CAHS
ACSS
Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Antimicrobial Resistance/ Antimicrobial Use in Food-Producing Animals in Canada:

Strategic Interventions to Strengthen Antimicrobial Stewardship

March 2025

The Canadian Academy of Health Sciences

70 George Street, 3rd Floor, Ottawa, Ontario, Canada, K1N 5V9

This report was prepared for the Government of Canada in response to a request from the Canadian Food Inspection Agency (CFIA) and the Public Health Agency of Canada (PHAC). It was undertaken with the approval of the Board of the Canadian Academy of Health Sciences (CAHS). The members of the Oversight Panel responsible for the report were selected by the CAHS for their special competencies and with regard for appropriate balance. Any opinions, findings, or conclusions expressed in this publication are those of the authors, the Expert Panel on the Assessment on AMR/AMU, and do not necessarily represent the views of their organizations of affiliation or employment, or the sponsoring organizations, the CFIA and PHAC.

Issued in electronic format only in English and French.

English version ISBN 978-1-9990034-8-7

French version ISBN 978-1-9990034-9-4

This report should be cited as: Canadian Academy of Health Sciences. (2025). *Antimicrobial Resistance / Antimicrobial Use in Food-Producing Animals in Canada: Strategic Interventions to Strengthen Antimicrobial Stewardship*. The Expert Panel on the Assessment on Antimicrobial Resistance (AMR)/Antimicrobial Use (AMU), Canadian Academy of Health Sciences.

This project was funded by the Canadian Food Inspection Agency and the Public Health Agency of Canada.

The Canadian Academy of Health Sciences

The CAHS provides independent and timely assessments that inform policy and practice to address critical health challenges affecting Canadians. The CAHS helps put change into action for a healthier Canada.

The CAHS recognizes Canadians of great achievement in health sciences. Founded in 2004, the CAHS now has almost 1,000 Fellows and elects new Fellows on an annual basis. The organization is governed by a voluntary Board of Directors and a Board Executive.

The CAHS brings together Canada's top-ranked health and biomedical scientists and scholars from all disciplines across our nation's universities and its healthcare and research institutes to make a positive impact on the urgent health concerns of Canadians. These Fellows reach out to other experts and engage with the public and key stakeholders to evaluate Canada's most complex health challenges and identify strategic, actionable solutions.

Since 2006, the CAHS has co-invested in rigorous, independent assessments that address key health issues with outcomes that have shaped its strategic policy and initiatives.

Acknowledgements

The CAHS would like to acknowledge and thank the following individuals and organizations for their contributions to the AMR/AMU assessment on food-producing animals.

The assessment would not have been possible without the leadership provided by the Chair, and the in-depth expertise and passion of our Expert Panel members, who generously donated their time to participate in many hours of evidence review, critical analysis, discussion, and revision that led to the production of this assessment. Thus, the CAHS acknowledges and sincerely thanks the following Expert Panel members for their input:

Jan Sargeant (Chair), University of Guelph

Panel members (in alphabetical order, by last name):

Julie Arsenault, Université de Montréal
Herman Barkema, University of Calgary
Sylvia Checkley, University of Calgary
Anne Deckert, University of Guelph
David Kelton, University of Guelph
Tim Nelson
Lindsay Nicolle, University of Manitoba
Simon Otto, University of Alberta
David Patrick, University of British Columbia
Andy Potter, University of Saskatchewan
John Prescott, University of Guelph
Javier Sanchez, University of Prince-Edward- Island
Cheryl Waldner, University of Saskatchewan

Conflicts of interest declarations have been reviewed and the CAHS is satisfied that there is no undue influence by panel members on the findings in this report.

The following staff members contributed by way of leadership, writing, research, and administration that made this project possible:

Rose Geransar (Scientific Writer and Lead)
Carlie Pagliacci (Administrator)
Kim Sheppard (Researcher)
Sarah Totton (Researcher)

Marc Ouellette, BSc, PhD, and Craig Stephen, DVM, PhD who served as peer reviewers of this work.

The following contractors contributed their services to this project:

ACER Consulting Ltd.
Roxana Badiei
Francine Watkins Translation Services Inc.
Léger
Mario Scaffardi Design Inc.

The CAHS would like to sincerely thank all of the key actors and organizations across Canada in the food-producing animal sectors and beyond who contributed their valuable time and input to this work.

