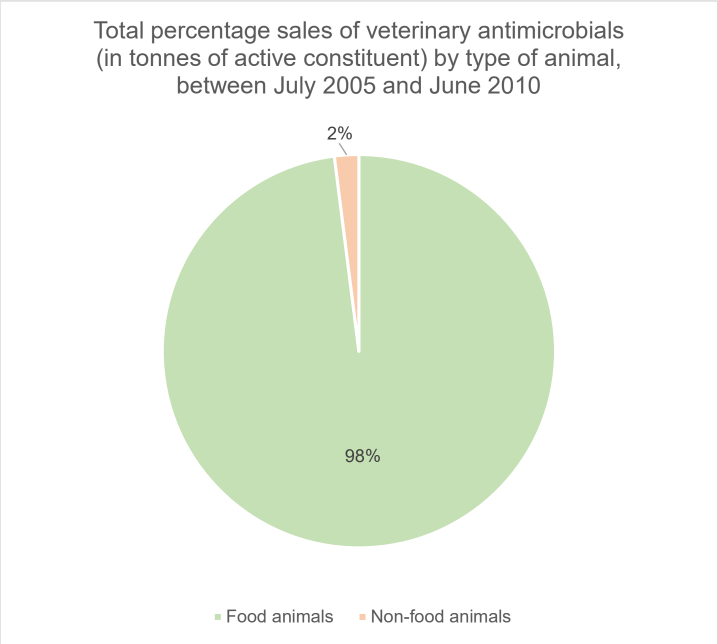


Figure 1: Total percentage sales of veterinary antimicrobials (in tonnes of active constituent) by type of animal, between June 2005 and June 2010, inclusive. Data from Australian Government (2014)[8].

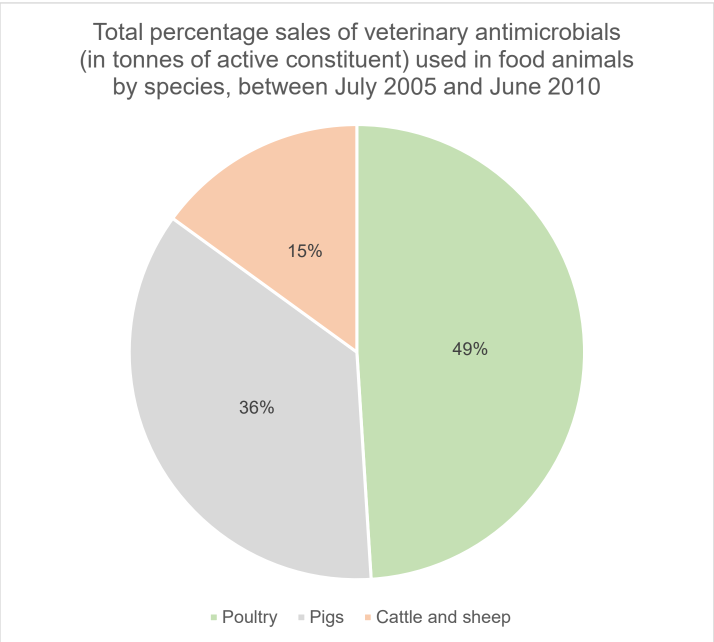


Figure 2: Total percentage sales of veterinary antimicrobials (in tonnes of active constituent) by species, between June 2005 and June 2010, inclusive. Data from Australian Government (2014)[8].

Table 1: Total sales of veterinary antimicrobials (in tonnes of active constituent) for use in food animals by species and year (July 2005 to June 2010). Table modified from Australian Government (2014)[8].

SPECIES	2005-6	2006-7	2007-8	2008-9	2009-10	Overall trend (2005-2010)
Cattle and sheep	163.8	149.7	125	106.9	133.3	↓
Poultry	385	318.6	351.9	276.4	406.4	↑
Pigs	106.1	103.1	103	98	104.2	↓
Other food animal species	0	0.1	0.1	0.1	0.2	↑
TOTAL	**655**	**571.5**	**580**	**481.5**	**644**	↓

b. Antibiotic classifications

Table 2: World Health Organisation classifications (critically-important classification and AWaRe classification) of veterinary antimicrobials sold in Australia (July 2005 – June 2010) and the purpose for which they are approved for use in food animals in Australia. [8,10,11]

Antimicrobial class	Importance classification for human health		Purposes for which they are approved in food animals*		
	*WHO classification**	*AWaRE classification*	*Therapy*	*Coccidiostat*	*Growth promoter*
Aminocoumarins	Unlisted[∞]	Unlisted[¥]	✓		
Aminoglycosides	CIA	Access / Watch / Reserve	✓		
Amphenicols	HIA	Access	✓		
Arsenicals	Unlisted[∞]	Unlisted[¥]			✓
Benzamides	Unlisted[∞]	Unlisted[¥]		✓	
Carbanilides	Unlisted[∞]	Unlisted[¥]		✓	
Cephalosporins	HIA / HPCIA[Δ]	Access / Watch / Reserve	✓		
Glycophospholipids	Unlisted[∞]	Unlisted[¥]			✓
Lincosamides	HIA	Access	✓		
Macrolides	HPCIA	Watch	✓		✓
Nitroimidazoles	IA	Access	✓		
Oligosaccharides	Unlisted[∞]	Unlisted[¥]	✓		✓
Robenidine	Unlisted[∞]	Unlisted[¥]		✓	
Tiamulin	IA	Unlisted[¥]	✓		
Penicillins & beta-lactamase inhibitors	HIA / CIA[Δ]	Access / Watch	✓		
Polyether ionophores	Unlisted[∞]	Unlisted[¥]		✓	✓
Polypeptides	IA	Unlisted[¥]	✓		
Quinoxaline	Unlisted[∞]	Unlisted[¥]	✓		✓
Streptogramins	HIA	Watch / Reserve	✓		
Sulfonamides & diaminopyramidine potentiators	HIA	Access	✓	✓	
Tetracyclines	HIA	Access / Watch / Reserve	✓		
Triazines	Unlisted[∞]	Unlisted[¥]		✓	

** IA = Important antimicrobials, HIA = highly important antimicrobials, CIA = critically important antimicrobials, HPCIA = highest priority critically important antimicrobials (WHO 2019).*

[∞] Antimicrobial classes described as 'unlisted' are not included in the WHO's list of critically important antimicrobials for human health i.e. they are not used in humans.

[¥] Antimicrobial classes described as 'unlisted' under the AWaRE classification do not appear in this list - most are not used in humans.

[Δ] Antimicrobial classes with two importance classifications include the cepalosporins - of which the first- and second-generation cephalosporins are HIAs and 3rd and higher generation cephalosporins are HPCIAs; and the penicillins - of which some (e.g. aminopencillins and those with beta-lactamase inhibitors) are CIAs, and others (e.g. amidinopenicillins) are HIAs.

Table 2 shows the classes of antimicrobial agents used in Australia in food animals, as named in the Australian Government's report *Quantity of Antimicrobial Products Sold for Veterinary Use in Australia,* published in 2014, and updated according to relevant available literature. The table documents the antimicrobial classes used, the purposes for which they are approved in food animals (therapy, coccidiostat and growth promotion) and their classifications according to the WHO's Critically-important Antimicrobials list and AWaRE (Access, Watch, Reserve) list.

The WHO's critically-important antimicrobials list ranks medically-important antimicrobials for risk management of antimicrobial resistance due to non-human use, based on: (1.) the availability of other therapies for treating serious bacterial infections in people, and (2.) the use of the antibiotic for infections arising from non-human sources[10]. The AWaRE list categorises antibiotics in terms of their importance in human medicine and their risk of resistance development, in order to guide their selection by medical practitioners for human patients[12].

As seen in **Table 2**, there is general alignment between the antibiotics ranked as highest priority critically-important (HP-CIA), and those on the Watch list (recommended only for specific, limited indications) and Reserve list (should only be used as a last resort when all other antibiotics have failed). The responsible use of antimicrobials for therapeutic indications in animals is broadly accepted as necessary in terms of its purpose to uphold animal health and welfare, and the table shows that a number of different medically-important antibiotics as defined by the WHO are used in Australia's food animals for this purpose (important, highly-important, critically-important and HP-CIA antibiotics). However, as discussed later in this report, antibiotic use for 'therapy' includes both therapeutic and prophylactic indications in the Australian Government's 2014 report, and usage levels for these different indications cannot be disaggregated.

Regulations around antibiotic use for growth promotion purposes, however, is variable in different jurisdictions. Growth promotion is generally not considered in line with responsible use practices, due to the associations between long courses of treatment at low doses for production purposes, and the development of antibiotic resistance with potential public health consequences[13–16]. Indeed, the use of growth promoters is thought to drive antimicrobial resistance by applying a prolonged sub-inhibitory selection pressure, enriching resistant bacteria, stimulating mutagenesis and promoting gene transfer between bacteria within the animal gut microbiome[13–16]. Furthermore, there are concerns that such practices may prop-up poor-welfare animal husbandry practices and environments[17–19] (see **Text Box 4**, later in this report).

Table 2 shows that six antimicrobial classes were licensed for use as growth promoters in Australia, although five of these are unlisted in terms of their importance in human healthcare. One class, however – the macrolides, which are HP-CIAs and on the Watch list - were approved as growth promoters, although label claims for growth promotion uses of medically-important antibiotics were voluntarily removed by industry following an agreement in 2017[20]. Prior to this in 2014, all products containing the macrolide tylosin were rescheduled to prescription-only ('S4')[21]. Growth promotion will be discussed in greater detail in section 1d.

Six antimicrobial classes are used as coccidiostats in Australia's food animal sector, most of which are unlisted in terms of their importance to human health. However, one class of antibiotic licensed for coccidiostat use is the sulphonamides and diaminopyramidine potentiators (e.g. trimethoprim), which are ranked as highly-important antimicrobials by the WHO**.** The use of coccidiostats in animal agriculture will be discussed in section 1d.

It is important to highlight that there are a number of medically-important antimicrobial classes not included in Table 2, as they are not registered for use in food-producing animals in Australia. These compounds most notably include three of the WHO's HP-CIA classes: the fluoroquinolones, colistin and

fourth-generation cephalosporins. This, in part, protects these agents from over-use in agriculture and veterinary settings, helping to preserve their efficacy for human medicine, and represents a progressive position regarding these particular HP-CIAs, rarely seen in other jurisdictions. However, the issue of co-resistance/co-selection highlights the deep complexities in the field of antimicrobial resistance, and how removing individual classes of antibiotics from use cannot replace broader use reductions and stewardship of *all* classes of antimicrobials. See **Text Box 1** for more information.

Text Box 1: Co-resistance

It is widely recognised in the scientific community that multi-drug resistance can occur through the mechanism of co-selection. Co-selection occurs when bacteria take up genetic elements, specifically plasmids, from other bacteria. Plasmids contain multiple genes, some of which confer resistance to a number of different antimicrobials (and antibacterial agents such as heavy metals). There are now many antimicrobial resistance genes that occur on plasmids alongside resistance genes to other classes of antibiotics. As a result, selection pressure favouring resistance to one class of antibiotic (e.g. tetracycline) can select for bacteria with plasmids containing resistance to several other antibiotics (e.g. cephalosporins). The phenomenon of co-selection is illustrated in a study by Kanwar et al. (2014)[22], amongst others.

Co-selection is one of the reasons why it is difficult to reverse resistance once it has been established in a bacterial population. It is insufficient to cease the use of one particular antibiotic if the resistance mechanisms are linked to resistance to other antibiotics.

Off-label uses

“Off-label” use of antibiotics is the prescription or authorisation to a client by a veterinarian allowing the use of a registered drug or veterinary chemical in a manner contrary to the approved label directions. Veterinarians are permitted to prescribe treatments off-label in order to broaden their treatment options for species for which there are no or limited licensed medicines for certain conditions. Off-label use in animals may include the application of drugs registered for human use. However, veterinarians in Australia must exercise “professional judgement” in selecting to use off-label medicines, understanding that such use is of concern to the community[23]. No literature was found providing further information and data on the off-label use of critically-important antibiotics in food animals in Australia. Such information for other countries is also rarely available.

c. Latest data

Unfortunately, no official data was found relating to the volume and classes of antimicrobials sold or used in food animals in Australia in the last two years. The most recent official government report for the whole country was published in 2014 and related to the monitoring period 2005-2010, as previously described in detail. However, a number of studies have been published by independent researchers, providing supplementary evidence of antimicrobial use practices in the country. See **Table 3** for an overview of findings from three studies from 2020, 2018 and 2009.

d. Reasons for use

Veterinary antibiotics are used in food animals in Australia for three main purposes: (1) **therapy** to treat a diagnosed disease in an individual animal or animals, under the direction of a veterinarian; (2) **prophylaxis** under the direction of a veterinarian to prevent disease in a healthy animal or group of

animals perceived to be at-risk of infection; and (3) for **production purposes**, with growth promoters administered via feed or water to a group of animals at low doses over longer periods of time to increase feed conversion efficiencies. The most recent data reported for types of antimicrobial use in food animals in Australia related to the time period 2005-2010, and are summarised in **Table 4.**

Table 3: Summary of findings from three studies documenting antimicrobial use practices in food animals in Australia[24–26].

Study title, year and reference	Food animal species involved	Summary of findings relating to antimicrobial use in Australia
Antimicrobial use and stewardship practices on Australian beef feedlots (2020); Badger et al.	Feedlot beef cattle	A self-administered questionnaire of 83 beeflot operators found monensin (coccidiostat) and virginiamycin (a streptogramin) to be the most commonly used in-feed antimicrobials. 42% of respondents used growth promoters, the majority of which reported using ionophores for this purpose. The most commonly used injectables were penicillin, oxytetracycline and tulathromycin (macrolide).
Antimicrobial labelling in Australia: a threat to antimicrobial stewardship? (2018); Hardefeldt et al.	All domestic species	A 2016 survey undertaken to investigate antimicrobial usage patterns by Australian veterinarians found that antimicrobial dose rates were varied and often inappropriate. For example, doses of procaine penicillin in cattle were often low, with 90% of respondents reporting doses that were unlikely to result in plasma concentrations above minimum inhibitory concentrations for common bovine pathogens. The authors report that antimicrobial labels often recommend incorrect dose rates and thus may be contributing to poor prescribing practices. They suggest changes to legislation are needed to ensure that antimicrobial drug labels are regularly updated to reflect the dose needed to effectively and safely treat common veterinary pathogens.
Antimicrobial use in the Australian pig industry: results of a national survey (2009); Jordan et al.	Pigs	An internet-based survey of 197 managers of large (>200 sow) pig herds (51%) in Australia found that most piggeries relied on drugs of low importance in human medicine (e.g. tetracyclines, penicillins and sulfonamides). For the two drugs of high importance in human medicine that can be legally prescribed to pigs in Australia, ceftiofur use was reported in 25% of herds and virginiamycin in none. Infections attributed to Lawsonia, Mycoplasma and Escherichia coli motivated the most use of antimicrobials.

Table 4: Total sales of veterinary antimicrobials (in tonnes of active constituent) used in food animals by type of use and year (July 2005 to June 2010). Table modified from Australian Government (2014)[8]

TYPE OF USE	2005-06	2006-07	2007-08	2008-09	2009-10	Trend
Therapy	271.6	230.4	262.3	199.1	288	↑
Coccidiostats	336.2	302.9	279.3	258.6	327.1	↓
Growth promotion	47.2	38.2	38.4	23.8	28.9	↓
TOTAL	**655**	**571.5**	**580**	**481.5**	**644**	↓

Of the total quantity of antimicrobials sold for use in food animals, the Australian Government[8] reported that an average of 51% were sold for coccidiostat use, 43% were sold for therapeutic or prophylactic purposes, and 6% were sold for growth promotion during the period 2005 and 2010. Unfortunately, their report does not disaggregate prophylactic and therapeutic uses, but refers to both under the term 'therapeutic use'. This is because it is difficult for registrant companies to estimate the proportions of products used for these purposes. Use of coccidiostats are usually administered for prophylactic purposes (See **Figure 3**).

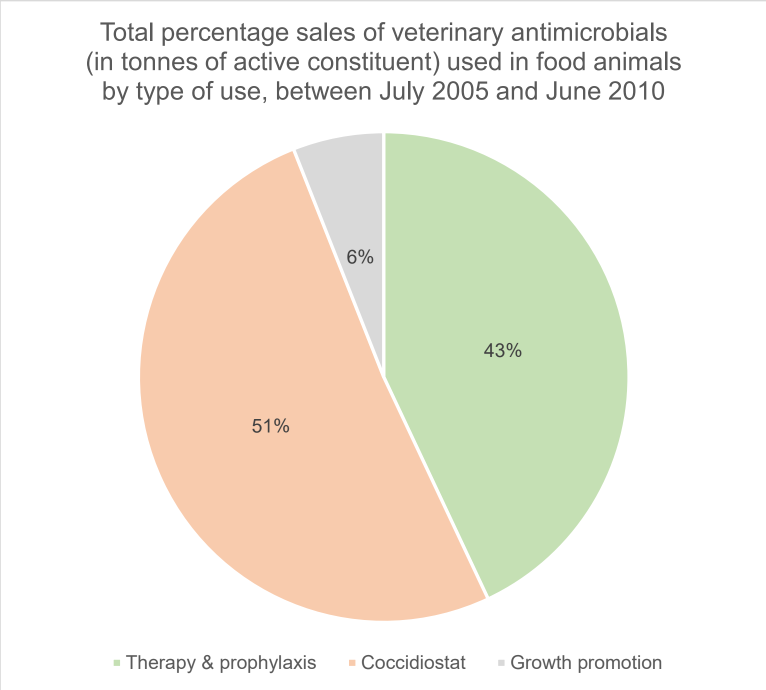


Figure 3: Total percentage sales of veterinary antimicrobials (in tonnes of active constituent) used in food animals by type of use, between June 2005 and June 2010. Data from Australian Government (2014)[8].

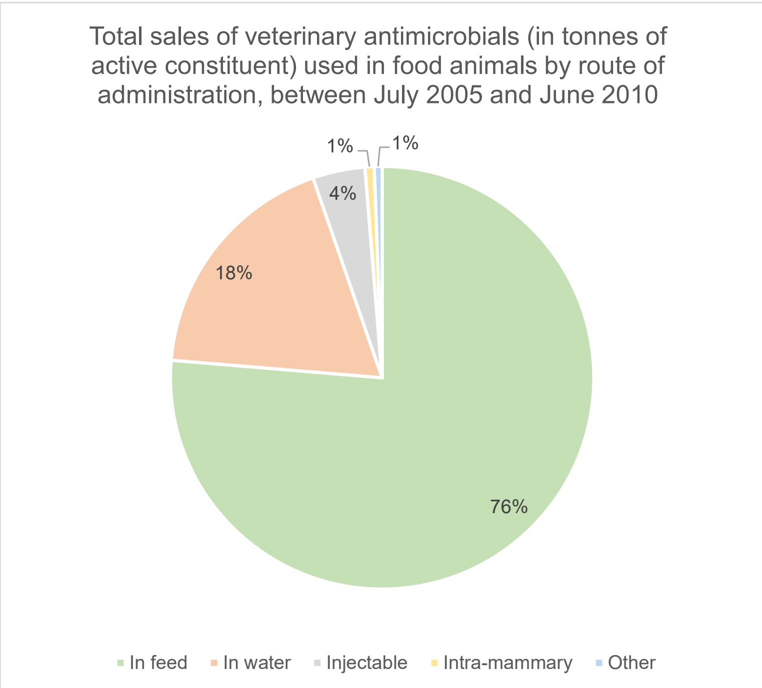


Figure 4: Total percentage sales of veterinary antimicrobials (in tonnes of active constituent) used in food animals by route of administration, between June 2005 and June 2010. Data from Australian Government (2014)[8].

The same report[8] reveals certain interesting insights into these types of use and drivers of use at individual species level over the monitoring period.

Coccidiostats

Coccidiostat use accounts for the greatest proportion of antimicrobial sales (51%) over the reporting period, 2005-2010. Some coccidiostats additionally control bacterial infections, e.g. the poultry disease necrotic enteritis caused by the bacterium *Clostridium perfringens*[27]. Of antimicrobial sales for poultry and cattle/sheep in Australia between 2005 and 2010, 62% and 65% were coccidiostats, respectively. All poultry coccidiostats were sold as in-feed preparations. All of the cattle/sheep coccidiostats sold were ionophores[8]. The four antimicrobials sold for coccidiostat uses in the greatest quantities between 2005 and 2010, in decreasing order of quantities sold, were monensin, dinitolmide, salinomycin and lasalacid. Other classes sold for coccidiostat uses (again, in decreasing order in terms of sales volumes) included nicarbazin, narasin, sulfaquinoxaline, semduramicin, robenidine, maduramicin and toltrazuril.[28]

Coccidiostat use is increasingly controversial in the livestock industry. Some proponents argue that the vast majority of coccidiostats are not listed as important for human health, with little documented evidence for resistance, cross-resistance or co-resistance to these compounds emerging in pathogens of consequence to human health[27]. Some also refer to their benefits in controlling the endemic disease coccidiosis, which can result in significant welfare problems and losses[29] and secondary infections of concern to human health[30]. They also allude to their collateral benefit in acting as a substitute growth promoter, with sustainability benefits:

"Preventing coccidiosis is essential for a better gut health and contributes to healthy animals, more animal welfare, a better defence against secondary infections (and because of that; the use of antibiotics) and a good feed conversion. In short: it is essential for sustainable poultry farming, which we very much need to meet the increasing demand for poultry."

- Industry representative, as quoted by Poultry World[31].

"These animal-only antimicrobials [coccidostats] are not used in human medicine and do not contribute to antibiotic resistance. The World Health Organisation, the World Animal Health Organisation (OIE), and the European Surveillance Programme of Veterinary Antibiotics have confirmed that coccidiostats have no impact to human health."

-British Poultry Council (2018)

"Coccidiosis is a parasitic disease and without doubt the most important parasitic disease in poultry and of major importance in other species such as pigs, rabbits and cattle. Even in the presence of high sanitary standards and good management, coccidiosis occurs with a serious potential impact on animal health and welfare and possible high mortality rates."

- Federation of Veterinarians of Europe (2016)[32]

Coccidiostats are classed as 'feed additives' in the EU, which means that their use is not subject to the same legislation or surveillance system as other antimicrobials. See **Text Box 2** for more details.

<u>Text Box 2:</u> Coccidiostat use in Europe

In Europe, coccidiostats are permitted for administration in feed to prevent coccidiosis occurring in food producing animals. Some coccidiostats are also used as therapeutic veterinary medicines to treat clinical signs of disease.

There are different types of coccidiostat agents – polyether synthetic ionophores (e.g. monesin), and synthetic products not of an ionophoric nature (e.g. sulphonamides, decoquinate), including combination products (e.g. sulphonamides with trimethoprim). The majority of coccidiostats are classed as feed additives under EU legislation. There are some coccidiostats that are classed as veterinary medicinal products, and as such are subject to different regulatory requirements and monitoring. There is no requirement to record ionophore coccidiostat use in European antibiotic monitoring and surveillance. There have been concerns raised in Europe about the risk of AMR developing from some coccidiostat use in food production; however, currently, there is limited conclusive evidence to suggest coccidiostat use in food production leads to AMR developing. The European Medicines Agency (EMA) maintain the classification of coccidiostats as feed additives. Nevertheless, the FVE state:

"FVE believes that all coccidiostats should be under veterinary prescription following clinical examination and diagnosis; this would allow for better surveillance and the veterinarian to diagnose and choose the best strategy to extend the useful life of coccidiostats, such as through 'shuttle use' or 'rotational use' or the use of vaccines."[32]

However, opponents of coccidiostat use argue that although most are not currently considered important to human health, we may need to deploy certain coccidiostats in human medicine as our arsenal of effective antibiotics declines, and retaining their efficacy is paramount. Colistin is an example of an antimicrobial previously used in animals, which is now used as a last-resort antimicrobial for certain resistant infections in people despite its adverse side-effects, as described in later in this section (see **Text Box 3**). Some anticoccidials are even being studied for possible future use as cancer therapy[32]. Development of resistance to coccidiostats in coccidia and bacteria with animal health implications has also been described in the scientific literature, and cross-resistance between various ionophore coccidiostats has also been shown[27]. The risk of resistance affecting animal patients coupled with the theoretical risk to humans may therefore warrant adoption of the 'precautionary principle' in terms of responsible use.

Furthermore, opponents with a broader view argue that routine antimicrobial use of any type that is considered 'essential' or 'indispensable' in order to rear animals is propping up sub-optimal environmental conditions and concealing fundamental problems with animal health, husbandry and management (see **Text Box 4**).

"Humans may theoretically be exposed to coccidiostat resistant bacteria from poultry in a number of ways, e.g. by handling live animals and their manure, through slaughtering and processing, and by preparation and consumption of poultry meat. Furthermore, bacteria of the human normal microbiota, which cover all skin and mucosal surfaces, might develop resistance if they are exposed to coccidiostats."

-Opinion of the Panel on Animal Feed of the Norwegian Scientific Committee for Food Safety[27]

"Polyether ionophores antibiotics, which are by far the most widely used coccidiostats, are currently not used in human medicine, but are being studied such as for possible future use as cancer therapy."

- Federation of Veterinarians of Europe (2016)[32]

"Consumers…should also be aware that, while the poultry industry has been reducing its use of medically-important antibiotics, its use of non-medically-important antimicrobials is at an all-time high and increased by nearly 100t in 2015 [in the UK]….Non-medically-important antimicrobials are used in the poultry industry to control the disease coccidiosis which frequently affects intensively reared birds. They are also believed to help control necrotic enteritis, another disease associated with intensive conditions."

- Coílín Nunan, Alliance to Save Our Antibiotics (2017), as quoted by Poultry World[33]

<u>Text Box 3:</u> Colistin: the 'animal antibiotic' repurposed for human use

Colistin is an antibiotic that has been used in veterinary medicine for decades, for the prevention and treatment of Enterobacteriaceae infections in food animals[34]. It was abandoned from clinical use in human patients in the 1970s, due to significant renal and neurological toxicity[35]. However, due to diminishing treatment options, it is now increasingly used in people to treat multidrug-resistant, Gram-negative bacterial infections, particularly in the intensive care setting. It is now listed as an HP-CIA by the WHO, amid growing concerns regarding the global dissemination of the plasmid-mediated colistin resistance gene (mcr-1), which has been found in bacterial species isolated from humans, animals and the environment[36,37].

This example demonstrates the potential future importance for human use of antimicrobials currently used exclusively in animals, as our arsenal of effective antibiotics declines due to antimicrobial resistance.

Therapeutic or prophylactic use?

Therapy and prophylactic use accounted for 43% of sales in Australia, 2005-2010[8], as show in **Figure 3**. As previously mentioned, the report does not disaggregate these types of use owing to challenges for the pharmaceutical companies in understanding how their products are used, post-sale. However, we can draw certain inferences from the classes of antimicrobials sold and the routes of administration that comprise therapeutic and prophylactic use.

As shown in **Figure 4**, in-feed preparations of antimicrobials accounted for a majority (76%) of all sales, and, indeed, in-feed preparations comprise the majority of sales for each of the species listed (poultry, pigs, cattle/sheep)[8]. Looking specifically at therapeutic and prophylactic antimicrobial sales, bacitracin accounted for the greatest percentage (30%) (see **Figure 5**), with macrolides/streptogramins and tetracyclines following, accounting for 24% and 23% of sales, respectively.

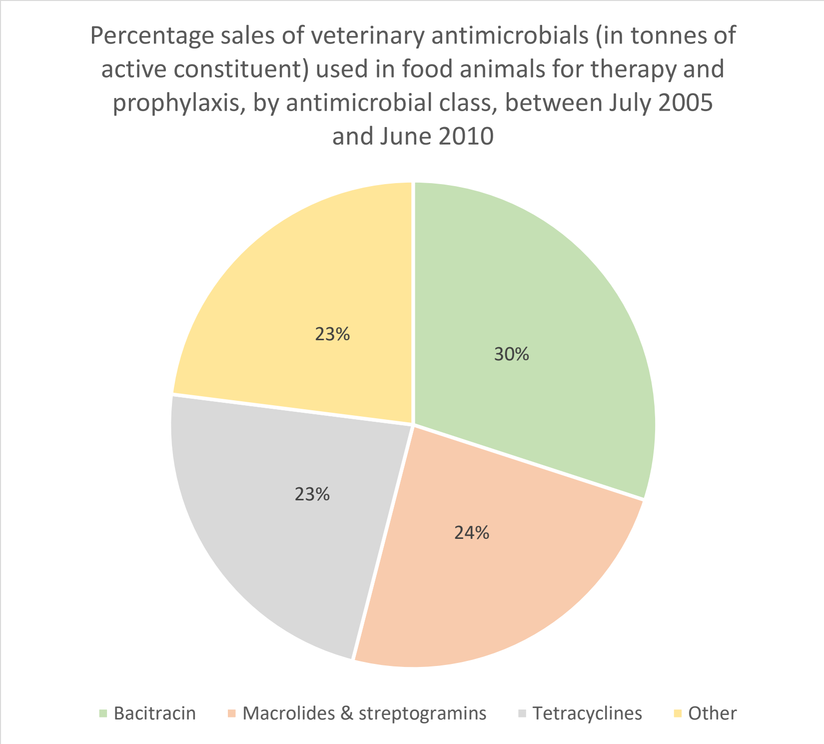


Figure 5: Total percentage sales of veterinary antimicrobials (in tonnes of active constituent) used in food animals for therapy and prophylaxis, by antimicrobial class, between June 2005 and June 2010. Data from Australian Government (2014)[8].

Bacitracin is used for the treatment and/or prevention of necrotic enteritis due to *Clostridium perfringens* types A and C in poultry and is administered in the feed. One feed company advertises bacitracin zinc in Australia as *"a vital management tool for broiler, layer and breeder farms in the prevention and control of Necrotic Enteritis, an economically devastating disease in poultry. By containing Necrotic Enteritis, and by maintaining a healthy gut, PRODUCT X improves feed efficiency, increases growth rates, improves layer performance and produces healthier birds."*[38] Such marketing claims imply a collateral production purpose in the use of bacitracin. Dose rates and recommended duration of treatment is not available online.

Most of the macrolides sold in Australia (2005-2010) were for administration in feed or water to pigs and poultry. The streptogramins were sold on a prescription-only basis in the feed to reduce the risk of acidosis due to high grain diets (which are common in feedlot systems of ruminant production), in cattle and sheep. They are also sold for the prevention of necrotic enteritis in broiler chickens caused by *Clostridium perfringens* sensitive to virginiamycin[8]. Generally, in-feed and in-water preparations facilitate group therapy or prophylactic treatments as they are easier to administer than individual animal treatments, for example, by injection. Although there are limited references available online regarding the exact purposes of use of these two antimicrobial drug classes in food animals in Australia, it can be inferred that some will have been used for prophylactic purposes during the monitoring period.

Although there are few that would object to the responsible use of antimicrobials in individual animals for clinical disease problems in order to protect animal health and welfare, routine prophylaxis is a source of debate. There has been a wave of support for mitigating antimicrobial use in animal agriculture in recent years. Much focus has been applied to *routine* prophylaxis, which is associated with high levels of group use with the potential to foster AMR, and is considered unnecessary as a replacement for good standards of animal husbandry and management.

Growth promotion

Growth promotion accounts for a relatively small proportion of use (6% over the reporting period 2005-2010)[8], and later developments in 2017 also contribute to a narrative of reduced support for growth promotion within the Australian livestock sector: In 2017, the livestock, veterinary pharmaceutical and animal feed industries voluntarily agreed to the removal of label claims for growth promotion from antimicrobials of importance to human health[20], meaning use of macrolides (a class of HP-CIAs holding the growth promotion label claim prior to 2017) for growth promotion purposes would become off label, as discussed in section 1b. However in the absence of a broader government ban on the use of antimicrobial growth promoters in food animal production, the use of a number of antimicrobials not listed by the WHO as important to human health such as avilamycin, olaquindox and bambermycin as growth promoters, persists.

"The Australian Chicken Meat Federation (ACMF) established a policy in 2007 that antibiotics should not be used for growth promotion purposes, and has been actively working with the product registrants since then to have growth promotion claims for chickens removed from labels. There are currently two products that remain registered for use in poultry that have growth promotion claims, however, neither of them are used in human medicine."

- Animal Industries' Antimicrobial Stewardship RD&E Strategy (2021)[21]

Growth promotion is still deployed in multiple jurisdictions across the world and has its roots in the earliest uses of antibiotics following their discovery. The use of antibiotics in animal agriculture began in the late 1930s, soon after they were discovered and made commercially available for use in human patients. As farm sizes grew, researchers trialled the use of mass medication in herds and flocks to control disease within concentrated animal operations, and to minimise the expensive labour required for the care of individual animals[39]. In the 1950s, scientists in the USA discovered that the addition of antibiotics with vitamin B12 to animal feed accelerated growth[40]. Despite early warnings of the risk of antimicrobial resistance from the scientific community[41], antibiotic use was soon globally widespread on farms, whaling and fishing fleets, processing plants and aquaculture operations to control disease, increase feed conversion, promote growth and preserve food[39].

The use of prolonged courses of low-dose antibiotics in feed for growth promotion became and remains common practice in some countries, yet their mechanism of action is not fully understood. However research suggests that their effects are derived from decreased competition for nutrients, a reduction in microbial metabolites that depress growth and the prevention of infections with pathogenic bacteria[42]. Use of growth promoters in agriculture generates improved growth rates and feed utilisation[43], and although research shows that these production gains are insufficient to offset the cost of the antibiotics[44], their popularity and widespread use continues across the world.

Their use leads to two main concerns. Firstly, the long courses of low dose antibiotics that characterise growth promotion are associated with the emergence of AMR, with potential public health consequences. Use of antibiotics as growth promoters applies a prolonged sub-inhibitory selection pressure, enriches resistant bacteria, stimulates mutagenesis and promotes gene transfer between bacteria within the animal gut microbiome[13,15,16,45]. Some studies have observed a dramatic reduction in the animal reservoir of enterococci resistant to the growth promoters avoparcin, avilamycin and virginiamycin, that were withdrawn from use in Scandinavia from 1995[46,47] – supporting the case for a ban on antimicrobial growth promotion for human health benefit.

The second concern is that growth promotion is a means of supporting sub-optimal farming practices, in which poor standards of hygiene, biosecurity, husbandry and management are concealed by the

routine use of antibiotics. Indeed, therapeutic antibiotic use increased in some sectors following national or EU bans on the use of growth promotion, due to a rise in infectious diseases. For example, growth promotion withdrawal in the EU was associated with an increased incidence of diarrhoea, weight loss and mortality due to *Escherichia coli* and *Lawsonia intracellularis* in early post-weaning pigs, and clostridial necrotic enteritis in broilers[48]. An effect of these infections was an increase in therapeutic use of antibiotics in food animals, including use of tetracycline, aminoglycosides, trimethoprim/sulphonamide, macrolides and lincosamides[48]. Opponents of growth promotion practices argue that such effects indicate underlying inadequacies in animal health and management, and that a focus on higher welfare systems may generate win-win benefits in terms of both antimicrobial use and animal welfare[49] (See **Text Box 4**).

Text Box 4: Sources relating to the association between antibiotic use and poor welfare practices

"The key risk factors for diseases that may require antimicrobial use in farm animals include: stress; low immunity; overcrowding; overheating; poor hygiene and biosecurity (processes to prevent new infections being introduced); diet change; housing system; mixing of unfamiliar animals; group size; temperature variation, and poor air quality….Routine use of antimicrobials (for growth promotion or to prevent infections), especially antibiotics and coccidiostats, is strongly discouraged as the focus of farm animal management must be on creating an optimum environment to meet the animals' needs."

– *RSPCA Australia (2019)*[50]

"In some farming systems, much reliance is placed on the routine use of antimicrobials for disease prevention or for the treatment of avoidable outbreaks of disease, such that these systems would be unsustainable in the absence of antimicrobials. The stress associated with intensive, indoor, large-scale production may lead to an increased risk of livestock contracting disease. One example relates to white veal production...In this industry, the disease risk is high, in particular bovine respiratory disease, and there is very high on-farm use of antimicrobial agents."

– EFSA/EMA (2017)[17]

"Antimicrobial use should not prop up poor husbandry or failing management systems. Where required, antimicrobials should be viewed as an acceptable veterinary treatment complementing good management, good nutrition, vaccination, biosecurity and farm hygiene."

– Responsible Use of Medicines in Agriculture (RUMA UK) (2015)[51]

"Corporate demand for cheap meat across the globe has driven such inhumane ways of rearing livestock. It's a system whose seemingly relentless pursuit of the highest returns positively encourages farmers to pack animals into overly-confined spaces and restrict their freedom to move, a restriction that leads to unnecessary illness. To counteract this practice, animals are dosed not just with unnecessary levels of antibiotics, but with antibiotics that are important – often critically so – to human medicine."

– ShareAction (2017)[18]

"The volume of antibiotics used in animals is continuing to increase worldwide, driven by a growing demand for foods of animal origin, often produced through intensive animal husbandry."

- Dr Kazuaki Miyagishima, Director of the Department of Food Safety and Zoonoses at WHO[19]

e. Trends in use

As shown in **Tables 1 and 4**, the use of antibiotics decreased slightly over the reporting period, with therapeutic use increasing slightly (from 272 to 288 tonnes), coccidiostat use decreasing slightly (from 336 to 327 tonnes) and growth promotion use reducing considerably (from 47 to 29 tonnes). In the different species, sales in antibiotics for use in cattle decreased over the reporting period, for poultry, sales increased, and for pigs, sales decreased slightly. In terms of antimicrobials of importance to human medicine, the following trends in sales of selected antimicrobial classes for use in food animals between 2005 and 2010 were observed: aminoglycoside sales decreased, cephalosporin sales increased, lincosamide sales increased, penicillin sales decreased, and amoxicillin-clavulanic acid penicillin sales increased. For the macrolides, sales for therapeutic purposes in food animals decreased over the reporting period, but sales for growth promotion purposes increased from 6.7 tonnes in 2005 to 10.7 tonnes in 2010. This trend in macrolide sales for growth promotion purposes is in contrast to the non-medically-important growth promoters, for which a decreasing trend in sales was observed.[8]

However, on a year-by-year basis, these levels of sales fluctuate significantly, possibly due to data reporting issues. Therefore these trends should be interpreted with caution and more recent data is certainly required in to order to draw conclusions about the general trajectory in types of antimicrobial use in the food animal sector.

f. Use in the human medical sector

Antimicrobial use in the human health sector in Australia is monitored via The Antimicrobial Use and Resistance in Australia (AURA) surveillance system. AURA collects and reports data from partner programmes across acute and community healthcare settings, and provides integrated reporting on priority organisms and antimicrobial use, and appropriateness of use, at a national level[52]. The most recent AURA report was published in 2019, and documents use between 2016 and 2017 using the Defined Daily Doses (DDD) per Occupied Bed Days (OBD) metric, which is specific to the human health care sector. The latest report found that in 2017, total antibiotic use in hospitals participating in the surveillance programme increased for the first time since 2013. The usage rate increased from 932.8 DDDs per 1,000 OBDs in 2016, to 956.8 DDDs per 1,000 OBDs in 2017[52].

Unfortunately, due to the differences in metrics used for antibiotic use reporting in the animal and human health sectors, official sources have not determined their relative contributions to total national antibiotic use. However, authors of one study[53] have extracted and extrapolated data from several sources to determine that across all antimicrobials of importance to human health, an average of 182,138 kg were sold for use each year in animals between 2005 and 2010, and 121,076 kg per year were used in humans. Sales of antimicrobials for animal use therefore comprised 60% of total antimicrobial sales by weight, during this time period. They also found that most antibiotic classes were predominantly used in either humans or animals; the only antibiotic classes with near-equal use between animals and humans were β-lactamase sensitive penicillins and extended-spectrum penicillins (see **Figure 6**).[53]

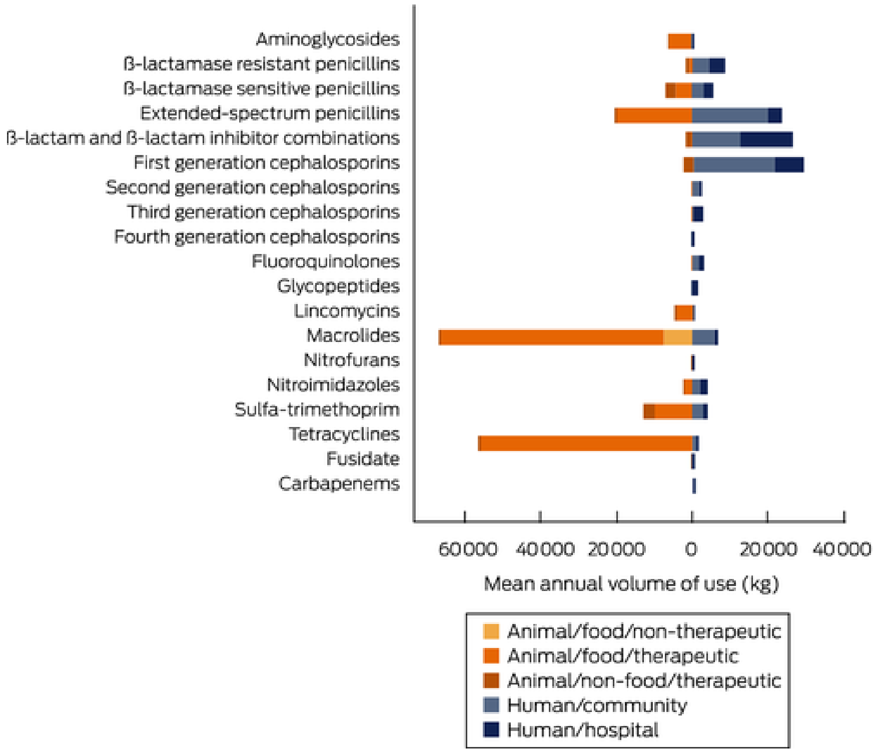


Figure 6: Comparative volume of antibiotic use in humans and animals in Australia, by indication and setting, excluding ionophore coccidiostats agents, which are used extensively in animals but are not believed to contribute to resistance in human pathogens. From Langham and Cheng (2019)[53].

2. Comparative antibiotic use across OECD countries

In this section, we discuss Australia's antimicrobial use in food animals in comparison to a selection of other OECD member countries.

a. *Comparing Australia's antimicrobial sales for food animals with other OECD countries, by volume*

As previously discussed, internationally harmonised surveillance systems are in their infancy and national reporting requirements relating to animal antimicrobial use are yet to be developed in many countries, including in Australia[54]. Although many resources and antimicrobial stewardship guidelines are available for veterinarians and food animal industries in Australia, for example for pigs and poultry[55,56], the most recent comprehensive evidence on the quantity of antimicrobials sold was published in the APVMA 2005-2010 report[8]. This report was constructed using sales data submitted by registrants of veterinary antimicrobial products, which is only indicative of overall trends in sales and is not necessarily an accurate reflection of antibiotic consumption, as discussed in section 1. However, the report indicates that the total sales of veterinary antimicrobials decreased slightly from 655 tonnes in 2005, to 644 tonnes in 2010, as displayed in **Table 1**.

For comparison with Australia, data on antimicrobial sales for use in food animal species in the other OECD countries of the Netherlands, UK and USA have been included in this report (see **Table 5**). Of relevance to the Netherlands and the UK, the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) publishes annual reports on the sales of veterinary antibiotics in 31 European countries[57]. The latest data related to sales in 2018 and were published in October 2020. The Netherlands and the UK sold 461 tonnes and 456 tonnes of veterinary antimicrobial agents for food-producing animals in 2010[58], respectively – figures that are lower than Australia's sales for the same year, but these crude comparisons do not account for differences in the sizes of animal populations. Sales of veterinary antimicrobials for food animals in The Netherlands and the UK decreased to 184 tonnes and 213 tonnes in 2018.

The United States require all sponsors of approved animal drug applications containing antimicrobials to report sales to the Food and Drug Administration (FDA)[59]. 13,287 tonnes of medically-important antimicrobial drugs were sold for use in food-producing animals in 2010 and 6,036 tonnes were sold in 2018. These figures both exceed the sales of antimicrobials for food animals in Australia in 2010, but again these comparisons do not account for differences in animal numbers.

Table 5 provides an overview of sales data for the four comparison countries, together with information on antibiotic sales surveillance systems.

Table 5: Antibiotic sales surveillance systems and data for the food animal sector from Australia, The Netherlands, UK and USA. Data derived from APVMA[8], ESVAC[57] and FDA[59].

	Australia	Netherlands	United Kingdom	United States
Data collection	Two reports (1999-2002; 2005-2010)	Annually (> 10 years)	Annually (> 10 years)	Annually (since 2008)
Authority	Australian Pesticides and Veterinary Medicines Authority (APVMA)	Federation of the Dutch Veterinary Pharmaceutical Industry (FIDIN)	Veterinary Medicines Directorate (VMD)	US Food and Drug Administration (FDA)
Source for data (approx. number)	Registrants (unknown)	Marketing Authorisation Holders (n=16)	Marketing Authorisation Holders (n=63)	Drug sponsors (unknown)
Total tonnes of antimicrobials sold (2010)	644	461	456	13287.1
mg/PCU (2010)	n/a*	146.1	67.9	n/a*
Total tonnes of antimicrobials sold (2018)	Unknown	183.9	212.9	6036.14
mg/PCU	n/a*	57.5	29.5	n/a*
Percentage change in antimicrobial sales, 2010 - 2018	Unknown	*Total tonnes:* ↓ by 60% *mg/PCU:* ↓ by 61%	*Total tonnes:* ↓ by 53% *mg/PCU:* ↓ by 57%	*Total tonnes:* ↓ by 55%

** Note that the metric mg/PCU are European metrics based on the estimated body weights of European livestock categories at the time of treatment, and therefore is not used by the Australian or American livestock sectors.*

It should be noted that due to multiple variations in collecting, analysing, and reporting data, simple country comparisons entail the risk of serious misinterpretations[60]. Failure to correct with animal population-based denominators such as population correction unit (PCU), and use of other country-specific metrics limit meaningful comparisons between reported AMU data from Australia and other OECD countries. However, **Table 5** shows a general downward trajectory in the sales of antimicrobials for use in food-producing animals across all comparison OECD countries (Netherlands, UK and USA) between 2010 and 2018, although a similar trajectory cannot be ascertained for Australia due to a lack of data for 2018.

b. Antibiotics used in Australia and prohibited in other countries

In Australia, growth promoters make up 4-7% of the total antimicrobials sold for use in food animals (23.8–47.2 tonnes), despite multiple recommendations against this practice from the Joint Expert Advisory Committee on Antibiotic Resistance (JETACAR) and academics[61–63]. In contrast, the use of antibiotics as growth promoters has been banned in the EU since 1 January 2006[64]. Since 2017, the use of antimicrobial drugs for production purposes has been phased out in the US, under guidance #213 from the FDA[65]. Certain drugs were withdrawn completely, others were converted to prescription status, and some were marketed without production (i.e. growth promotion) indications[66].

The following antibiotics were registered for use as growth promoters in Australia according to the 2014 government report[8]:

- Roxarsone (Arsenical)
- Flavophospholipol (Glycophospholipid)
- Kitasamycin (Macrolide)
- Tylosin (Macrolide)

- Avilamycin (Oligosaccharide)
- Lasalacid (Polyether ionophore)
- Monensin (Polyether ionophore)
- Narasin (Polyether ionophore)
- Salinomycin (Polyether ionophore)
- Olaquinodox (Quinoxaline)

On the other hand, the use of fluoroquinolones, colistin and fourth-generation cephalosporins in food-producing animals is prohibited in Australia, but permitted in most of the other OECD countries[57].

c. *The ASTAG system*

Importance ratings for antimicrobials inform decision-makers about the risks to human health of using antimicrobial classes, some with a specific focus on the risks to human health of antimicrobial resistance as a consequence of animal antibiotic use. This helps to prioritise resources to regulate and monitor use of the most important antimicrobials. Although the WHO CIA list has been recognised as the global standard for ranking important antimicrobials for human medicine, implementation of the WHO recommendations to restrict HP-CIA use in food animals[67] varies from country to country according to the local context, such as differences in agricultural practices and resistance patterns[68]. In addition, many countries have opted over the years to develop their own national importance ratings – including Australia.

The Australian Strategic and Technical Advisory Group on AMR (ASTAG) published Australia's critically-important antimicrobials list[69] with three tiers: High, Medium, and Low importance to human health. The ASTAG categories of some antibiotics are in agreement with the WHO CIA list[10] (i.e. for some antibiotics, 'High' in ASTAG's list corresponds to 'Critically-important' in the WHO list, 'Medium' corresponds to 'Highly-important', and 'Low' corresponds to 'Important'). Examples of antimicrobial classes for which ASTAG and WHO importance ratings are well aligned include the carbapenems, cephalosporins (all generations), fluoroquinolones, glycopeptides, lincosamides and polymyxins.

However, there are several notable differences in the ranking of antimicrobial classes between the two systems. Macrolides, moderate-spectrum penicillins (e.g. amoxicillin and ampicillin) and several aminoglycosides (e.g. neomycin, framycetin and streptomycin) are classified as Low in ASTAG's list, but are rated as Critically-important in the WHO's CIA list. These differences in importance ratings may be due to the relatively low use of these antimicrobials in Australia, as resistance is already widespread in many human pathogens[70]. Another explanation would be that some of the pathogens of interest to the WHO represent less significant health burdens in Australia[69]. See **Table 6** for a list of antimicrobial agents and their ASTAG and the WHO importance categorisations.

Table 6: ASTAG and WHO[10,69] classifications of antimicrobials in terms of their importance to human health.

Antimicrobial class	Importance classification	
	ASTAG	WHO classification
Aminocoumarins	n/a	n/a
Aminoglycosides		Critically important
Neomycin	Low	Critically important
Framycetin	Low	Critically important
Gentamicin, tobramycin	Medium	Critically important
Amikacin	High	Critically important
Spectinomycin	Medium	Critically important
Streptomycin	Low	Critically important
Dihydrostreptomycin	Low	Critically important
Paromomycin	Low	Critically important
Apramycin	Medium	Critically important
Amphenicols		Highly important
Chloramphenicol	Low	Highly important
Florfenicol	Low	Highly important
Antileprotics	High	n/a
Antimycobacterials	High	n/a
Amprolium	n/a	n/a
Arsenicals	Low	n/a
Bambermycins	Low	n/a
Benzamides	n/a	n/a
Carbanilides	n/a	n/a
Carbapenems	High	Critically important
Coumermycins	Low	n/a
Cephalosporins		
1st and 2nd Generation	Medium	Highly important
3rd and 4th Generation	High	Critically important
Anti-MRSA Cephalosporins	High	n/a
Fosfomycins	High	Critically important
Fluoroquinolones/Quinolones	High	Critically important
Fusidanes	High	Highly important
Glycopeptides	High	Critically important
Glycophospholipids	n/a	n/a
Glycylcyclines	High	Critically important
Ionophores	Low	n/a
Lincosamides	Medium	Highly important
Lincopeptides	High	n/a
Macrocyclic lactones	High	n/a
Macrolides	Low	Critically important
Monobactams	High	Critically important
Nitrofurans	High	Important
Nitroimidazoles	Medium	Important
Nystatin	n/a	n/a
Oligosaccharides	n/a	n/a
Orthosomycins	Low	n/a
Oxazolidinones	High	Critically important
Penicillins & beta-lactamase inhibitors		
Antistaphylococcal penicillins	Medium	Highly important
Moderate-spectrum penicillins (amoxicillin, ampici	Low	Critically important
Narrow-spectrum penicillins	Low	Highly important
Broad-spectrum penicillins	Medium	Critically important
Pleuromutilins (tiamulin)	Low	Important
Polyether ionophores	n/a	n/a
Polymyxins	High	Critically important
Polypeptides	Low	Important
Pseudomonic acids	Medium	Highly important
Quinoxaline	Low	n/a
Robenidine	n/a	n/a
Rifamycins	High	Critically important
Streptogramins	High	Highly important
Sulfonamides & diaminopyramidine potentiators		Highly important
Sulfadiazine, Silver sulfadiazine, Trimethoprim, Pro	Low	Highly important
Sulfamethoxazole-trimethoprim, Sulfadoxine-pyrir	Medium	Highly important
Tetracyclines	Low	Highly important
Triazines	n/a	n/a

n/a: not listed or not currently used in humans

Similarly to Australia, the European Medicines Agency (EMA) also uses its own ranking system, as agreed by the Antimicrobial Advice ad hoc Expert Group (AMEG), for the importance of antibiotics: Category A – "Avoid", Category B – "Restrict", Category C – "Caution", and Category D – "Prudence"[71]. This list has been developed and refined according to a number of criteria, including the likelihood and possible consequences of AMR transfer from animals to humans, and the availability of alternative antibiotic classes in veterinary medicine with lower AMR risks[72]. Whereas Category A (Avoid) antimicrobials under the EMA system are not authorised as veterinary medicines in the European Union and cannot be used in food-producing animals, the other categories are allowed. The EMA recommends that use of Category B antimicrobials is restricted in animals. These antimicrobial classes align closely with the WHO HP-CIA list, with the exception that macrolides are considered HP-CIAs by the WHO, but listed in Category C (Caution) by the EMA and are therefore subject to prudent use guidelines but no recommended restrictions.

In the USA, the importance ranking for antimicrobials is listed in Appendix A of the FDA's Guidance for Industry (GFI) #152[73] (see below **Table 7** for the comparison with the WHO's classification). The three tiers of "Critically-important", "Highly-important", and "Important" are used for classification, and the ranking process is based upon five criteria (in order of importance):

1. The antimicrobial is used to treat enteric pathogens that cause food-borne disease;
2. The antimicrobial is the sole therapy or one of few alternatives to treat serious human disease, or the drug is an essential component with other antimicrobials in the treatment of human disease;
3. The antimicrobial is used to treat enteric pathogens in non-food-borne disease;
4. There is no cross-resistance within the drug class and an absence of linked resistance with other drug classes;
5. There is difficulty in transmitting resistance elements within or across genera and species of organism.

Unlike the EMA's ranking system that closely resembles the WHO list, the FDA's list contains several notable differences, demonstrating a less restrictive approach:

- Several antibiotics present in the WHO list are not included in the FDA's ranking system (including fosfomycins, fusidanes, glycylcyclines, nitrofurans, nitroimidazoles, pleuromutilins, polypeptides, pseudomonic acids and sulphonamides);
- Aminoglycosides, carbapenems, fourth-generation cephalosporins, glycopeptides, oxazolidinones, moderate-spectrum (amoxicillin, ampicillin) and broad-spectrum penicillins, polymyxins and rifamycins are ranked as 'Critically-important' by the WHO but 'Highly-important' by the FDA;
- Monobactams are classified as 'Critically-important' by the WHO but 'Important' by the FDA;
- 1st and 2nd generation cephalosporins are ranked as 'Highly-important' by the WHO but 'Important' by the FDA.

The FDA's antimicrobial classification list was published in 2003 and may not be representative of the actual risks of using each antibiotic according to current understanding of antimicrobial resistance. This was recognised recently when the FDA published a concept paper[74] to revise the approach for ranking antimicrobial drugs. Rather than emphasising the treatment of foodborne infections in humans (as described in the original GFI #152), the concept paper considers more broadly the importance of these drugs in human medicine, based on availability of treatment options and seriousness of human illness[75]. Public comments were requested until 16th March 2021. If the revised ranking list and risk assessment methodology were to be adopted by the FDA, they would replace those included in GFI #152 and the list would align more closely with the WHO list.

Table 7: FDA and WHO[10,73] classifications of antimicrobials based on their importance to human health.

Antimicrobial class	Importance classification	
	FDA	WHO classification
Aminocoumarins		n/a
Aminoglycosides	Highly important	Critically important
Neomycin	Highly important	Critically important
Framycetin	Highly important	Critically important
Gentamicin, tobramycin	Highly important	Critically important
Amikacin	Highly important	Critically important
Spectinomycin	Highly important	Critically important
Streptomycin	Highly important	Critically important
Dihydrostreptomycin	Highly important	Critically important
Paromomycin	Highly important	Critically important
Apramycin	Highly important	Critically important
Amphenicols		Highly important
Chloramphenicol	Highly important	Highly important
Florfenicol	n/a	Highly important
Antileprotics	n/a	n/a
Antimycobacterials	n/a	n/a
Amprolium	n/a	n/a
Arsenicals	n/a	n/a
Bambermycins	n/a	n/a
Benzamides	n/a	n/a
Carbanilides	n/a	n/a
Carbapenems	Highly important	Critically important
Coumermycins	n/a	n/a
Cephalosporins		
1st and 2nd Generation	Important	Highly important
3rd Generation	Critically important	Critically important
4th Generation	Highly important	Critically important
Anti-MRSA Cephalosporins	n/a	n/a
Fosfomycins	n/a	Critically important
Fluoroquinolones/Quinolones	Critically important	Critically important
Fusidanes	n/a	Highly important
Glycopeptides	Highly important	Critically important
Glycophospholipids	n/a	n/a
Glycylcyclines	n/a	Critically important
Ionophores	n/a	n/a
Lincosamides	Highly important	Highly important
Lincopeptides	n/a	n/a
Macrocyclic lactones	n/a	n/a
Macrolides	Critically important	Critically important
Monobactams	Important	Critically important
Nitrofurans	n/a	Important
Nitroimidazoles	n/a	Important
Nystatin	n/a	n/a
Oligosaccharides	n/a	n/a
Orthosomycins	n/a	n/a
Oxazolidinones	Highly important	Critically important
Penicillins & beta-lactamase inhibitors	Highly important	
Antistaphylococcal penicillins	Highly important	Highly important
Moderate-spectrum penicillins (amoxicillin, ampicilli	Highly important	Critically important
Narrow-spectrum penicillins	Highly important	Highly important
Broad-spectrum penicillins	Highly important	Critically important
Pleuromutilins (tiamulin)	n/a	Important
Polyether ionophores	n/a	n/a
Polymyxins	Highly important	Critically important
Polypeptides	n/a	Important
Pseudomonic acids	n/a	Highly important
Quinoxaline	n/a	n/a
Robenidine	n/a	n/a
Rifamycins	Highly important	Critically important
Streptogramins	Highly important	Highly important
Sulfonamides & diaminopyramidine potentiators	n/a	Highly important
Sulfadiazine, Silver sulfadiazine, Trimethoprim, etc.	n/a	Highly important
Sulfamethoxazole-trimethoprim, etc.	n/a	Highly important
Tetracyclines	Highly important	Highly important
Triazines	n/a	n/a

n/a: not listed or not currently used in humans

Although addressing context-specific challenges is crucial to developing effective AMR strategies, the variety of rating systems in use globally makes international harmonisation more challenging. Harmonisation of approaches to antimicrobial use and stewardship in the food animal sector may be important in negotiations between potential trading partners, as indicated by the NGO and media narrative around the implications of a UK-Australia trade deal[76]. However, the WHO CIA list is still recognised as the global reference by many countries, organisations and industries.

> *"..Antimicrobial ratings systems…formally define the importance of each individual agent in human health by assigning them to a position on a graduated scale of 'importance' comprising up to four categories of risk. Until recently, these published ratings have only had a modest impact on antimicrobial stewardship at the frontline of medical and veterinary practice, although they will undoubtedly have a substantial influence into the future…Faithful application of these rating systems at all levels of decision making to do with antimicrobial use is now seen as central to the protection of animals, humans and economies from the scourge of AMR."*
>
> Antimicrobial ratings: the importance of importance, Jordan (2019)[77]

d. Regulations on antibiotics of 'medium' and higher importance

Antimicrobials with a 'High' ASTAG ranking are generally not registered by APVMA for use in food-producing animals, unless under exceptional circumstances. The circumstances under which 'High' ranking antimicrobials can be used in animals are as follows: "*based on culture and susceptibility testing, there are no effective alternate agents and the animal is not destined for human consumption*." However, there are certain exceptions, with antibiotics such as virginiamycin and ceftiofur having 'High' ASTAG ratings and being used in food-producing animals[69].

All veterinary antimicrobials with ASTAG 'Medium' or 'High' ratings are for 'therapeutic' uses only – which includes both therapeutic and prophylactic indications (i.e. they cannot be used as growth-promoters)[69]. However, the use of certain antibiotics that are *not* of 'High' importance according to the ASTAG ratings but are categorised as HP-CIAs in the WHO list (i.e. the macrolides) may be used with fewer restrictions in Australia as growth promoters.

There are limited regulations in many countries on the accessibility, use, monitoring and reporting of veterinary antimicrobials. Beyond restrictions on the use and marketing of growth promoters in the EU, USA and some other jurisdictions, and restrictions on the use of specific classes of antibiotics in Australia, antimicrobials of 'Medium' or higher importance classifications according to ASTAG ratings can be utilised in many OECD countries under veterinary advice (sometimes with additional justifications if use is off label, as discussed in section 1).

e. Use of antibiotics for group prophylaxis

According to the latest report on the quantity of antimicrobials sold for veterinary use in Australia[8], it is difficult for registrant companies to estimate the proportions of products used for therapeutic or prophylactic purposes. Therefore, both of these indications are categorised as "therapeutic" within antimicrobial sales data[8].

Unfortunately, there is also no differentiation between prophylactic and therapeutic use of antibiotics within sales data reported for the Netherlands, UK and the USA[57,59].

3. Current surveillance, monitoring and reporting requirements for antimicrobial use in the Australian food animal sector

This section reviews the current activities for surveillance, monitoring and reporting AMU and AMR in the food animal sector in Australia, and the resourcing and funding allocated to these activities. Implementation of the National Antimicrobial Resistance Strategy and recommendations from the JETACAR report will be explored in detail.

a. Monitoring and reporting requirements

There is currently a legal requirement for pharmaceutical companies to provide to the APVMA an annual return detailing the quantities of veterinary chemicals that were imported, manufactured or exported during that year[78]. However, these data are not regularly published in the public domain. As discussed in the previous sections, two reports on the quantity of antimicrobials sold for veterinary use in Australia are available; the latest one published in 2014 reported data collected between 2005 and 2010[8], revealing tonnes of active antimicrobial constituents sold each year. No information was reported regarding the size of the animal populations in which they were used.

However, several surveys reporting antimicrobial use practices have been published, providing valuable insights[79] (see **Table 3**). For example, Hardefeldt *et al.* (2017) investigated antimicrobial classes used and the appropriateness of their use in bovine practice for surgical prophylaxis[80]. Findings showed that antimicrobial drug choice was appropriate for the reported surgical conditions (i.e. procaine penicillin and oxytetracycline accounting for 93% of use). However, under-dosing and incorrect timing of administration were common.

Many guidelines (i.e. prescribing guidelines for veterinarians) and recommendations are widely available for food producers and veterinarians in Australia[55,56,81], to promote judicious use of antimicrobials. These guidelines contribute to antimicrobial stewardship initiatives promoted by the livestock industries, including specific guidelines from the Australian cattle feedlot industry[82] and the Australian Chicken Meat Federation (ACMF)[83]. However, these guidelines and recommendations are not accompanied by legally enforceable monitoring and reporting requirements.

b. Compliance with the Government's National Antimicrobial Stewardship plan

The National Antimicrobial Resistance Strategy ("The 2015 Strategy")[84] represents the first national, cross-sectoral response to the AMR threat in Australia. In this report, seven objectives are outlined to ensure an effective and sustainable response can be coordinated, and together, all stakeholders can work to minimise AMR and safeguard human health, animal health and agricultural productivity. The objectives are as follows:

1. Increase awareness and understanding (through communication, education and training);
2. Antimicrobial stewardship;
3. One Health surveillance;
4. Infection prevention and control;
5. Research;
6. International partnership; and
7. Governance.

Priority Areas for Action for each objective are also provided to focus various stakeholders on the most urgent issues. Most importantly, a One Health approach is emphasised repeatedly to ensure all sectors are engaged to tackle AMR coherently. **Table 8** provides the full description of the objectives and priority areas for action.

Table 8: Objectives and priority areas for action. Information collated from the 2015 Strategy[84].

Objectives	Priority Areas for Action
Objective 1: Increase awareness and understanding of AMR, its implications, and actions to combat it through effective communication, education and training	1.1 Strengthen consumer awareness initiatives to improve understanding of antimicrobial resistance and the importance of using antibiotics appropriately
	1.2 Increase support for human and animal health professionals in reinforcing key messages with patients and clients
	1.3 Strengthen communication and education initiatives for health professionals and health care team members
	1.4 Develop a stakeholder engagement and communication plan to support whole-of-society awareness of, and participation in implementing the Strategy
Objective 2: Implement effective antimicrobial stewardship practices across human health and animal care settings to ensure the appropriate and judicious prescribing, dispensing and administering of antimicrobials	2.1 Ensure that tailored, evidence-based antibiotic prescripbing guidelines are available for all sectors
	2.2 Ensure the availability of evidence-based, best-practice and nationally consistent approaches to AMS across human health and animal care settings
	2.3 Develop tailored, evidence-baseed resources to support the implementation of AMS programmes
	2.4 Review existing accreditation and quality assurance programmes to ensure they appropriately support and encourage compliance with best practice AMS approaches
	2.5 Strengthen existing measures to better support appropriate and judicious use
Objective 3: Develop nationally coordinated One Health surveillance of AMR and antimicrobial usage	3.1 Establish the foundations for national One Health surveillance
	3.2 Agree the objectives of surveillance for each sector, ensuring they align with the overarching objectives for the national One Health surveillance system
	3.3 Develop lists of priority organisms and associated antimicrobials for national reporting
	3.4 Agree and implement a uniform standard for laboratory testing methods for antibacterial susceptibility
	3.5 Improve human health surveillance
	3.6 Improve animal health and agriculture surveillance
	3.7 Investigate requirements for surveillance in food
Objective 4: Improve infection prevention and control measures across human health and animal care settings to help prevent infections and the spread of AMR	4.1 Ensure the availability of evidence-based, best-practice and nationally consistent standards for IPC across human health and animal care settings
	4.2 Review existing accreditation and quality assurance programmes to ensure they appropriately support and encourage compliance with best practice IPC measures
	4.3 Develop additional initiatives and resources to strengthen IPC in all human health care settings
	4.4 Further develop initiatives and resources to strengthen IPC in the livestock industry
	4.5 Further develop resources to strengthen IPC in veterinary practice
	4.6 Encourage continued increases in vaccination rates to prevent infections
Objective 5: Agree a national research agenda and promote investment in the discovery and development of new products and approaches to prevent, detect and contain AMR	5.1 Identify current gaps and agree national research and development priorities
	5.2 Coordinate national research activities and the sharing of information
	5.3 Explore opportunities to increase support for research and development, including incentives for greater private sector investment
	5.4 Explore opportunities to support the translation of promising research findings into new products, policies and approaches
Objective 6: Strengthen international partnerships and collaboration on regional and global efforts to respond to AMR	6.1 Active engagement with multilateral organisations and relevant forums to contribute to regional and global action on antimicrobial resistance
	6.2 Lead regional initiatives to increase capacity to respond to antimicrobial resistance
	6.3 Learn from international best practice
	6.4 Participate in international surveillance initiatives
	6.5 Establish closer ties with international collaborations to link Australia's national research agenda with what is happening internationally
Objective 7: Establish and support clear governance arrangements at the local, jurisdictional, national and international levels to ensure leadership, engagement and accountability for actions to combat AMR	7.1 Identify, establish and maintain linkages between implementation partners across all sectors
	7.2 Work with stakeholders to develop an Implementation Plan for the Strategy
	7.3 Establish baseline measures to inform monitoring and evaluation of the Strategy
	7.4 Review regulation (legislated and other) relevant to antimicrobial resistance and antibiotic usage

The Implementation Plan[85] then translates the Strategy into action. Each objective and its corresponding Priority Areas for Action are broken down into focus areas with activities to be undertaken by the Australian Government, state and territory governments, non-governmental organisations, professional bodies and research organisations. These activities are grouped into ‘One Health’, ‘Human Health’ and ‘Animal Health and Agriculture’ sectors, to define the responsibilities of different stakeholders under each domain of the One Health framework.

Development of this Plan was overseen by the AMR Prevention and Containment (AMRPC) Steering Group. They were also assigned responsibility for monitoring the implementing the Strategy. Examples of activities undertaken in the animal health and agriculture sector are listed below:

- Zoetis Australia provide presentations to animal health professionals and producers within the feedlot and pig industries to improve their understanding of the global and national situation regarding AMR, and the importance of responsible use of the management of AMR as an industry (Objective 1; Priority area for action 1.2)[86];
- The National Centre for Antimicrobial Stewardship surveys attitudes to antimicrobial prescribing in companion and production animals. They develop and assess methods for monitoring AMU at the veterinary practice level (Objective 2; Priority area for action 2.2)[87,88];
- The Australian Chicken Meat Federation is developing a framework for AMS implemented within each of the major chicken meat companies for internal reporting (Objective 2; Priority area for action 2.2)[89];
- The Australian Pesticides and Veterinary Medicines Authority and the Australian Government Department of Agriculture and Water Resources regularly report imports, exports and manufacture of active constituents in veterinary medicines (Objective 3; Priority area for action 3.1)[28];
- Meat and Livestock Australia research and develop evidence-based infection prevention and control measures for adoption into industry standards for managing infectious cattle diseases, including bovine respiratory disease, on feedlots (Objective 4; Priority area for action 4.4)[90];
- The Australian Government Department of Health work with research bodies and other relevant stakeholders to identify future research priorities (Objective 5; Priority area for action 5.1);
- The University of Queensland develop curricula and teaching methods that include improvements in AMR awareness and mitigation in veterinary schools in developing countries (Objective 6; Priority area for action 6.1)[91];
- AMRPC Steering Group work with the ASTAG on AMR to identify indicators and set targets to monitor progress against the objectives of the National AMR Strategy (Objective 7; Priority area for action 7.3).

These examples represent a broad spectrum of multidisciplinary antimicrobial stewardship activities; however, only one Progress Report is currently publicly available[92]. Two years after the Strategy was released, a Progress report was published to highlight the work undertaken and identify challenges and gaps affecting the activities. Achievements in the animal health and agriculture sectors specified in this report are summarised as follows:

- In August 2017, the Australian Chief Veterinary Officer wrote to Australian registered veterinarians. The letter provided a reminder of prudent and responsible use of antimicrobials in veterinary practice, to limit and minimise the spread of AMR (Objective 1);
- The Australian Chicken Meat Federation and Rural Industries Research and Development Corporation are collaborating on a range of initiatives, including an AMS framework and a review of AMS implementation and external verification of programmes within each of the major chicken meat companies[93]. They are also developing evidence-based resources to support the implementation of a chicken meat stewardship framework that can be easily tailored for other poultry meat industries (Objective 2);
- The Australian Government Department of Health is funding a literature review to determine the extent to which AMR is present in food, the extent to which food is a route of transmission of AMR, and to identify gaps to inform decision-making around surveillance requirements and future work (Objective 3)[94];
- The Australian Veterinary Association (AVA) has recently updated the infection, prevention and control principles and procedures in the AVA Guidelines for veterinary personal biosecurity. This provides the latest information about infection control and how to deal with high risk situations, and is relevant to veterinary practices of all types (Objective 4)[95];

- Murdoch University (AMR and Infectious Diseases laboratory) and New South Wales Department of Primary Industries, funded by the Australian Government Department of Agriculture and Water Resources, are studying risk management of critical antimicrobial resistant bacteria in food-producing animals. A semi-automated enumeration assay is being developed to study standard (e.g. as used in surveillance) and enhanced tests (e.g. selective recovery) for the detection of the occurrence of critically-important AMR bacteria in animal faeces and food products (Objective 5);
- The University of Queensland commenced a study identifying current antimicrobial usage and AMR in commensal *E. coli* on integrated chicken-fish farms in Myanmar and supported the development of research capacity in AMR diagnosis at the University of Veterinary Science, Myanmar (Objective 6)[91];
- The AMR Prevention and Containment (AMRPC) Steering Group, previously managed by the Secretaries of the Departments of Health and Agriculture and Water Resources, with the Australian Chief Medical Officer (CMO) and Chief Veterinary Officer (CVO), has convened to provide leadership on AMR and oversee the development and implementation of the Strategy (Objective 7).

There is clear evidence of actions being initiated under each objective set out in the First National Antimicrobial Resistance Strategy. However, no further reports are available to assess the progress of such initiatives and activities after 2017. It is also unclear whether any changes were actioned in response to the challenges identified in the 2017 Progress report. Furthermore, in implementing the activities outlined above, it appears that the objectives are being addressed individually under separate objectives and sectors (i.e. human health and animal health), rather than as part of a coherent One Health programme of work as envisioned in the Strategy.

It can be noted that the human health sector appears to receive more attention and regulatory support compared to the animal health sector in Australia. For instance, the Antimicrobial Use and Resistance in Australia (AURA) surveillance system ensures comprehensive, coordinated and effective surveillance of AMR and AMU in human health. No parallel can be found for animal health and agriculture.

The Second National Antimicrobial Stewardship Plan (2020 Strategy)[96] celebrated the progress made in response to the first Strategy. Progress included development of a One Health Antimicrobial Resistance online hub, which includes an “Activity and Research Directory”[97] to showcase activities led by multiple stakeholders and provide a platform for sharing information and improving collaboration on AMR related initiatives.

Furthermore, “Food” and “Environment” are added as sectors in the report, which previously included “Human Health”, “Animal Health”, and “Agriculture”. The 2020 Strategy also encompasses other classes of antimicrobials such as antifungals and antivirals.

Another important difference between the 2015 and 2020 strategies is the arrangement of the seven objectives. Although the principles of the seven objectives are similar between the two strategies, ‘Governance’ has been moved from the 7th objective in the 2015 Strategy to the 1st objective in the 2020 Strategy. ‘Prevention and Control of Infection’ was also moved up from the 4th to the 2nd Objective, which suggests increased prioritisation of these objectives.

Rather than listing the objectives in a linear manner, the 2020 Strategy included a more structured model to demonstrate how each objective fits into the national vision of combatting AMR: Objectives 6 and 7 form the foundations of all of the actions; the four ‘pillar’ Objectives (Objectives 2-5) are positioned in the centre; and Objective 1 serves as an overarching principle (see **Figure 7**).

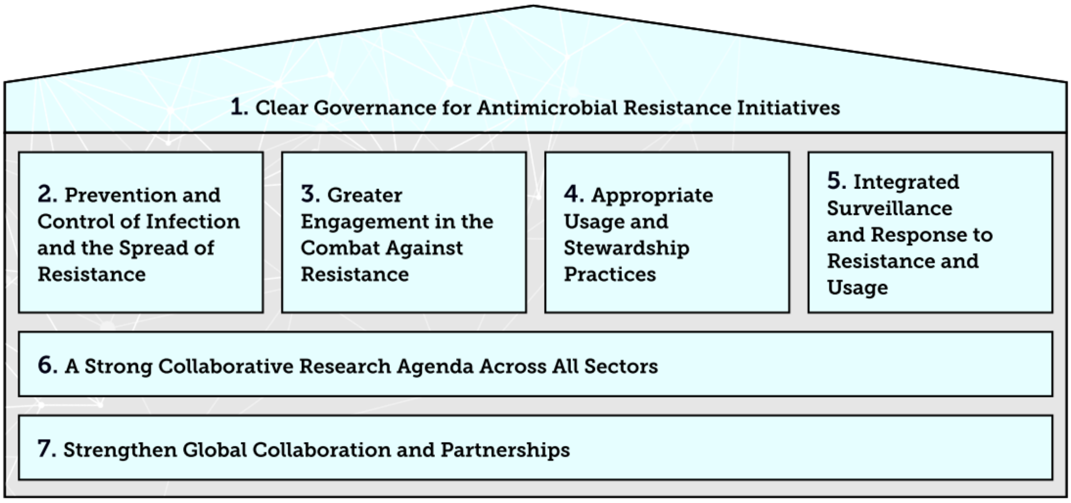


Figure 7: Objectives of the 2020 Strategy. From the Second National Antimicrobial Stewardship Plan – 2020 and beyond[96].

The One Health Master Action Plan (OHMAP)[98] was later published in 2021 to provide practical guidance for implementing the 2020 Strategy. Priority and focus areas were listed for each objective, as well as the One Health sectors expected to contribute to each focus area. No further reports are available to evaluate the progress of the 2020 Strategy and to monitor the compliance of the stakeholders.

c. *Implementation of the JETACAR recommendations*

The **1999 Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) report** laid out 22 recommendations for the “appropriate future management of antibiotic use in food-producing animals” in Australia[99]. The recommendations fall under seven key principles, as follows:

- Regulatory controls (recommendations 1-9);
- Monitoring and surveillance (recommendations 10-11);
- Infection prevention strategies and hygiene measures (recommendations 12-14);
- Education (recommendations 15-17);
- Further research (recommendation 18);
- Communication (recommendations 19-20); and
- Coordination (recommendations 21-22).

The Australian Government strongly supported the intent of these JETACAR recommendations and promised to establish:

- An Expert Advisory Group on Antibiotics/Antimicrobial Resistance (EAGAR), under the auspices of the National Health and Medical Research Council (NHMRC), to provide continuing advice on antibiotic resistance and related matters (2000-2007); and
- A Commonwealth Interdepartmental JETACAR Implementation Group (CIJIG) to oversee and coordinate the continuing government response to the JETACAR, to respond to the policy advice received from EAGAR, and to seek funding for implementation purposes (2000-2004).

However, although the government supports and accepts the recommendations, it is not clear from information in the public domain what actions were taken, or how impactful the actions were[100].

The CIJIG later published a progress report on the government response to the JETACAR Report[61]. The establishment and duties of the CIJIG and EAGAR were explained in more detail. In August 2000 at the Australian Health Ministers Conference (AHMC), an AHMC JETACAR Taskforce was appointed to monitor and report to the Minister for Health and Ageing on the implementation of the government response. The Primary Industries Ministerial Council (PIMC) also appointed the PISC Taskforce on JETACAR to monitor the JETACAR implementation from the animal industry perspective. Further progress and reports are not available in the public domain.

In 2013, the **Senate (Finance and Public Administration References Committee)**[101] scrutinised the progress on the implementation of the recommendations of the 1999 JETACAR report once more, and critically evaluated actions enacted and not enacted. The table below shows a summary of government actions taken to address AMR.

Table 9: Summary of significant elements relevant to the recommendations of the 1999 JETACAR report on AMR in Australia. Taken from the Senate Progress report[101].

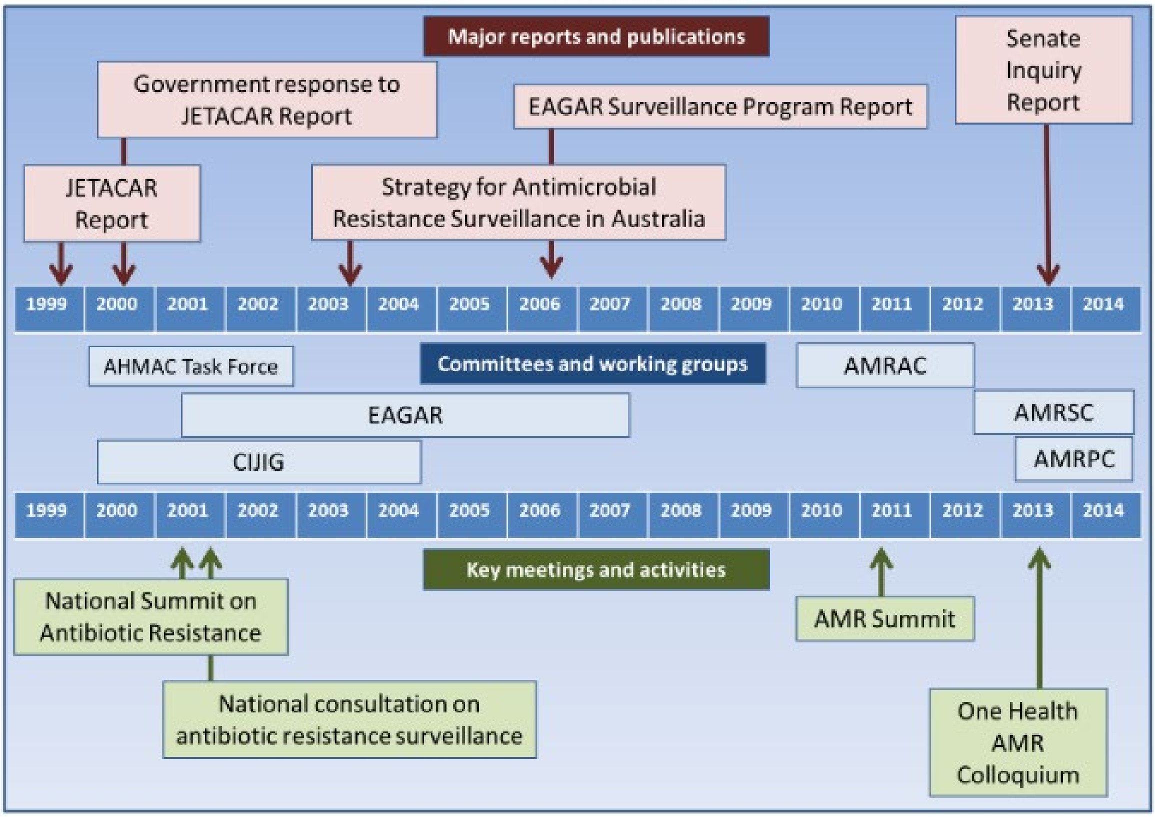
Date	Significant element	Role/Outputs/Comments
2000 – 2002	Australian Health Ministers' Conference JETACAR Taskforce	• oversaw activities arising from the JETACAR report • provided conduit for human health related issues to Health Ministers
2000 – 2004	CIJIG (Commonwealth Interdepartmental JETACAR Implementation Group)	• responsible for promoting implementation of JETACAR recommendations • reported through the Australian Health Ministers' Conference JETACAR Taskforce
Apr 2001	Australian Infection Control Association – National Surveillance of Healthcare Associated Infection in Australia	• report developed in response to JETACAR • study of surveillance activities, policies and programs across Australia
May 2001	National Summit on Antibiotic Resistance	• involved participants from human health, food and primary industries • proposed priorities for national action
2001	National consultation on antibiotic resistance surveillance	• part of the post-JETACAR Report consultation • workshops and focus groups involved all states and territories seeking input to a antibiotic resistance surveillance plan
2003	Strategy for Antimicrobial Resistance Surveillance in Australia	• published in Communicable Diseases Intelligence journal • proposed a comprehensive strategy to address JETACAR recommendations relating to surveillance
2001 – 2007	EAGAR (Expert Advisory Group on Antimicrobial Resistance)	• role of expert advisory group under the oversight of the NHMRC • produced outlines of a comprehensive set of projects to address JETACAR recommendations
Aug 2006	EAGAR Comprehensive Integrated Surveillance Program to Improve Australia's Response to Antimicrobial Resistance	• contained the outlines for nine projects that would address surveillance of antimicrobial resistance and antibiotic use
2010 – 2012	NHMRC AMRAC (Anti Microbial Resistance Advisory Committee)	• established by NHMRC in 2010 • AMRAC's term expired on 30 June 2012
Feb 2011	Antimicrobial Resistance Summit – A call to urgent action	• jointly convened by the ASID and the ASA • a proposed plan of action was published in the Australian Medical Association journal
2012 – ongoing	AMRSC (Antimicrobial Resistance Standing Committee)	• established in the review of committee structures under the COAG Standing Council on Health

Criticisms were received regarding the Australian Government's response to the JETACAR report. Professor Peter Collignon, infectious disease physician and a member of JETACAR, stated that '*a lot of [the recommendations] have been done only partially or not at all'*, including the proposal for comprehensive AMR and AMU surveillance across all sectors that was developed by EAGAR but never released.

Professor Matthew Cooper commented that a major drawback for full implementation of the JETACAR recommendations may have been the involvement of dozens of departments and governmental agencies, such that no one agency or minister was responsible or accountable. Numerous committees and groups were established and disbanded (including EAGAR and CIJIG), compromising programme continuity and suggesting a lack of coordination.

The Senate report concluded with 10 further recommendations. The Government's response to these recommendations was generally inconclusive (i.e. 'agreed in-principle' or 'partially agreed'), with little guarantee and commitment to action[102].

Multiple reports, publications, committees, meetings and activities were initiated following the 1999 JETACAR report (see the timeline in **Figure 8**) for AMU[26] and AMR[103,104] in both the human and animal sectors. For the animal and agricultural sectors, lessons could be learnt and strategies adapted from achievements in the human health sector, especially regarding the AURA surveillance system. This may provide valuable insights into operationalising an effective surveillance system, which is needed in the animal health field.



<u>Figure 8</u>: Key events relating to antimicrobial surveillance and governance in the food animal sector in Australia between 1999 and 2014. From Surveillance and Reporting of Antimicrobial Resistance and Antibiotic Usage in Animals and Agriculture in Australia (2014)[79].

d. Integrity of data on AMR and AMU in the Australian food sector

In this section, we provide an overview of the peer-reviewed and industry studies that document the prevalence of antimicrobial resistance, in particular zoonotic pathogens in samples and bacterial isolates from food animal species in Australia, and some reports regarding antimicrobial use. This section is not a literature review to summarise findings such as prevalence rates, or comment on study quality; it is intended to provide an indication of the volume of research, and of how current, comprehensive and independent this body of research is, for each species.

As a measure of volume, the following tables provide a summary of the papers found during a non-systematic online web search, and of the papers identified and confidentially shared with FAI by World Animal Protection (document: 'Antibiotic resistance list from collated studies_WAP 23 Nov 20'). As an indicator of how current the body of research is for each species and risk, the papers are listed in reverse chronological order and the date of publication (newest first) and data collection period are included, the latter to account for studies utilising retrospective/historical data sets or that experienced publication delays. To provide a crude indication of how comprehensive each paper is, the sample size in terms of number of specimens collected from food animals or the number of bacterial isolates analysed is provided. Finally, to facilitate a subjective assessment of independence, the affiliations of the authors and the source of funding for each piece of research is provided.

Broiler chickens and laying hens: E. coli, Enterococcus, Campylobacter, Salmonella and environmental risk

Tables 10-14 provide an overview of the papers found for AMR risk from broiler chickens and laying hens in Australia. There was a substantial body of research for most pathogens, with the largest number of papers (11) found in relation to Campylobacter in broiler chickens. However, evidence was somewhat more lacking for laying hens, Salmonella and for the risks presented by environmental contamination by AMR determinants from poultry. The majority of papers were published within the last 10 years, indicating relevance to current risks in the food sector, although it should be noted that lag-times of between 1 and 13 years between sample collection/analysis and paper publication were observed. The most common time delay between sample collection and paper publication was four years. Sample sizes used in the studies ranged from 34 to 1746 animal samples, although the actual sample size was not explicitly provided by certain authors that preferentially detailed the number of bacterial isolates analysed instead. Sample sizes were most frequently in the range 100-320, and studies were therefore relatively small compared to the largest study conducted by Barton and Wilkins (2001), featuring 1746 samples[104]. In terms of affiliations, the papers reflected a variety of university, government and industry-led studies.

In terms of their findings, a mixed picture is presented by the selection of poultry papers reviewed, in which some highlight present or emerging dangers of AMR of public health importance from poultry products in Australia, with others portraying a very low risk of AMR, attributed to Australia's antimicrobial stewardship and farming policies. There is a general narrative of low risks of resistance to critically-important antimicrobials, which would be a logical conclusion as certain HP-CIAs are not licensed for use in the Australian food animal sector. However, other research opposed these findings, confirming the presence of resistance to antimicrobials of importance to human health. In particular, in finding resistance to antimicrobials not licensed for food animal use in the samples, researchers have highlighted the risks presented by historical antibiotic use, possible off-label use, and an increasingly globalised food supply chain, in which breeding stock, food animals and their products together with antimicrobial resistance determinants are exchanged across international borders.

“The findings are extremely favourable compared to resistance profiles for chicken isolates described internationally. While the fluoroquinolone resistance in the Campylobacter isolates deserves further investigation, there was a general reduction in AMR observed in comparison with the 2004 study. These results highlight the efficacy of the chicken industry’s past and current antimicrobial stewardship efforts and identify further areas for investigation and improvement.”

-Australian Chicken Meat Federation (2018)[105]

“This study establishes the presence of resistance to critically-important antimicrobials among clinical E. coli isolates from Australian food-producing animals, largely attributed to globally disseminated fluoroquinolone- and extended-spectrum cephalosporin-resistant E. coli lineages."

-Abraham et al (2015)[106]

In short, substantial work has been assimilated in recent years to determine the prevalence and risks of AMR attributed to poultry and poultry products in Australia, with industry reports balanced in number although not always corroborated in their conclusions by university-led research. Multiple papers are published for the key food-borne pathogens E. coli, Enterococcus and Campylobacter, many with relatively small samples sizes, although evidence for laying hens, Salmonella resistance and the risks presented by environmental contamination could be expanded.[107]

Pigs: E. coli, Enterococcus, Campylobacter and Salmonella

Tables 15-18 provide an overview of the papers found for AMR risk from pigs in Australia. There was a substantial body of research for most pathogens, with the largest number of papers (10) found in relation to E. coli. The majority of papers were published within the last 10 years, indicating relevance to current risks in the food sector, although lag-times of between 0 and 9 years between sample collection/analysis and paper publication were observed. The most common time delay between sample collection and paper publication was 4 years. Sample sizes used in the studies ranged from 60 to 1100 animal samples, although the actual sample size was not explicitly provided by certain authors that preferentially detailed the number of bacterial isolates analysed instead. Sample sizes were most frequently in the range 100-300, and studies were therefore relatively small compared to the largest study conducted by Breda et al (2017), featuring 1100 samples[108]. In terms of affiliations, the papers reflected a variety of university, NGO, government and industry-led studies.

In terms of findings, the selection of studies portray a generally more concerning picture around antimicrobial resistance arising in pigs compared to in poultry, with many of the researchers reporting the presence of food-borne pathogens of resistant and multi-drug resistant strains, particularly with resistance to first-line and commonly used antimicrobials. Some attribute this to the greater use of antibiotics in the pig sector compared to the poultry sector. Once again, some conclude that resistance determinants to antimicrobials of critical importance to human health are absent or of low prevalence.

"'This study shows that non-susceptibility to first-line antimicrobials is common among E. coli and Salmonella spp. isolates from healthy slaughter-age pigs in Australia. However, very low levels of non-susceptibility to critically-important antimicrobials (CIAs), namely third-generation cephalosporins and fluoroquinolones were observed. Nevertheless, the isolation of two ciprofloxacin-resistant E. coli isolates from Australian pigs demonstrates that even in the absence of local antimicrobial selection pressure, fluoroquinolone-resistant E. coli clonal lineages may enter livestock production facilities despite strict biosecurity."

-Kidsley et al (2018)[109]

"In South Australian pigs, thermophilic Campylobacter species showed widespread resistance (60–100%) to tylosin, erythromycin, lincomycin, ampicillin and tetracycline. No resistance was seen to ciprofloxacin."

-Hart et al (2004)[110]

"..The different treatment practices in poultry and pigs have resulted in differences in resistance profiles in Campylobacter isolates. Antibiotics are used more frequently in pigs."

-Obeng et al (2012)[111]

One additional paper was also found regarding antimicrobial use in the Australian pig sector, but was not included in the tables because it relates to antimicrobial usage patterns and not a specific pathogen. Jordan et al (2009)'s findings were based on a survey of 197 pig herds, representing an estimated 51% of all large pig herds in Australia, and found that most piggeries relied on drugs of low importance in human medicine (e.g. tetracyclines, penicillins and sulfonamides). Of the drugs of high importance in human medicine that can be legally prescribed to pigs in Australia, ceftiofur use was reported in 25% of herds.[112]

Aquaculture: AMR and AMU

Table 19 provides a summary of three papers found regarding AMR and AMU in the Australian aquaculture industry. It appears there are few studies on this subject. The single university-led study on AMR in aquaculture was published in 2005 using data collected between 2000 and 2004, and findings may therefore not reflect the situation today. However, the presence of resistance determinants to multiple antibiotics in their samples, despite the fact that no antibiotics are licensed for aquaculture in Australia, are concerning and warrant further investigation.

Two antibiotic use reports for the company Tassal were also found. These suggest a trend of increasing use of antibiotics between 2017 and 2019, from a baseline of zero use in 2017 to 62 g/tonne in 2019, and a reduced usage 2019-2020 to 27 g/tonne. To understand antibiotic usage patterns more broadly across the aquaculture industry in Australia, further data from more companies and with a longer timeline are required.

Beef cattle: All pathogens

Table 20 provides an overview of the nine papers found for AMR risk from beef and dairy cattle in Australia. A number of studies were found covering the specific food-borne pathogens Campylobacter, Entercoccus, E. coli and Salmonella, however more research is required to provide a more comprehensive body of evidence. The majority of papers were published within the last 10 years, indicating relevance to current risks in the food sector, although it should be noted that lag-times of between one and seven years between sample collection/analysis and paper publication were observed. Sample sizes used in the studies were very variable up to 1500 animal samples, although the actual sample size was not explicitly provided by certain authors that preferentially detailed the number of bacterial isolates analysed instead. In terms of affiliations, Australian government departments, industry bodies or commercial companies were involved in all of the cattle studies (or combinations of these), together with university researchers.

In terms of their findings, the studies predominantly indicate low levels of antimicrobial resistance determinants arising from cattle holdings, particularly relating to antimicrobials of significance to animal health. Some, however, document relatively high levels of resistance to antimicrobials not considered significant to human health. Where resistance to critically-important antimicrobials was detected, it was attributed to ‘globally disseminated E. coli lineages’[113], as opposed to domestic antibiotic use selection pressures.

Due to the relatively small number of cattle studies, with particular research gaps in relation to dairy cattle, and specific important zoonotic pathogens such as Campylobacter and E. coli, these findings should be interpreted with caution before further evidence is published.

“The results of AMR testing identified high levels of resistance to antimicrobials that are not critically or highly-important to human medicine with resistance to flavomycin (80.2%) and lincomycin (85.4–94.2%) routinely observed. Conversely, resistance to antibiotics considered critically or highly-important to human medicine such as tigecycline, daptomycin, vancomycin and linezolid was not present in this study. There is minimal evidence that Australian cattle production practices are responsible for disproportionate contributions to AMR development and in general resistance to antimicrobials of critical and high importance in human medicine was low regardless of the isolate source."

-Barlow et al (2017)[114]

Table 10: Summary of a selection of research papers documenting antimicrobial resistance in E. coli in samples and bacterial isolates from poultry in Australia [94,103–105,113,115–119]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Broiler chickens and laying hens	*E. coli*	Escherichia coli and Salmonella spp. isolated from Australian meat chickens remain susceptible to critically important antimicrobial agents (Abraham et al, 2019)	Implemented by university institution, and funded by Australian Government's Department of Agriculture and Water Resources.	2016	200 pooled samples	"The results provide strong evidence that resistance to highest priority CIA's is absent in commensal E. coli and Salmonella isolated from Australian meat chickens, and demonstrates low levels of resistance to compounds with less critical ratings such as cefoxitin, trimethoprim/sulfamethoxazole, and tetracycline... Nevertheless, industry and government need to proactively monitor AMR and antimicrobial stewardship practices to ensure the long-term protection of both animal and human health."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian meat chickens (ACMF, 2018)	Commercial chicken processors, study funded by The Department of Agriculture and Water Resources	2016	220 samples	"In general, the results of this survey demonstrate either nil or substantially low carriage of resistance to antimicrobials used in human medicine. The findings are extremely favourable compared to resistance profiles for chicken isolates described internationally. While the fluoroquinolone resistance in the Campylobacter isolates deserves further investigation, there was a general reduction in AMR observed in comparison with the 2004 study. These results highlight the efficacy of the chicken industry's past and current antimicrobial stewardship efforts and identify further areas for investigation and improvement."
		Superbugs in the supermarket? Assessing the rate of contamination with third-generation cephalosporin-resistant gram-negative bacteria in fresh Australian pork and chicken (McLellan et al, 2018)	Implemented and funded by university institutions	2014	60 specimens	"We found low rates of multidrug-resistant gram negative bacteria in Australian chicken and pork meat, but potential 3rd generation cephalosporin resistant gram negative bacteria are common (93% specimens)."
		Factors affecting the presence, genetic diversity and antimicrobial sensitivity of Escherichia coli in poultry meat samples collected from Canberra, Australia (Vangchhia et al, 2018)	University institutions, study funded by Canberra Hospital Private Practice Trust Fund	2013-14	306 samples	"The results of this study demonstrate that poultry meat products are likely to be contaminated with a genetically diverse community of E. coli. The presence of E. coli in a sample is likely largely a consequence of contamination of the meat by the bird's own fecal E. coli. The fecal E. coli clonal communities present in the birds is expected to vary with farm, season and rearing method."
		First detection of extended-spectrum cephalosporin- and fluoroquinolone-resistant Escherichia coli in Australian food-producing animals (Abraham et al, 2015)	Veterinary diagnostic laboratories; Study funded by Zoetis and an Australian Research Council Linkage Grant	2013-14	32 clinical isolates	"This study establishes the presence of resistance to critically important antimicrobials among clinical E. coli isolates from Australian food-producing animals, largely attributed to globally disseminated fluoroquinolone- and Extended-spectrum cephalosporin-resistant E. coli lineages."
		Prevalence of Antimicrobial Resistance in Enterococci and Escherichia coli in Meat Chicken Flocks During a Production Cycle and Egg Layer Pullets During Rearing (Obeng et al, 2014)	Implemented by university institutions and Biosecurity department of Australian Government	Unknown	302 samples	"This study demonstrates that newly hatched chicks are already colonized with resistant bacteria which persist through the production cycle and can potentially contaminate eggs and chicken carcasses. This study also confirms that poultry are a potential source of pathogenic E. coli strains."
		Antibiotic resistance, phylogenetic grouping and virulence potential of Escherichia coli isolated from the faeces of intensively farmed and free range poultry (Obeng et al, 2012)	Implemented by university institutions and Biosecurity department of Australian Government	2008-9	311 samples	"This study demonstrates that antibiotic resistance has declined in E. coli isolates from the level detected in intensive meat chickens by an earlier study in 2000. In addition it demonstrates that, at least under Australian conditions there is no significant difference in resistance in E. coli between intensively and free range raised meat chickens..Resistance in free-range layers was substantially lower than the resistance observed in meat chickens."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations. In E. coli from poultry and pork the prevalence of AMR for ampicillin (38% and 28.2%), streptomycin (19% and 17.4%), tetracycline (47% and 44.5%) and trimethoprim / sulphamethoxazole (22% and 13%) was notably higher than in beef E. coli isolates."
		Antimicrobial Resistance in Bacteria of Animal Origin (Australian Government, 2007)	Commercial chicken processors/Department of Agriculture and Water Resources	2003-4	303 samples	"With the exception of streptogramins and E. faecium, nil or a very low prevalence of resistance to antimicrobials of importance to human medicine was observed. No resistance was detected amongst E. coli to either cefotaxime or ceftiofur (both third generation cephalosporins). Resistance to ciprofloxacin was detected in only one E. coli isolate from chickens (0.4%) but not in any Campylobacter spp. Amongst E. coli from chickens (n = 269), resistance was detected to ampicillin, tetracycline and trimethoprim/sulfamethoxazole (33%, 44% and 27% of isolates, respectively) and there was little or no resistance to the other antimicrobial agents. Multi- and multiple-resistance was also detected in chicken E. coli isolates..with only 2.6% of chicken isolates having multiple resistance and one isolate resistant to two quinolone-type antibiotics."
		Antibiotic Resistance in Bacteria Isolated From Poultry: A report for the Rural Industries Research and Development Corporation (Barton and Wilkins, 2001)	Report written by university researchers and funded by the Rural Industries Research and Development Corporation.	1999-2000	1746 samples	"Acquired resistance to multiple classes of antibiotics was seen in E coli...There was a significant amount of resistance to ampicillin, streptomycin, tetracycline and trimethoprim in isolates from laboratories A and B and surprisingly, resistance to cephalothin in isolates from one of the laboratories (laboratory A) (cephalosporins are not registered for use in chickens). There was negligible resistance to gentamicin and no resistance to fluoroquinolones (ciprofloxacin) – neither of these antibiotics is registered for use in food producing animals. As is the norm with livestock isolates, multiple resistance was commonly seen."

Table 11: Summary of a selection of research papers documenting antimicrobial resistance in Enterococcus in samples and bacterial isolates from poultry in Australia [94,103–105,120,121]

Species	Risk	Study title	Affiliations	Data collection period	Sample size range	Summary of findings
Broiler chickens and laying hens	*Enterococcus*	Genomic, Antimicrobial Resistance, and Public Health Insights into Enterococcus spp. from Australian Chickens (O'Dea et al, 2019)	Study implemented by members of university institutions and the Australian Chicken Meat Federation, and funded by the Australian Government's Department of Agriculture and Water Resources.	2016	200 pooled samples	"Our study has provided further insight into the widespread occurrence and characteristics of the potentially pathogenic Enterococcus species E. faecalis and E. faecium in Australian meat chickens. Although some enterococcal isolates were found to be resistant to multiple antimicrobials, vancomycin resistance was not detected...This detailed genomic study comparing poultry-derived E. faecium isolates with human sepsis-associated isolates combined with phenotypic antimicrobial resistance data provides evidence that poultry E. faecium is not a primary source of vancomycin-resistant E. faecium in Australia."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian meat chickens (ACMF, 2018)	Commercial chicken processors, study funded by The Department of Agriculture and Water Resources	2016	220 samples	"No resistance was detected to aminoglycosides or chloramphenicol and low resistance was detected to linezolid and vancomycin.. Among the enterococci isolates, 17.5% isolates were classified as MDR (clinical resistance to three or more drug classes). Resistance and presence of resistance genes to tetracycline (40.3-46.3%) was common among Enterococcus spp. reflecting historical use in the chicken industry. Elevated frequency of quinupristin-dalfopristin (54.5%) resistance among E. faecium may be a consequence of past virginiamycin use... Although not entirely comparative, it can be highlighted that there has been a significant reduction in phenotypic resistance to erythromycin in Enterococcus isolates from Australian meat chickens since the earlier study in 2004. This could reflect the reduction in use of macrolides in the industry since the introduction of the Mycoplasma vaccines in the 1990s... In general, the results of this survey demonstrate either nil or substantially low carriage of resistance to antimicrobials used in human medicine. The findings are extremely favourable compared to resistance profiles for chicken isolates described internationally...These results highlight the efficacy of the chicken industry's past and current antimicrobial stewardship efforts and identify further areas for investigation and improvement."
		Comparison of antimicrobial resistance patterns in enterococci from intensive and free range chickens in Australia (Obeng et al, 2013)	Implemented by university institutions and Biosecurity department of Australian Government	2000, 2008-9	311 samples	"In conclusion, this revealed a significant difference in phenotypic resistance and resistance genes in free range meat chickens compared with egg laying birds. This suggests that meat chickens (particularly free range) are a potential source of resistant E. faecalis and E. faecium strains....This study provides evidence that, despite strict regulation imposed on antibiotic usage in poultry farming in Australia, enterococcal species of poultry origin persist with varying levels of resistance to a variety of antibiotics."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations. E. faecalis isolates from poultry were disguished from beef and pork E. faecalis isolates by high prevalences of resistance to erythromycin (48%) and tetracycline (76%). The absence of detection of Enterococcus amongst Enterococcus faecium amongst isolates from all retail meat sources was unexpected."
		Antimicrobial Resistance in Bacteria of Animal Origin (Australian Government, 2007)	Commercial chicken processors/Department of Agriculture and Water Resources	2003-4	303 samples	"With the exception of streptogramins and E. faecium, nil or a very low prevalence of resistance to antimicrobials of importance to human medicine was observed. Only one enterococci isolate was vancomycin resistant (low-level vanC), whilst high-level resistance to gentamicin were not detected in any enterococci. Enterococci from chickens (n=217) showed a high prevalence (68%) of resistance to erythromycin. Resistance to virginiamycin in enterococci from chickens was common (28.7% excluding consideration of E. faecalis which is intrinsically resistant to virginiamycin)."
		Antibiotic Resistance in Bacteria Isolated From Poultry: A report for the Rural Industries Research and Development Corporation (Barton and Wilkins, 2001)	Report written by university researchers and funded by the Rural Industries Research and Development Corporation.	1999-2000	1746 samples	"Acquired vanA vancomycin resistance was detected in E faecium isolates and somewhat surprisingly in E hirae which is normally intrinsically resistant only to low concentrations of vancomycin. Resistance to virginiamycin and bacitracin was also common in E faecium...Resistance to other antibiotics was widespread and in accordance with expectations because these organisms are known to be intrinsically resistant to many antibiotics."

Table 12: Summary of a selection of research papers documenting antimicrobial resistance in Campylobacter in samples and bacterial isolates from poultry in Australia[94,111,122–130]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Broiler chickens and laying hens	*Campylobacter*	Molecular characterization of Campylobacter spp. recovered from beef, chicken, lamb and pork products at retail in Australia (Wallace et al, 2020)	Study was conducted by members of university institutions and government departments, and was funded by AgriFutures, NHMRC and various government departments.	2017-9	616 isolates from 1490 samples of chicken, lamb, pork and beef	"Our results indicate Australia's AMR prevalence in Campylobacter spp. from retail products is very low. Our results also suggest prevalence of resistance in Campylobacter spp. from foods of animal origin may be increasing, but ongoing surveillance is needed to confirm such a trend."
		Emergence of Fluoroquinolone-Resistant Campylobacter jejuni and Campylobacter coli among Australian Chickens in the Absence of Fluoroquinolone Use (Abraham et al, 2020)	Study implemented by members of university institutions and the Australian Chicken Meat Federation, and funded by the Australian Government's Department of Agriculture and Water Resources.	2016	200 pooled samples	"In conclusion, this study demonstrates a favorable AMR status among the majority of C. jejuni and C. coli isolates with regard to resistance to key antimicrobials important to human health. However, the present study reveals the emergence of fluoroquinolone-specific drug resistance in small subpopulation of C. jejuni and C. coli among Australian isolates from the guts of meat chickens in the absence of fluoroquinolone use."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian meat chickens (ACMF, 2018)	Commercial chicken processors, study funded by The Department of Agriculture and Water Resources	2016	220 samples	"In general, the results of this survey demonstrate either nil or substantially low carriage of resistance to antimicrobials used in human medicine. The findings are extremely favourable compared to resistance profiles for chicken isolates described internationally. While the fluoroquinolone resistance in the Campylobacter isolates deserves further investigation, there was a general reduction in AMR observed in comparison with the 2004 study. These results highlight the efficacy of the chicken industry's past and current antimicrobial stewardship efforts and identify further areas for investigation and improvement."
		Comparison of epidemiologically linked Campylobacter jejuni isolated from human and poultry sources (Lajhar et al, 2015)	Study conducted by researchers from CSIRO, university and government researchers, and funded by funded by CSIRO.	2011	26 isolates	"Despite the small sample size, a combination of typing methods, flaA-SVR and P-BIT support that contact with raw or consumption of undercooked chicken is one of the important sources of campylobacteriosis and evaluated the risk of strains to humans. [These findings] could be considered as further evidence and a warning signal for the importance of poultry as potential vehicles of campylobacteriosis and a risk factor in campylobacteriosis preceding neuropathy."
		Antimicrobial resistance and genetic characterization of Campylobacter spp. from three countries (Wieczorek et al, 2013)	Study conducted by university researchers, international research institutes and CSIRO, and funded by the Commonwealth Scientific and Industrial Research Organization.	2010-2	20 isolates	"Only two (10%) Australian isolates were resistant, one to tetracycline and one to nalidixic acid. Polish isolates (12; 54.5%) carried multiresistance with the most common pattern (9 strains; 40.9%) ciprofloxacin, nalidixic acid, and tetracycline. All Malaysian strains were resistant to at least three antimicrobials, with 9 isolates carrying multiresistance to 8 antimicrobials."
		Antimicrobial susceptibilities and resistance genes in Campylobacter strains isolated from poultry and pigs in Australia (Obeng et al, 2012)	Implemented by University of South Australia	2008-9	311 samples	"No significant difference between isolates from free range egg layers and meat chickens ($P < 0{\cdot}05$) was found. However, there were significant differences between the pig strains and all the groups of poultry strains ($P < 0{\cdot}05$) with regard to carriage of resistance genes. In addition, pulsed field gel electrophoresis of selected resistant isolates from the poultry and pig revealed closely related clonal groups."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations. AMR resistance to all antimicrobials tested in Campylobacter from chicken was low (≤4%). Resistance to quinolones was not observed in any E. coli or Campylobacter isolates."
		Antimicrobial Resistance in Bacteria of Animal Origin (Australian Government, 2007)	Commercial chicken processors/Department of Agriculture and Water Resources	2003-4	303 samples	"With the exception of streptogramins and E. faecium, nil or a very low prevalence of resistance to antimicrobials of importance to human medicine was observed. Resistance to ciprofloxacin was detected in only one E. coli isolate from chickens (0.4%) but not in any Campylobacter spp. Tetracycline and erythromycin resistance (21% and 11% respectively) were detected in Campylobacter spp. from chickens (n=131). There was no multiple-resistance found in enterococci or Campylobacter isolated from chickens."
		Antibiotic resistance in Campylobacter jejuni and Campylobacter coli isolated from poultry in the South-East Queensland region (Miflin et al, 2007)	This study was conducted by members of Department of Primary Industries and Fisheries and was funded by the Rural Industries Research and Development Corporation (Chicken Meat Program).	Unspecified	152 isolates	"Our study has provided solid evidence that the majority of Queensland poultry isolates of Campylobacter shows little resistance to antibiotics that are either used in the poultry industry or of public health significance."
		Tetracycline resistance of Australian Campylobacter jejuni and Campylobacter coli isolates (Pratt and Korolik, 2005)	Conducted and funded as part of a university studentship.	Unspecified	46 isolates from humans and chickens	"These data indicate that the tet(O) gene, previously reported in Campylobacter strains throughout the world, is present in Australian Campylobacter."
		Antibiotic Resistance in Bacteria Isolated From Poultry: A report for the Rural Industries Research and Development Corporation (Barton and Wilkins, 2001)	Report written by university researchers and funded by the Rural Industries Research and Development Corporation.	1999-2000	1746 samples	"Among key findings is the absence of fluoroquinolone resistance in campylobacter (or E coli or salmonella) reflecting the fact that fluoroquinolones are not registered in Australia for use in livestock species...Resistance to ampicillin was very widespread, but resistance patterns to other antibiotics differed between the Laboratories. There was no resistance to fluoroquinolones and very little resistance to gentamicin."

Table 13: Summary of a selection of research papers documenting antimicrobial resistance in Salmonella in samples and bacterial isolates from poultry in Australia[94,105,116,131,132]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Broiler chickens and laying hens	*Salmonella*	Escherichia coli and Salmonella spp. isolated from Australian meat chickens remain susceptible to critically important antimicrobial agents (Abraham et al, 2019)	Implemented by university institution, and funded by Australian Government's Department of Agriculture and Water Resources.	2016	200 pooled samples	"The results provide strong evidence that resistance to highest priority CIA's is absent in commensal E. coli and Salmonella isolated from Australian meat chickens, and demonstrates low levels of resistance to compounds with less critical ratings such as cefoxitin, trimethoprim/sulfamethoxazole, and tetracycline... Nevertheless, industry and government need to proactively monitor AMR and antimicrobial stewardship practices to ensure the long-term protection of both animal and human health."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian meat chickens (ACMF, 2018)	Commercial chicken processors, study funded by The Department of Agriculture and Water Resources	2016	220 samples	"In general, the results of this survey demonstrate either nil or substantially low carriage of resistance to antimicrobials used in human medicine. Susceptibility to all antimicrobials tested was observed in 92.5% of the 53 Salmonella isolates. No multidrug resistant bacteria were detected. None of the Salmonella were microbiologically resistant to ceftiofur, ciprofloxacin, chloramphenicol, florfenicol, colistin, gentamicin or tetracycline. Resistance was detected at low frequency to ampicillin, streptomycin and trimethoprim. None of the six isolates that were microbiologically resistant to cefoxitin carried any beta lactam genes required for cefoxitin resistance which suggests that there is measurement variation in the assay, the breakpoints may be inappropriate, or there exists previously uncharacterised resistance mechanisms."
		Antimicrobial resistance of non-typhoidal Salmonella isolates from egg layer flocks and egg shells (Pande et al, 2015)	Study conducted by university researchers and funded by the Australian Government.	Unspecified	145 isolates	"The work described here highlights the low rates of antimicrobial resistance in Salmonella isolated from Australian layer flocks. Regular surveillance over a larger geographical area and comprehensive nationwide sampling is, however, needed to identify any changes in antimicrobial resistance patterns in Salmonella isolates in the egg industry."
		Salmonella enterica isolated from infections in Australian livestock remain susceptible to critical antimicrobials (Abraham et al, 2014)	Study conducted by university and government researchers, and funded by New South Wales Department of Primary Industries.	2014	4 poultry isolates	"The resistance attributes confirm that Salmonella isolates recovered from livestock infections in NSW, Australia, have demonstrated a lower prevalence of antimicrobial resistance in comparison with other countries where the use of critical antimicrobials in food-producing animals is less regulated. The absence of fluoroquinolone resistance is most likely due to the fact that this drug class cannot be legally used in food animals in any state of Australia...The fact that fewer Salmonella isolates in the collection were obtained from pigs and poultry compared with ruminants may reflect the lower incidence of clinical salmonellosis in these intensively raised animal species."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations. Resistance to tetracycline (16%) was observed for Salmonella isolates from chicken...Naladixic acid resistance was present in only a single Salmonella isolate (1%) from chicken."

Table 14: Summary of a selection of research papers documenting antimicrobial resistance in the environment arising from poultry in Australia[133]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Broiler chickens and laying hens	*Environmental contamination with AMR determinants*	Antibiotic Resistance Genes in Antibiotic-Free Chicken Farms (Liu et al, 2020)	The study was conducted by university personnel and funded by the National Health and Medical Research Council.	Unspecified	34 samples	"The results provide a baseline for the occurrence of resistance genes in the chicken production system without direct selective pressure. The ARG profiles for the two farms were similar. The ARGs with high human clinical importance, such as the beta lactamase resistance genes blaSHV, blaCTX-M, cphA, the fluoroquinolone resistance gene qnrB and the virginiamycin resistance gene vatE, detected at very low abundances (~10−6 to 10−5) in the samples. The ARGs with higher abundances, particularly tetM, strB and sul2, were likely due to their carriage by bacterial species naturally present in the chicken faecal microbiota, or because these genes have been already spread widely in the environment and were not the result of selection due to antibiotic use."

Table 15: Summary of a selection of research papers documenting antimicrobial resistance in E. coli in samples and bacterial isolates from pigs in Australia[94,103,109,113,134–139]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Pigs	*E. coli*	Pork and the superbug crisis: How higher welfare farming is better for pigs and people (World Animal Protection, 2018)	World Animal Protection - NGO conducted and funded	2018	300 samples	"Bacterial contamination was found. Of the 300 samples across 3 supermarkets… E. coli was found ranging from 36 - 70% of samples from each supermarket..Moderate to high levels of resistance were found to ampicillin/tetracycline in E. coli.. Multi-drug resistance was found in Woolworths (E. coli) only. No resistance to drugs of highest critical importance to human health was found."
		Antimicrobial Susceptibility of Escherichia coli and Salmonella spp. Isolates From Healthy Pigs in Australia: Results of a Pilot National Survey (Kidsley et al, 2018)	Study conducted by researchers from university institutions, government and the pork industry. Study funded by Australian Pork Limited and a Research Council.	2015	201 isolates	"This study shows that non-susceptibility to first line antimicrobials is common among E. coli and Salmonella spp. isolates from healthy slaughter age pigs in Australia. However, very low levels of non-susceptibility to critically important antimicrobials (CIAs), namely third generation cephalosporins and fluoroquinolones were observed. Nevertheless, the isolation of two ciprofloxacin-resistant E. coli isolates from Australian pigs demonstrates that even in the absence of local antimicrobial selection pressure, fluoroquinolone-resistant E. coli clonal lineages may enter livestock production facilities despite strict biosecurity."
		Superbugs in the supermarket? Assessing the rate of contamination with third-generation cephalosporin-resistant gram-negative bacteria in fresh Australian pork and chicken (McLellan et al, 2018)	Implemented and funded by university institutions	2014	60 specimens	"We found low rates of multidrug-resistant gram negative bacteria in Australian chicken and pork meat, but potential 3rd generation cephalosporin resistant gram negative bacteria are common (93% specimens)."
		Antibiotic resistant Escherichia coli in southeastern Australian pig herds and implications for surveillance (Breda et al, 2017)	Conducted by university researchers and funded by the Cooperative Research Centre for High Integrity Pork.	2013-4	1100 samples	"Twenty (6.1%) of the E. coli isolates were resistant to 3rd generation cephalosporin antibiotics and 24 (7.4%) to the aminoglycoside antibiotic gentamicin. Genetic analysis revealed six different extended spectrum β-lactamase (ESBL) genes, four of which have not been previously reported in Australian pigs. Critically, the prevalence of 3GC resistance was higher in non-pathogenic (non-ETEC) isolates and those from clinically normal (non-diarrhoeal) samples. This highlights the importance of non-ETEC E. coli as reservoirs of antimicrobial resistance genes in piglet pens. Antimicrobial resistance surveillance in pig production focused on diagnostic specimens from clinically-affected animals might be potentially misleading. We recommend that surveillance for emerging antimicrobial resistance such as to 3GC antibiotics should include clinically healthy pigs."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian pigs (Australian Pork Limited, 2017)	This project was funded by Australian Pork Ltd and the Department of Agriculture and Water Resources.	Unspecified	200 samples	"No resistance to critically important drugs including colistin, fluoroquinolones and third-generation cephalosporins, was identified in either E. coli or Salmonella isolates, and only a small number of isolates showed reduced susceptibility to fluoroquinolones...It is recommended that the Salmonella and E. coli isolates showing reduced susceptibility to fluoroquinolones... are subjected to whole genome sequence analysis to further elucidate their epidemiology, likely origins and public health significance."
		Phenotypic and genotypic profiling of antimicrobial resistance in enteric Escherichia coli communities isolated from finisher pigs in Australia (Jordan et al, 2016)	Study conducted by researchers from universities and government departments and funded by Australian Pork Limited.	2007	72 pooled samples	"The prevalence of E. coli isolates showing no resistance to any of the drugs was 50.2%. Ceftiofur resistance was very low (1.8%; CI 0.8–3.9%) and no ARGs associated with 3rd-generation cephalosporin resistance were detected. By contrast, ampicillin (29.4%, CI 22.8–37.0%), florfenicol (24.3%, CI 17.8–32.3%) and gentamicin (CI 17.5%, 10.7–27.2%) resistance prevalence varied greatly between farms and associated ARGs were common. The most common combined resistance phenotype was ampicillin–florfenicol. The use of registered antimicrobials in Australian pigs leads to the enteric commensal populations acquiring associated ARGs. However, despite a high intensity of sampling, ARGs imparting resistance to the critically important 3rd-generation cephalosporins were not detected."
		First detection of extended-spectrum cephalosporin- and fluoroquinolone-resistant Escherichia coli in Australian food-producing animals (Abraham et al, 2015)	Veterinary diagnostic laboraties; Study funded by Zoetis and an Australian Research Council Linkage Grant	2013-14	114 clinical isolates	"This study establishes the presence of resistance to critically important antimicrobials among clinical E. coli isolates from Australian food-producing animals, largely attributed to globally disseminated fluoroquinolone- and Extended-spectrum cephalosporin-resistant E. coli lineages."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations...In E. coli from poultry and pork the prevalence of AMR was ≥15% for ampicillin, streptomycin and tetracycline."
		Antimicrobial Resistance in Bacteria of Animal Origin (Australian Government, 2007)	Commercial processors/Department of Agriculture and Water Resources	2003-4	200 samples	"Amongst E. coli from pigs (n = 182), greater than 30% of isolates were resistant to ampicillin, chloramphenicol, florfenicol, tetracycline and trimethoprim/sulfamethoxazole. Multi-resistance (defined here as isolates resistant to two or more antibiotics) and multiple-resistance (defined here as isolates resistant to four or more antibiotics) was common amongst E. coli from pigs and involved up to six antibiotics. A small proportion (3%) of pig E. coli isolates expressed resistance to gentamicin. "
		Antimicrobial Resistance in Campylobacter spp., Escherichia coli and Enterococci Associated with Pigs in Australia (Hart et al, 2004)	Study conducted by researchers from academic institutions.	Unspecified	453 samples	"Escherichia coli strains showed widespread resistance to tetracycline and moderately common resistance (30–60%) to ampicillin and sulphadiazine. Resistance to more than one antibiotic was common. Pigs from New South Wales were also sampled and differences in resistance patterns were noted, perhaps reflecting different antibiotic use regimens in that state."

Table 16: Summary of a selection of research papers documenting antimicrobial resistance in Enterococcus in samples and bacterial isolates from pigs in Australia[94,103,136,139–141]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Pigs	*Enterococcus*	Pork and the superbug crisis: How higher welfare farming is better for pigs and people (World Animal Protection, 2018)	World Animal Protection - NGO conducted and funded	2018	300 samples	"Bacterial contamination was found. Of the 300 samples across 3 supermarkets… Enterococcus was found ranging from 36% to 90% of samples from each supermarket.. Moderate to high levels of resistance were found to tetracycline/streptogramins in enterococcus. Multi-drug reisstance was found in Coles (enterococcus) only. No resistance to drugs of highest critical importance to human health was found."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian pigs (Australian Pork Limited, 2017)	This project was funded by Australian Pork Ltd and the Department of Agriculture and Water Resources.	Unspecified	200 samples	"No resistance to vancomycin and linezolid was identified in Enterococcus isolates..It is recommended that.. the multidrug-resistant enterococci and a selection of multidrug-resistant Campylobacter and enterococci isolates are subjected to whole genome sequence analysis to further elucidate their epidemiology, likely origins and public health significance."
		Antimicrobial and heavy metal resistance in commensal enterococci isolated from pigs (Fard et al, 2011)	Study conducted by researchers from academic institutions.	Unspecified	192 bacterial isolates	"The findings show that resistance to antibiotics of high clinical significance for nosocomial Enterococcus infections is absent, whereas antimicrobial resistance was detected for some other antibiotics including bacitracin, flavophospholipol, tetracycline, tiamulin, tylosin and virginiamycin...confirming previous findings that healthy pigs can act as a reservoir of antimicrobial resistant enterococci that can be transferred to humans. In particular, commensal non-pathogenic enterococci such as E. gallinarum, E. casseliflavus and E. hirae/durans carry resistance genes that could be transferred to more pathogenic species E. faecalis and E. faecium. In general, the high levels of resistance to tetracycline, bacitracin, tiamulin and tylosin reflect the widespread usage of these antibiotics in the Australian pig industry."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations."
		Antimicrobial Resistance in Bacteria of Animal Origin (Australian Government, 2007)	Commercial processors/Department of Agriculture and Water Resources	2003-4	200 samples	"With the exception of streptogramins and E. faecium, nil or a very low prevalence of resistance to antimicrobials of importance to human medicine was observed. A small proportion (3%) of pig E. coli isolates expressed resistance to gentamicin. A high proportion (74.8%) of Enterococcus spp. from pigs were resistant to erythromycin. Virginiamycin resistance was common (43.3%) in pig E. faecium isolates although little or no resistance to other antimicrobial agents was detected in the remaining enterococci from pigs. "
		Antimicrobial Resistance in Campylobacter spp., Escherichia coli and Enterococci Associated with Pigs in Australia (Hart et al, 2004)	Study conducted by researchers from academic institutions.	Unspecified	453 samples	"The enterococci demonstrated little resistance (0–30%) to vancomycin or virginiamycin, but the overall results from the antibiotic sensitivity testing of the enterococci have demonstrated how widespread their resistance has become."

Table 17: Summary of a selection of research papers documenting antimicrobial resistance in Campylobacter in samples and bacterial isolates from pigs in Australia [136,139,142]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Pigs	*Campylobacter*	Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian pigs (Australian Pork Limited, 2017)	This project was funded by Australian Pork Ltd and the Department of Agriculture and Water Resources.	Unspecified	200 samples	"All Campylobacter isolates were susceptible to fluoroquinolones. Nevertheless, it is recommended that the Salmonella and E. coli isolates showing reduced susceptibility to fluoroquinolones, the multidrug-resistant enterococci and a selection of multidrug-resistant Campylobacter and enterococci isolates are subjected to whole genome sequence analysis to further elucidate their epidemiology, likely origins and public health significance."
		Antimicrobial susceptibilities and resistance genes in Campylobacter strains isolated from poultry and pigs in Australia (Obeng et al, 2012)	Implemented by University of South Australia	2008-9	Unspecified: randomly selected from a prevalence study carried out on different piggeries (39 piggeries and 10 piggery environmental samples)	"There were significant differences between the pig strains and all the groups of poultry strains ($P < 0{\cdot}05$) with regard to carriage of resistance genes. In addition, pulsed field gel electrophoresis of selected resistant isolates from the poultry and pig revealed closely related clonal groups...Our results suggest the resistant strains are persisting environmental isolates that have been acquired by the different livestock species. Furthermore, the different treatment practices in poultry and pigs have resulted in differences in resistance profiles in Campylobacter isolates. Antibiotics are used more frequently in pigs"
		Antimicrobial Resistance in Campylobacter spp., Escherichia coli and Enterococci Associated with Pigs in Australia (Hart et al, 2004)	Study conducted by researchers from academic institutions.	Unspecified	453 samples	"In South Australian pigs, thermophilic Campylobacter species showed widespread resistance (60–100%) to tylosin, erythromycin, lincomycin, ampicillin andtetracycline. No resistance was seen to ciprofloxacin."

Table 18: Summary of a selection of research papers documenting antimicrobial resistance in Salmonella in samples and bacterial isolates from pigs in Australia[109,136]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Pigs	*Salmonella*	Antimicrobial Susceptibility of Escherichia coli and Salmonella spp. Isolates From Healthy Pigs in Australia: Results of a Pilot National Survey (Kidley et al, 2018)	Study conducted by researchers from university institutions, government and the pork industry. Study funded by Australian Pork Limited and a Research Council.	2015	69 isolates	"This study shows that non-susceptibility to first line antimicrobials is common among E. coli and Salmonella spp. isolates from healthy slaughter age pigs in Australia. However, very low levels of non-susceptibility to critically important antimicrobials (CIAs), namely third generation cephalosporins and fluoroquinolones were observed."
		Surveillance for antimicrobial resistance in enteric commensals and pathogens in Australian pigs (Australian Pork Limited, 2017)	This project was funded by Australian Pork Ltd and the Department of Agriculture and Water Resources.	Unspecified	200 samples	"No resistance to critically important drugs including colistin, fluoroquinolones and third-generation cephalosporins, was identified in either E. coli or Salmonella isolates, and only a small number of isolates showed reduced susceptibility to fluoroquinolones...It is recommended that the Salmonella and E. coli isolates showing reduced susceptibility to fluoroquinolones... are subjected to whole genome sequence analysis to further elucidate their epidemiology, likely origins and public health significance."

Table 19: Summary of a selection of research papers documenting antimicrobial resistance in samples and bacterial isolates and antimicrobial use in salmon in Australia[143–145]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Aqua-culture	*Marine sources of AMR determinants*	Global Salmon Initiative Sustainability Indicticators - online tool (GSI 2020)	Report on Tassal antibiotic use, data collected by industry group, GSI.	Antimicrobial use reported 2013-2020.	Whole supply chain	Use in 2017: 0 g/tonne; 2018: 0.24 g/tonne; 2019: 62.28 g/tonne; 2020: 27.39 g/tonne.
		Sustainability Report 2017 (Tassal, 2017)	Report by Tassal, commercial seafood company	Antimicrobial use in salmon reported 2012-2017.	Whole supply chain	No antibiotics used in the first half of 2017; 17.16 grams per tonne used in the latter half of 2016.
		Antimicrobial resistance in bacteria isolated from aquaculture sources in Australia (Akinbowale et al, 2005)	Study conducted by researchers from University of South Australia.	2000-4	104 isolates	"Resistance to ampicillin, amoxycillin, cephalexin and erythromycin was widespread; resistance to oxytetracycline, tetracycline, nalidixic acid and sulfonamides was common but resistance to chloramphenicol, florfenicol, ceftiofur, cephalothin, cefoperazone, oxolinic acid, gentamicin, kanamycin and trimethoprim was less common. All strains were susceptible to ciprofloxacin. Multiple resistance was also observed and 74.4% of resistant isolates had between one and ten plasmids with sizes ranging 2–51 kbp. Conclusions: No antibiotics are registered for use in aquaculture in Australia but these results suggest that there has been significant off-label use."

Table 20: Summary of a selection of research papers documenting antimicrobial resistance in samples from cattle in Australia[94,103,113,114,146–150]

Species	Risk	Study title	Affiliations	Data collection period	Sample size	Summary of findings
Cattle	All resistance determinants	Molecular characterization of Campylobacter spp. recovered from beef, chicken, lamb and pork products at retail in Australia (Wallace et al, 2020)	Study was conducted by members of university institutions and government departments, and was funded by AgriFutures, NHMRC and various government departments.	2017-9	616 isolates from 1490 samples of chicken, lamb, pork and beef	"Our results indicate Australia's AMR prevalence in Campylobacter spp. from retail products is very low. Although consumption of contaminated poultry is well established as a key risk factor for campylobacteriosis, foods derived from other animals can result in Campylobacter infection. We found that isolates from pork represented a diverse array of STs, many not found among isolates from beef, chicken or lamb. Our results also suggest prevalence of resistance in Campylobacter spp. from foods of animal origin may be increasing, but ongoing surveillance is needed to confirm such a trend."
		Antimicrobial resistance status of Enterococcus from Australian cattle populations at slaughter (Barlow et al, 2017)	Study conducted by researchers from CSIRO (private innovation business) and government. Funded by Meat & Livestock Australia and the Commonwealth Scientific and Industrial Research Organisation (CSIRO).	2014	1501 samples	"Enterococcus were isolated from 805 (88.5%) beef cattle faeces, 244 (84.1%) dairy cattle faeces and 247 (82.3%) veal calf faeces with a total of 800 enterococci subsequently selected for AMR testing. The results of AMR testing identified high levels of resistance to antimicrobials that are not critically or highly important to human medicine with resistance to flavomycin (80.2%) and lincomycin (85.4–94.2%) routinely observed. Conversely, resistance to antibiotics considered critically or highly important to human medicine such as tigecycline, daptomycin, vancomycin and linezolid was not present in this study. There is minimal evidence that Australian cattle production practices are responsible for disproportionate contributions to AMR development and in general resistance to antimicrobials of critical and high importance in human medicine was low regardless of the isolate source."
		First detection of extended-spectrum cephalosporin- and fluoroquinolone-resistant Escherichia coli in Australian food-producing animals (Abraham et al, 2015)	Veterinary diagnostic laboraties; Study funded by Zoetis and an Australian Research Council Linkage Grant	2013-4	169 isolates	"The 324 E. coli isolates from different sources exhibited a variable frequency of resistance to tetracycline (29.0–88.6%), ampicillin (9.4–71.1%), trimethoprim/ sulfamethoxazole (11.1–67.5%) and streptomycin (21.9–69.3%), whereas none were resistant to imipenem or amikacin. Resistance was detected, albeit at low frequency, to ESCs (bovine isolates, 1%; porcine isolates, 3%) and FQs (porcine isolates, 1%). Most ESC- and FQ-resistant isolates represented globally disseminated E. coli lineages (ST117, ST744, ST10 and ST1). This study uniquely establishes the presence of resistance to CIAs among clinical E. coli isolates from Australian food-producing animals, largely attributed to globally disseminated FQ- and ESC-resistant E. coli lineages."
		Prevalence and Antimicrobial Resistance of Salmonella and Escherichia coli from Australian Cattle Populations at Slaughter (Barlow et al, 2015)	Study conducted by researchers from CSIRO (private innovation business) and government.	2013	1500 samples	"E. coli was readily isolated from all types of samples (92.3% of total samples), whereas Salmonella was recovered from only 14.4% of samples and was more likely to be isolated from dairy cattle samples than from beef cattle or veal calf samples. The results of AMR testing corroborate previous Australian animal and retail food surveys, which have indicated a low level of AMR. Multidrug resistance in Salmonella isolates from beef cattle was detected infrequently; however, the resistance was to antimicrobials of low importance in human medicine. Although some differences in AMR between isolates from the different types of animals were observed, there is minimal evidence that specific production practices are responsible for disproportionate contributions to AMR development."
		Salmonella enterica isolated from infections in Australian livestock remain susceptible to critical antimicrobials (Abraham et al, 2014)	Conducted by researchers from university institutions and government departments, and funded by the government.	2007-11	21 beef cattle, 85 dairy cattle	"Most isolates (66.1%) remained susceptible to all antimicrobials; 8.5% of the isolates were resistant to four or more antimicrobials. Antimicrobials with the highest prevalence of resistance were sulfafurazole (28.5%), ampicillin (17.0%), tetracycline (15.8%) and trimethoprim (8.5%). There was no resistance to fluoroquinolones or third-generation cephalosporins...Overall, the comparatively favourable resistance status of S. enterica in Australian livestock represents minimal public health risk associated with MDR strains and supports a conservative approach to the registration of antimicrobial drug classes in food-producing animals."
		Antimicrobial susceptibility of Salmonella isolates recovered from calves with diarrhoea in Australia (Izzo and House, 2011)	Conducted by researchers from the University of Sydney and funded by Intervet/Schering-Plough Animal Health.	Unspecified	597 samples	"Most of the Salmonella isolates were not resistant to any of the antimicrobials tested. No resistance was seen to amikacin and nalidixicacid, and only one isolate was resistant to ceftiofur or amoxicillin-clavulanic acid. The most common antimicrobial resistance was tostreptomycin, ampicillin or combination sulfonamides. Multi-drug resistance was detected in S. ser. Anatum, S. ser. Bovismorbificans,S. ser. Muenster, S. ser. Newport and S. ser. Typhimurium. Isolates from dairy beef properties were more likely to be resistant to ampicillin, kanamycin, neomycin, sulfamethoxazole/trimethoprim and tetracycline ($P < 0.05$) and were more likely to exhibit multi-drug resistance...The prevalence of antimicrobial resistance in Salmonella isolates from dairy calves in Australia is low compared withthat reported overseas. From a human health perspective, resistance to antimicrobials used in the treatment of human salmonellosis was infrequent."
		Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food (Barlow and Gobius, 2008)	Food Science Australia, funded by the Department of Health and Ageing	2007-8	100 samples	"The results of testing isolates from 12 monthly sampling rounds for AMR indicates that resistance to the majority of antimicrobials tested is low (<10%). However, it is notable that the data indicates trends of higher prevalences of AMR in particular food / bacterium combinations...In E. coli from poultry and pork the prevalence of AMR was ≥15% for ampicillin, streptomycin and tetracycline, in contrast to beef E. coli isolates where prevalence of resistance to these antimicrobials was ≤11%. Similarly, E. faecalis isolates from poultry were distinguished from beef and pork isolates by high prevalences of resistance to erythromycin (48%) and tetracycline (76%)."
		Antimicrobial Resistance in Bacteria of Animal Origin (Australian Government, 2007)	Commercial processors/Department of Agriculture and Water Resources	2003-4	204 samples	"Amongst E. coli isolates from cattle (n = 194), there was only a very low prevalence of resistance to florfenicol (1 %) and tetracycline (3 %). The only notable resistance involving enterococci from cattle were 9.5% of E. faecium isolates (n = 21) expressing resistance to both erythromycin and virginiamycin. Only small differences were observed between the prevalence and patterns of AMR in E. coli and Enterococcus spp. derived from feedlot cattle, grass-fed cattle and dairy cattle."
		Mass screening for antimicrobial resistant Escherichia coli in dairy cows in northern New South Wales (Jordan et al, 2005)	Conducted by members of the New South Wales Department of Primary Industries.	2001-2	30 herds	"..Only a small proportion of commensal E coli shed by dairy cattle in northern New South Wales had resistance to antimicrobials that have been commonly used in dairy cattle and which are often associated with multiple resistance in other settings. Specific multiple resistance phenotypes were rare and were confined to particular herds where as sulfamethoxazole resistance was widespread but had a low prevalence."

e. *Evidence of AMR along the supply chain*

In this section, we provide a summary overview of a small selection of key studies relating to AMR in the various domestic food animal sectors along the supply chain. Please refer to section 3d for more evidence on this subject.

The Australian Government Department of Agriculture and Water Resources initiated the **Pilot Surveillance Program for Antimicrobial Resistance in Bacteria of Animal Origin**[103] as part of the national action plan for AMR surveillance in food-producing animals (emphasised in both the JETACAR report - recommendation 10, and 2015 Strategy[84]). Data were collected between November 2003 and July 2004. Key findings from this report are as follows:

Cattle:

- E. coli: very low prevalence of resistance to florfenicol (1%) and tetracycline (3%);
- Enterococcus faecium: resistance to erythromycin and virginiamycin (9.5%).

Pigs:

- E. coli: greater than 30% of isolates were resistant to ampicillin, chloramphenicol, florfenicol, tetracycline and trimethoprim/sulfamethoxazole; Multi-resistance (isolates resistant to two or more antibiotics) was common amongst E. coli (over 50%);
- Enterococcus spp.: a high proportion (74.8%) were resistant to erythromycin; a little less than half of E. faecium isolates were resistant to virginiamycin (43.4%).

Chickens:

- E. coli: notable resistance to ampicillin (33%), tetracycline (44%) and trimethoprim/ sulfamethoxazole (27%); Multi-resistance was detected in 2.6% of isolates;
- Enterococci spp.: high prevalence of resistance to erythromycin (68%) and virginiamycin (28.7%);
- Campylobacter spp.: detected resistance to tetracycline (21%) and erythromycin (11%).

This report provides evidence of antimicrobial resistance in the major food animals in Australia. However, according to the ASTAG classification[69], all but one antibiotic listed above is of low importance to human medicine, thus these findings have not initiated immediate action, even when a high prevalence was detected. However, virginiamycin is a streptogramin antibiotic, which is classified as ‘highly-important’. Analysis and conclusions drawn from such results are also complicated by the fact that macrolides (including erythromycin) are ranked as ‘critically-important’ on the WHO CIA list[68] compared to ‘low’ on the ASTAG list. Additionally, florfenicol, tetracycline, ampicillin and chloramphenicol are all classified as ‘low importance’ on the ASTAG list and ‘highly-important’ on the WHO CIA list. The challenges arising from the lack of harmonisation between national and WHO antimicrobial importance classifications have been discussed in previous sections.

Another important survey titled ‘**Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food prepared for the Australian Government Department of Health and Ageing**’ was published in 2008[94]. Three out of four of the retail foods studied were of animal origin (poultry, beef and pork). The significant results were as follows:

Beef

- E. coli: Resistance to one or more antimicrobials was observed in 19% of isolates. Resistance to ampicillin (11%), streptomycin (7%) and tetracycline (7%) was most commonly observed.

There was also evidence of resistance to amoxicillin/clavulanic acid (3%), cefazolin (3%), kanamycin (2%) and trimethoprim/sulfamethoxazole (5%).
- Enterococcus: Resistance to one or more antimicrobials was observed in 27% of isolates. Resistance to tetracycline (15%) and tigecycline (10%) was most commonly observed. There was also evidence of resistance to chloramphenicol, erythromycin, flavomycin, kanamycin and streptomycin (prevalence ≤7%).

Pork

- E. coli: Resistance to one or more antimicrobials was observed in 80.4% of isolates. Resistance to tetracycline (44.5%), ampicillin (28.2%), streptomycin (17.4%), chloramphenicol (13%) and trimethoprim/sulfamethoxazole (13%) was most commonly observed. There was also evidence of resistance to florfenicol (8.7%), amoxicillin/clavulanic acid (3.3%), cefazolin (3.3%), kanamycin (3.3%) and gentamicin (1.1%).
- Enterococcus: Resistance to one or more antimicrobials was observed in 22% of isolates. Resistance to tetracycline (17%) was most commonly observed. There was also evidence of resistance to chloramphenicol, erythromycin, flavomycin, kanamycin, streptomycin, and tigecycline (prevalence ≤7%).

Poultry

- E. coli: 65% of isolates were resistant to one or more antimicrobials. Resistance to tetracycline (47%), ampicillin (38%), trimethoprim/sulfamethoxazole (22%) and streptomycin (19%) was most common. There was also evidence of resistance to kanamycin (8%) and gentamicin (4%).
- Enterococcus: Resistance to one or more antimicrobials was observed in 81% isolates. A high prevalence of resistance to tetracycline (76%) and erythromycin (48%) was observed.
- Salmonella: 23% were resistant to one or more antimicrobials. Resistance to tetracycline was most commonly observed (16%).
- Campylobacter: Overall level of AMR was very low.

A high prevalence multi-drug resistance was detected in bacteria isolated from retail beef, pork and poultry. The resistant bacteria could have originated from the animals themselves or from the post-harvest environment, for example during transport, processing and storage, and therefore may not be directly linked to antimicrobial use on farms.

As shown in the previous examples, the Australian Government has contributed funding to surveillance programmes to determine and monitor AMR levels in different species in Australia. However, university institutions and livestock industry bodies have also significantly contributed to the body of evidence, including the following studies and their findings:

Cattle

- A study investigated the AMR status of Enterococcus from cattle populations at slaughter and found evidence of resistance to flavomycin (80.2%) and lincomycin (85.4-94.2%)[114];
- Barlow et al. (2020) found that the majority of bacteria (Salmonella, E. coli, and Enterococcus) from cattle (beef, dairy, and veal) are wild-type for all antimicrobials tested. The non-wild type populations also showed little resistance to highly or critically-important antimicrobials (e.g., third-generation cephalosporins, quinolones and oxazolidinones)[151].

Pigs

- A surveillance project for AMR in enteric commensals and pathogens found[136]: for E. coli and Salmonella, a high prevalence of resistance to tetracycline, ampicillin and streptomycin (55-77%); intrinsic resistance to lincosamides and streptogramins in Enterococcus (E. faecalis only) and a high prevalence of resistance to macrolides. For Campylobacter they found intrinsic

resistance to lincosamides, and a high prevalence of resistance to macrolides (73.2-74.5%), ketolides (67.5%) and tetracyclines (53.5%).

- Another national survey found similar results in E. coli and Salmonella isolated from healthy Australian finisher pigs[109]. In E. coli and Salmonella, resistance was detected to ampicillin (60.2 and 20.3%), tetracycline (68.2 and 26.1%), chloramphenicol (47.8 and 7.3%), and trimethoprim/sulfamethoxazole (33.8 and 11.6%).

Poultry (meat)[105,116]

A surveillance study for antimicrobial resistance in enteric commensals and pathogens in Australian meat chickens[105] and another survey investigating AMR in E. coli and Salmonella from caecal samples of chickens at slaughter[116] both reported low carriage of resistance to important antimicrobials for humans:

- For E.coli, 47 to 63% of isolates were susceptible to all tested antimicrobials, and 5.8% were classified as multi-drug resistant (MDR)[105,116].
- For Enterococcus, no resistance to aminoglycosides or chloramphenicol was reported.17.5% of isolates were resistant to three or more drug classes. Resistant genes to tetracycline (40.3-46.3%) were common. Resistance to quinupristin-dalfopristin (54.5%) was also detected among E. faecium[105].
- For Salmonella, the studies found susceptibility in 92.5% Salmonella isolates with no MDR detected. Some evidence of resistance to streptomycin, ampicillin, and cefoxitin was found[152].
- For Campylobacter, the studies found susceptibility to all antibiotics in 63% of C. jejuni and 86.5% of C. coli isolates. The most commonly detected resistance was to tetracycline, nalidixic acid and ciprofloxacin (a fluoroquinolone). As fluoroquinolones are not approved for use in Australian food animals, it is suspected that anthropozoonosis (i.e. human to chicken transmission) or transmission from wildlife occurred[105].
- Results showed a significant decrease in the prevalence of AMR determinants in poultry meat compared to a study in 2001[104]. For example, E. coli isolates were resistant to almost all antimicrobials tested in 2001, compared to less than 50% in a similar paper published in 2019[152].

Overall, these studies suggest there are relatively low levels of resistance to HP-CIAs as categorised by the WHO in cattle and poultry in Australia. However, more significant levels of resistance to critically-important antimicrobials (according to the WHO CIA list) macrolides, ketolides, ampicillin, and streptomycin were detected in Australian pig populations. Again, this may be attributed to the fact that they are classified as Low importance on ASTAG's list and higher levels of use may be seen in pig production than in some of the other livestock species.

f. Comparison with the OIE/WHO/FAO recommendations

Considering the development of the WHO's global action plan on AMR[153], OIE's Terrestrial and Aquatic Animal Health Codes[154,155] and FAO/WHO's Codex Alimentarius Code of Practice[156], there is no shortage of initiatives and recommendations to establish unified AMU and AMR surveillance systems with robust monitoring and reporting requirements.

The WHO's Global Action Plan on AMR reflects a global consensus that AMR poses a profound threat to human health. Therefore, this plan was developed to "ensure continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them." Five strategic objectives were included:

- To improve awareness and understanding of AMR;
- To strengthen knowledge through surveillance and research;
- To reduce the incidence of infection;
- To optimise the use of antimicrobial agents; and
- To ensure sustainable investment in countering antimicrobial resistance.

Member state actions, secretariat actions and international and national partners' actions were then specified under each objective. The document provides a comprehensive list of expectations of different stakeholders and promotes a collaborative approach to combat AMR[153].

Chapter 6.9 of **OIE's Terrestrial Code**[154] and chapter 6.3 of **OIE's Aquatic Code**[155] include approaches to monitoring the quantities and usage patterns of antimicrobial agents used in food-producing/aquatic animals. Different sources and reporting formats for antimicrobial usage data are recommended for the development and standardisation of antimicrobial monitoring systems. However, these codes primarily focus on informing monitoring options rather than calling for action.

FAO/WHO's Codex Alimentarius[156] includes a code of practice to "minimise and contain antimicrobial resistance" (CAC/RCP 61-2005)[157]. This document defines the respective responsibilities of authorities and groups involved in the authorisation, production, control, distribution and use of veterinary antimicrobials. For instance, amongst their duties, the regulatory authorities are responsible for quality control of veterinary antimicrobial drugs and surveillance programmes; duties of the veterinary pharmaceutical industry include marketing and export, and research; and veterinarians are responsible for off-label use, recording and training[156].

These reports from the multilateral agencies OIE, WHO and FAO provide general guidelines on monitoring and reporting AMR and AMU, recommending that member states strengthen surveillance in the animal health and agriculture sectors[158]. However, recognising the significant differences between local contexts, they leave the details of implementation to member states.

The Australian Government adopted OIE/WHO/FAO recommendations into their national strategies, but these strategies are yet to be actioned. As discussed in previous sections, the Australian Government has not reported on AMU in animals since 2014. However, it did introduce its own One Health Master Plan[98] in 2021. Examples of focus areas from this report include:

- Focus area 4.2.8: Build monitoring, auditing and feedback processes into existing frameworks across relevant sectors;
- Focus area 5.4.2: Explore capability for real-time collection, analysis and reporting of antimicrobial resistance and use data across all relevant sectors.

Establishing a national animal sector surveillance programme for AMR and AMU is also highlighted in the Animal Sector National Antimicrobial Resistance Plan 2018[159].

g. *Comparison with other OECD countries*

As discussed in previous sections of this report, the Australian AMU and AMR monitoring and reporting process still lacks certain elements, such as annual reporting and active surveillance. The lack of federally-funded AMU and AMR surveillance programmes focused on animals is in contrast to the systems in place in some other OECD countries, from which insights and learnings can be drawn. In this section, we look at a selection of other OECD countries and their AMU/AMR surveillance systems.

The Netherlands: Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands (MARAN)[160]

Since 2002, veterinary antibiotic use in the Netherlands has been published annually in the MARAN report, which includes sales and use of antimicrobial veterinary medicinal products monitored by the Netherlands Veterinary Medicines Institute (SDa). Both livestock farms and veterinarians are benchmarked according to their antibiotic usage. Antibiotic usage is expressed in number of defined-daily dosage animal (DDDA) and is stratified by animal species. These data cover approximately 98% of all sales in the Netherlands. An impressive decrease in sales by 69% was seen over the period 2009-2020, demonstrating the importance of antibiotic use monitoring systems to track and drive progress.

Since 2012, MARAN has been combined with the NethMap report with corresponding data from human healthcare. The resulting joint reports demonstrate the opportunity for the human and veterinary sectors to practically collaborate on One Health initiatives.

Denmark: Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP)[161]

DANMAP was established in 1995 to annually monitor antimicrobial use in the human and veterinary sectors and AMR in human and animal pathogens, including both zoonotic and indicator bacteria. As all antibiotics are available by prescription only, the Register of Medicinal Statistics records the data through national databases Medstat and Vetstat. For instance, data on all sales of veterinary prescription medicines from pharmacies, private companies, feed mills and veterinarians are all sent into Vetstat. The Defined Animal Daily Dose (DADD) metric is used to quantify AMU.

This was the first national surveillance programme to be initiated by a country and forms a successful blueprint that has been replicated by other countries. These achievements can be attributed to adequate funding (funded jointly by multiple governmental departments), planning and collaboration, and the large economic reliance on high-quality agricultural produce in a small country[79].

United Kingdom: UK Veterinary Antibiotic Resistance and Sales Surveillance Report (UK-VARSS)[162]

Similarly to EU member states, the UK also publishes an annual report on the sales of veterinary antibiotics by administration route, animal species and antibiotic class, in the form of the VARSS report[162]. A wide range of animal species are covered, including pigs, meat poultry, laying hens, gamebirds, cattle, aquaculture and companion animals. These data relate primarily to pharmaceutical sales in the absence of a mandatory, national surveillance system for actual antimicrobial use or prescription, as seen in the Netherlands and Denmark. However, some livestock sectors, for example the pig and poultry sectors, have voluntarily developed industry-led antibiotic usage reporting systems, with reports regularly made available in the public domain.

Data on antibiotic resistance are collected under two surveillance schemes: the harmonised antibiotic resistance monitoring scheme, mandatory under EU legislation (Decision 2013/652/EU, see below), and clinical surveillance. The latter evaluates antibiotic resistance via passive surveillance and relies on private veterinary surgeons submitting samples to APHA veterinary laboratories.

EU Legislation on monitoring and reporting of antimicrobial resistance (Decision 2013/652/EU)[163]

This harmonised antibiotic resistance monitoring scheme has mandated all EU Member States to monitor and report AMR in zoonotic and commensal bacteria from healthy food-producing animals and food products at retail, since 2013. The scope of this Decision covers the following bacteria:

- Salmonella spp.;
- Campylobacter jejuni and Campylobacter coli;
- Indicator commensal Escherichia coli; and
- Indicator commensal Enterococcus faecalis and Enterococcus faecium.

Salmonella spp., and E. coli producing the following enzymes are also subject to strict monitoring and reporting requirements:

- Extended-Spectrum beta-Lactamases (ESBL);
- AmpC beta-Lactamases (AmpC); and
- Carbapenemases.

Canada: Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)[164]

CIPARS was established in 2002 and monitors trends in annual antimicrobial use and antimicrobial resistance in selected bacterial organisms from human, animal and food sources across Canada. The amalgamation of human data with animal data demonstrates a One Health approach.

Antibiotic usage data are assessed based on two data sources: (a) total sales for use in animals, on crops and in marine and freshwater finfish aquaculture; and (b) questionnaires administered by veterinarians to producers (specifically in the broiler chicken, grower-finisher pig and turkey sectors). The combination of national and on-farm surveillance builds a reliable framework for understanding the active ingredients of antibiotics distributed and used in the country. Units of Population Correction Unit (PCU), Canada Defined Daily Doses (DDDvetCA) and DDDvetCA per 1000 animal-days at risk are widely used to represent AMU in the different sectors[165].

For antibiotic resistance, data are collected from the following sources:

- Human healthcare systems;
- Retail meat;
- Abattoir;
- Farm (feedlot cattle, broiler chickens, grower-finisher pigs, turkeys);
- Animal clinical isolates; and
- Feed and feed ingredients.

United States: National Antimicrobial Resistance Monitoring System (NARMS)[166]

The US Centers for Disease Control and Prevention (CDC), the US Department of Agriculture (USDA), the US Food and Drug Administration (FDA) and state and local health departments collaborated to establish NARMS in 1996. This surveillance scheme aims to track resistance in enteric bacteria from humans, retail meats and food-producing animals at the time of slaughter. However, this scheme does not involve collection of data on antibiotic use.

Reporting annual sales of antibiotic drugs to the FDA has, however, been a mandatory requirement according to Section 105 of the Animal Drug User Fee Amendments of 2008 (ADUFA) and amended section 512 of the Federal Food, Drug, and Cosmetic Act (2016)[167] (see section 2a). Sponsors of

antimicrobial drug products must submit the following information: (1) a listing of each antimicrobial active ingredient contained in the product; (2) a description of each product sold or distributed by unit, including the container size, strength, and dosage form of such product units; (3) for each such product, a listing of the target animal species, indications, and production classes that are specified on the approved label; (4) for each such product, the number of units sold or distributed in the United States (i.e. domestic sales) for each month of the reporting year; and (5) for each such product, the number of units sold or distributed outside the United States (i.e. quantities exported) for each month of the reporting year. Each report must also provide a species-specific percentage of each product sold for cattle, swine, chicken and turkeys[168]. Results of this data collection are regularly published by the FDA in reports entitled ‘Summary Report On Antimicrobials Sold or Distributed for Use in Food-Producing Animals’.

In summary, the Netherlands, Denmark, the UK, Canada and the USA have all established continuous monitoring and reporting (voluntary and mandatory) requirements for AMU and AMR. Although the Australian Government also acknowledges that combatting antimicrobial resistance is a long-term objective, regular reporting of AMU and AMR remains an outstanding action in Australia’s response to antimicrobial resistance when compared with these other OECD countries (see **Table 21**).

Table 21: Comparison of AMU/AMR surveillance programmes from selected OECD countries.[79,103,160–162,164,166]

Program/Institute	Country/Region	Program status	Type of activity	Funding model, governance	Program focus	Population	Sampling type, methods	Data	Organisms	Report type/frequency
Pilot Surveillance Program for Antimicrobial Resistance in Bacteria of Animal Origin	Australia	Sample collection: Nov 2003 – Jul 2004	Pilot surveillance program	Government	Program initiate as part of Government's response to Recommendation 10 of JETACAR report	Cattle; Pigs, Chickens	Gut content obtained from healthy animals at 31 slaughter establishments	AMR data for isolates recovered from caecal specimens	E. coli, Enterococcus, Campylobacter	Single report
Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands (Nethmap-MARAN 2021)	Netherlands	Current	Reports on antimicrobial sales data and AMR data in veterinary field	Government program; Central Veterinary Institute	Sales of veterinary antibiotics; AMR in food animals	Pigs; Veal calves; Cattle; Broilers; Turkeys; Rabbits	Antibiotic sales data from the federation of the Dutch veterinary pharmaceutical industry (FIDIN); Range of sampling programs (eg intestine of randomly picked broilers, pigs, veal calves at slaughter)	Overall antibiotic sales data and usage data per animal species; AMR in food borne pathogens and commensal indicator bacteria; Total sales data of antimicrobial agents in animal husbandry; AMR in bacteria of animal origin and of relevance to public health	Salmonella; Campylobacter; E coli; Enterobacteriaceae; MRSA	Combined report of NETHMAP (human) and MARAN published annually
The Netherlands Veterinary Medicines Institute (SDa)	Netherlands	Current (established 2010)	Creating transparency in and setting benchmark indicators for consumption of antimicrobials in livestock production, based on consumption data	Government program	Veterinary prescription data from practice management system	Pig; Veal calf; Broiler; Cattle; Turkey; Rabbit	Data collected by private animal sectors and sent to the SDa after encryption of identifiers	Complete consumption of antimicrobials as registered on individual farm level, for all pig, veal calf, and broiler farms in the Netherlands; Animal defined daily dosages per year (ADDD/Y)	N/A	SDa monitors, analyses, and reports data on consumption of antimicrobials annually, making trends in consumption patterns in the various sectors transparent
Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP)	Denmark	Current (established 1995)	Systematic and continuous monitoring program of antimicrobial drug consumption (VetStat) and antimicrobial resistance in animals, food and humans	Funded jointly by the Ministry of Health, the Ministry of Science, Innovation and Higher Education, and the Ministry of Food, Agriculture and Fisheries	Antimicrobial consumption and resistance	Food animals (pigs, cattle, broilers, etc.); Food of animal origin; Humans	Healthy production animals at slaughter	Animal AMR data from vet practices, laboratories, slaughterhouses	Zoonotic bacteria (Salmonella, Campylobacter, C. difficile); Indicator bacteria (Enterococcus, E. coli, ESBL producers)	Annual report

Program/Institute	Country/Region	Program status	Type of activity	Funding model, governance	Program focus	Population	Sampling type, methods	Data	Organisms	Report type/frequency
VetStat (Stege et al., 2003, Dupont and Stege, 2013)	Denmark	Current (established 2000)	Usage surveillance; Data on all medicine prescribed by veterinarians have been registered at the farm and species level	Danish Ministry of Food, Agriculture and Fisheries	Antimicrobials administered to food animals	Food animals	Pharmacies, veterinarians and feed mills	Data entry via website or upload includes veterinarian, receiving herd, product name and amount, species, age group, diagnostic group. Kg active compoud. ADD (Animal Daily Dose) per 100 animals	n/a	Range of reports including monthly statements reporting antimicrobial use by species, journal articles, conference publications
UK Veterinary Antibiotic Resistance and Sales Surveillance Report (UK-VARSS)	UK	Current	Combines UK data on antimicrobial sales for animal use with England and Wales AMR data for veterinary pathogens and food-borne pathogens	Government program under the Veterinary Medicines Directorate (VMD)	Sales of veterinary antibiotics; AMR in food animals	Estimates made of animal population to link with antimicrobial sales data; AMR data focuses on food producing animals in England and Wales	Antimicrobial sales data converted to active ingredient (mg), sold for food producing animals/population correction unit (PCU); Active screening for indicator and zoonotic bacteria	Antimicrobial sales data; AMR data from clinical specimens and targeted surveillance; AMR data for 25 bacterial species, 26 antibiotics from 14 Animal Health and Veterinary Laboratories Agency (AHVLA) labs	Salmonella, Campylobacter, E coli, etc. (25 bacterial species in total)	Annual report
Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)	Canada	Current	Monitors trends in antimicrobial use and antimicrobial resistance in selected bacterial organism from human, animal and food sources across Canada	Public Health Agency of Canada program	Creation of evidence-based policies to control antimicrobial use; Identification of measures to contain the emergence and spread of resistant bacteria between animals, food and people	Food production animals, food and humans	Both active and passive surveillance; Track trends in antimicrobial use and resistance in selected species of enteric bacteria obtained at different stages of food production and from human clinical laboratory submissions	Integrates data on zoonotic foodborne bacteria from public health laboratories with that from animal and food-chain isolates	Resistance surveillance in Salmonella, Campylobacter, and the indicator organisms, Enterococci and E coli	Annual reports, short reports and quarterly summaries
National Antimicrobial Resistance Monitoring System (NARMS)	United States	Current (established 1996)	Collaboration among state and local public health departments, CDC, U.S. FDA, and USDA	Collaboration between the US FDA, U.S. Department of Agriculture, CDC and state and local health departments	National public health surveillance system tracking changes in AMR of certain bacteria found in ill people (CDC), retail meats (FDA), and food animals (USDA) in the U.S.	50 US States	Participating public health labs submit to CDC for AMR testing (Salmonella, Campylobacter, E coli, Shigella, Vibrio)	AMR data	Salmonella; Campylobacter; E coli; Vibrio	Annual reports (most recently available for 2018) and interactive maps. Helps protect public health by providing information about emerging bacterial resistance, ways in which resistance is spread, and how resistant infections differ from susceptible infections

h. Funding allocation

The NHMRC's Expert Advisory Group on Antimicrobial Resistance (EAGAR) estimated in 2006 that a comprehensive integrated surveillance programme to improve Australia's response to AMR would require additional funding of $3.475m for 3 years. It was assumed that the costs of surveillance of antimicrobial usage in the community and in food animals would be absorbed within existing budgets at that time[169]. In addition, surveillance of AMR in bacteria isolated from food animals and products were not prioritised, such that some of the costs required were not included in calculations. See **Table 22**.

However, several one-off surveillance programmes for AMR in the food sector received funding from the State, Territory or departments of the Australian government, specifically the Department of Home Affairs (DoHA) and the Department of Agriculture, Fisheries and Forestry (DAFF). These programmes included the OzFoodNet survey of Campylobacter and a pilot AMR Surveillance programme, costing $469,525[169] in total. See **Figure 9.**

Table 22: Preliminary cost estimates and priorities for action for a comprehensive integrated surveillance programme to improve Australia's response to antimicrobial resistance. Taken from the EAGAR report, 2006[169]

Surveillance of antimicrobial use		**Year 1 already funded**	**Year 1 new funding**	**Year 2 Ongoing funding**	**Year 3 Ongoing funding**	**Priority**
1	Surveillance of the use of antimicrobials in hospitals	160,000		160,000`	160,000	1
2	Surveillance of the use of antimicrobials in the community	0[1]		0[1]	0[1]	1
3	Surveillance of the use of antimicrobials in food animals.	0[1]		0[1]	0[1]	2
Surveillance of antimicrobial resistance (AMR)						
4	Active surveillance of AMR in pathogens of importance in human health.	280,000		300,000	300,000	1
5	Surveillance of multi-resistant organisms				300,000[2]	2
6	Passive surveillance of AMR in bacteria of importance in human health		600,000	500,000		1
7	Active surveillance of AMR in bacteria isolated from food animals and aquaculture		385,000	385,000	385,000	4
8	Surveillance of AMR in bacteria isolated from food and food products	340,000		Review when pilot program completed		3
9	Surveillance for AMR in animal pathogens with implications for public health.	Not costed				5
		780,000	985,000	$1.345 m	$1.145 m	
	Total additional funding for 3 years.		**$3.475 m**			

NOTE:
1 Costs absorbed within existing budget.
2 Data will be captured as part of Project 6 once the AMR data capture program is deployed nationally.

Budget

Funding from State/Territory and Commonwealth Governments to date for surveillance of AMR in food is as follows:

a.)	OzFoodNet survey of Campylobacter *(Funded by DoHA)*		**$52,525**
b.)	Salmonella passive surveillance (MDU & IMVS) *(Funded by DoHA and DAFF)*		**$77,000**
c.)	Pilot AMR Surveillance program *(Funded by DoHA, DAFF and the States/Territories)*		**$340,000**
	• Sample collection	52,000	
	• Bacterial isolation	112,000	
	• Freight, materials & packaging	2,000	
	• AMR testing (Vitek & Campylobacter)	110,000	
	• Salmonella serotyping	4,000	
	• Project management	60,000	

Figure 9: Budget of the project 'Surveillance for antimicrobial resistance in bacteria isolated from food and food products'. Adapted from the EAGAR report, 2006[169].

Following the Senate Inquiry[101], the Australian Commission on Safety and Quality in Healthcare (ACSQHC) became responsible for establishing a national centre for AMR surveillance. This was funded with $11.9 million, which covered activities for three years, from the 2013-2014 Health Budget to support the development of the Australian National AMR Prevention and Containment Strategy[79]. The National Health and Medical Research Council (NHMRC) invested over $107 million in funding for research relating to AMR from 2009-2019[100]. The Minister for Health, Greg Hunt, announced on 19 November 2020 that the Australian Government was committing $22.5 million in their 2020 budget to address the priorities identified in Australia's National Antimicrobial Resistance Strategy – 2020 & Beyond[170]. However, it is unclear how these budgets are broken down between projects undertaken in the human, animal and food sectors, and what percentage was allocated for building a surveillance programme.

Federal funding allocated to national surveillance systems in the animal health sector is not comparable to that provided in the human health sector, i.e. AURA. Although a One Health surveillance system is repeatedly emphasised in the national strategies to combat antimicrobial resistance, there is still limited evidence of significant financial support for the food and agriculture sector to establish integrated monitoring and reporting programmes. The current budget only enables ad hoc rather than ongoing surveillance of AMR and AMU in animal health[92]. Furthermore, the Australian Veterinary Association also recommended that the Government should match-fund research into AMR in the human health sector, by funding the equivalent investment to support AMR research in animals[171].

There is insufficient available data to accurately calculate the percentage of GDP allocated to enhance surveillance, monitoring and reporting programmes for AMR and AMU in the Australian food animal sector.

> *"The costs of implementing a fit-for-purpose resistance surveillance system would be negligible compared to the economic losses incurred by having to treat antibiotic-resistant infections in large numbers in the population … the Australian Groups on Antimicrobial Resistance (AGAR)'s budget, currently AUD$300 000 per year, would probably need to be doubled, plus an initial injection of $1 million to get the system running."*
>
> \- Graeme Nimmo (2011)[172]

i. *Comparison of Australia's spending on AMR with other OECD countries*

There are currently no published reports comparing spending on surveillance, monitoring and reporting of antibiotic use and AMR in the food animal sector across different OECD countries. Funding availability from governments are often designated to a range of agencies and institutions for various related objectives and strategies. For example:

- Horizon Europe, EU's key funding programme for research and innovation, indicated a EUR 1 million budget for developing a "roadmap towards the creation of the European partnership on One Health antimicrobial resistance (OH AMR)" during 2021-2022[173];
- The UK government initiated the Fleming fund, a £265 million UK aid programme, to improve disease surveillance in low and middle-income countries[174];
- The US Congress appropriated USD 170 million in 2020 to fight AMR, supporting antimicrobial resistance initiatives in all 50 state health departments and other research institutions[175];
- The Canadian Institutes of Health Research (CIHR) invested more than $96 million in AMR-related research between 2011 and 2016[176].

Insufficient published information is available to specifically compare governmental spending in the selected OECD countries on AMU and AMR surveillance initiatives, and funding for monitoring and reporting activities may be contained within broader programme budgets. Furthermore, some funding may be exclusively allocated for AMR surveillance in the human health sector[175], and others may be inclusive of both human and animal sectors[173,176].

Providing a broader view of funding capacity, the annual Tripartite AMR country self-assessment survey (TrACSS)[177], jointly administered by FAO, OIE and the WHO since 2016, provides valuable insights into member countries' progress with their AMR national action plans (NAPs). The TrACSS is a component of the global action plan on antimicrobial resistance (GAP-AMR), monitoring and comparing actions taken by each country to ensure the global objectives are attained. It is a self-assessment survey that asks for a rating of national capacity and progress on a five-point scale from A to E, which corresponds to: no, limited, developed, demonstrated and sustained capacity. Availability of funding sources was assessed as a component of the question "development of national action plans", with countries choosing from the following five responses:

- A: No national AMR action plan;
- B: National action plan under development;
- C: National AMR action plan developed;
- D: National AMR action plan approved by government that reflects Global Action Plan objectives, with a budgeted operational plan and monitoring arrangements; and
- E: National AMR action plan has funding sources identified, is being implemented, and has relevant sectors involved with a defined monitoring and evaluation process in place.

49 high income countries, including Australia, completed the survey for 2019-2020[178] (115 countries in total provided data). Among the high-income countries, which is defined according to World Bank income classification, 15 countries reported that their National AMR action plans had funding sources identified, were being implemented, and had relevant sectors involved with a defined monitoring and evaluation process in place (level E, the highest tier). These countries included the US and the Netherlands. 18 countries reported that their national AMR action plans were approved by government and reflected their Global Action Plan objectives, with a budgeted operation plan and monitoring arrangement (level D, the second highest tier). These countries included the UK, Denmark and Australia. Canada was ranked at level C, which corresponds with a national AMR action plan being developed but without any further actions[179].

4. Conclusion

The aim of this report was to synthesise information and evidence around the governance of antimicrobial use and resistance in relation to the food animal sector in Australia. The results of this literature review highlight the strengths and weaknesses of Australia's antimicrobial stewardship programmes.

The strengths include Australia's progressive stance on the use of certain antimicrobials listed as 'highest priority critically-important' (HP-CIA) antimicrobials to human health by the World Health Organisation (WHO): specifically, the fluoroquinolones, colistin and fourth-generation cephalosporins are not approved for use in food animals, a position rarely seen in other jurisdictions. It is thought that this has led to the relatively low prevalence of resistance to antimicrobials of importance to human health (as defined by Australia's ASTAG group) detected in food-borne pathogens from livestock sources.

The weaknesses of Australia's antimicrobial stewardship programmes include the lack of regular public reporting of antimicrobial use and resistance data from the food animal sector. Two reports are available in the public domain, but the most recent report was published in 2014. In contrast, a number of other comparison OECD countries have reported these data on an annual basis for over 10 years. In addition, antimicrobial growth promoters are still permitted in Australia. Although the antibiotics currently used for this purpose are not medically-important antimicrobials, other comparison OECD countries have either banned or are phasing out all growth promoter use.

Approaches to antimicrobial stewardship in the food animal sector vary widely between countries, and this report provides an overview of the situation in Australia, based on information available in the public domain. Certain aspects of Australia's antimicrobial stewardship policies and governance reflect a progressive position, with apparent positive impacts in terms of the prevalence of antimicrobial resistance detected in the food chain. However, in order to align with the actions and progress made by certain other OECD countries, and to honour commitments made in various government strategies and reports, remaining gaps in antimicrobial governance should be addressed. This should include the implementation of robust surveillance and public reporting regarding antimicrobial use and resistance in food animals in Australia.

Recommendations from World Animal Protection

While we commend the Australian Government for deciding not to register certain antibiotics of critical importance for human health for use in animal agriculture, there are further actions that should be taken to help improve animal welfare and safeguard the effectiveness of antibiotics. Following the findings of this report, World Animal Protection recommends the following reforms:

1. Mandatory annual public reporting

We encourage the Government to introduce mandatory annual public reporting for antimicrobial sales and use data nationwide in Australia as happens in the US and UK. This reporting should indicate whether the antimicrobials were used for treatment of a sick animal (therapeutic), for treatment of a group of animals after clinical diagnosis (metaphylactic), for prevention of disease in groups of animals (prophylactic), or for growth promotion. The data should also provide information on which species of animal the antimicrobials were administered to, and what type of farm the animals were housed in, whether conventional, indoor, outdoor, free-range or organic. We recognise this will require cooperation between the State, Territory, and Federal Governments to create a uniform reporting system. We encourage the Government to look at examples of monitoring and reporting systems from places such as Denmark, the Netherlands, the US, and the UK. These provide leading examples for Australia to follow.

This reform will help provide transparency and oversight so we can see if the antimicrobial stewardship plans, and guidelines are working to ensure more responsible use. While the Government and the agriculture industry claim they have a good story to tell on antibiotics, until we can see what is being used and for what purpose, there is no accountability. This issue is too significant to leave in the shadows – we need clear reporting and oversight. Millions of lives depend on it.

2. Ban the use of antibiotics for growth promotion

Australia should immediately ban the use of antibiotics for growth promotion. The evidence is clear that this practice creates unnecessary risk. Using low dose, sub-therapeutic levels of antibiotics for an extended period of time can foster resistance, helping to create superbugs. Australia should follow the 90 other countries that have already banned antibiotic use for growth promotion – some of which took this step in the 1990s. The time for action on this issue is now. While we recognise that there have been some moves within the industry to reduce or restrict the use of antibiotics for growth promotion, we need consistency on this issue to help ensure safety and, importantly, public confidence in how the agriculture industry is using antibiotics. To ensure consistency and public confidence, and to guarantee compliance for trade purposes, regulation needs to be introduced at a Commonwealth level.

3. End the routine use of antimicrobials for group prophylaxis

Australia should end the use of antimicrobials for the prevention of disease in groups of animals. If animals are prone to disease because of their housing conditions, their diets, or because their genetics put them at increased risk, we need to address the root cause, not use antibiotics to allow poor welfare practices to continue. We cannot allow antimicrobials to be used simply so we can continue raising animals for quick and cheap meat. It is not worth the risk of losing the benefits of modern medicine.

The EU has taken a leading position by introducing a ban on the use of antibiotics for group prophylaxis. This ban is to be accompanied by changes to help improve the welfare of animals on farms, to reduce the risk of sickness and disease. Simple improvements like reducing stocking density, ending the use of cages, ensuring a more natural diet, and using breeds that are less prone to disease can help greatly reduce the need for antibiotics. World Animal Protection recommends the adoption of Farm Animal Responsible Minimum Standards for all conventional farms across Australia.[10] The changed legislation in the EU has occurred alongside the growing cage free movement which has seen a commitment to phase out the use of conventional cages for animal farming by 2027.[11] This demonstrates the connection between improved animal welfare and more responsible use of antibiotics.

Australia needs to act now to begin the process of phasing out the use of antibiotics in groups of animals that are not sick. It is not a responsible way to use antibiotics and it puts animal welfare and human health at risk.

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[10] See, Farm animal responsible minimum standards (FARMS), https://www.farms-initiative.com/

[11] See, eg, BBC, 'Caged Animal Farming: EU aims to end practice by 2027 (BBC Online, 30 June 2021) available at < https://www.bbc.com/news/world-europe-57668658>

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