Finally, the CAHS thanks the Canadian Food Inspection Agency and the Public Health Agency of Canada for providing funding for this work, and acknowledges that this report does not necessarily reflect the views of the sponsors or other entities within the Government of Canada.

Message from the CAHS President

On behalf of the Canadian Academy of Health Sciences (CAHS), I am pleased to introduce this Assessment Report on Antimicrobial Resistance (AMR) and Antimicrobial Use (AMU) in Food Producing Animals.

This important document will undoubtedly inform policy makers and support Canada as it considers its next steps on the issue.

The CAHS would like to express its sincere appreciation to the Chair of the Panel, Jan Sargeant, as well as the members of the Panel for their immense contributions to this assessment.

The report was strengthened by the extensive consultations undertaken throughout the process.

I would also like to thank the peer-reviewers who provided excellent feedback on the draft report and the members of the CAHS Scientific Affairs Committee for their guidance throughout the process.

Finally, I would like to recognize the Canadian Food Inspection Agency (CFIA) and Public Health Agency of Canada (PHAC) who funded this assessment.

Sincerely,

Trevor Young, President

Message from the CAHS AMR/AMU Chair

Our Expert Panel ("the Panel") has contributed its time and diverse range of expertise to identifying promising strategic interventions to support stewardship of antimicrobials in food-producing animals in Canada. It is with great pleasure that we release our final report.

The panel received an ambitious scope of work provided by the sponsor of this assessment and a relatively short time to accomplish our task. The collective experience and wisdom of the panel was truly the critical integrative lens that enabled the CAHS to integrate key evidence from the vast body of literature and other evidence relevant to this assessment.

The fundamental framework through which the issue of antimicrobial resistance/antimicrobial use was viewed is that of stewardship. This focus on stewardship acknowledges the complex and diverse economic and social landscapes faced by Canadian producers, while cultivating a sense of responsibility on part of all users for the sustainable use of antimicrobials for generations to come.

The four critical interconnected themes identified resonate the messaging of our dedicated and passionate key actors whom we consulted throughout this assessment, and review of international case studies. Those themes are:

- Leadership and political commitment
- Supporting veterinarians and producers in maintaining animal health
- Integrating antimicrobial stewardship principles
- Enhancing surveillance and measurement of antimicrobial use.

Five strategic interventions were identified, each of which would enhance stewardship, and collectively would have a profound impact on antimicrobial use in food-producing animals.

Canada is now presented with a transformative opportunity for collaborative advancement in antimicrobial resistance/antimicrobial use. The panel hopes that this assessment will inform policymakers and all of the key actors as they consider actions and policies.

Jan Sargeant, DVM, MSc, PhD, FCAHS - Panel Chair

Executive Summary

Antimicrobial Resistance in Canada

Antimicrobial resistance (AMR) represents a profound threat to human and animal health, driven by intricate transmission pathways and interconnections between humans, animals, and the environment. An estimated 15 people per day died in Canada in 2018 due to AMR infections, a number that is expected to increase substantially over time unless urgent action is taken. If AMR continues to increase at the current rate, by 2050, the cumulative loss to Canada's GDP has been estimated to be $388 billion (Council of Canadian Academies, 2019). A key modifiable driver of AMR is antimicrobial use (AMU) across the One Health spectrum. This includes the use of antimicrobials in food-producing animals.

The Canadian Academy of Health Sciences (CAHS), with financial support from the Canadian Food Inspection Agency (CFIA) and the Public Health Agency of Canada (PHAC), conducted the present assessment on AMR and AMU in food-producing animals in Canada. The assessment is intended to support the Pan-Canadian Action Plan on AMR (the PCAP).

The primary charge as worded by the project sponsors (CFIA and PHAC) was as follows: "Given that it is well understood that the overuse and misuse of antimicrobials drives AMR, what are the promising and strategic interventions that can be implemented to further strengthen the prudent use of antimicrobials in food-producing animals in Canada, to mitigate the risk of AMR to human health?" Additional sub-questions were included by the sponsor addressing animal health (see Chapter 1).

The Assessment on Antimicrobial Resistance/Antimicrobial Use in Food-Producing Animals

Antimicrobial stewardship (AMS) lies at the core of managing AMR/AMU in food-producing animals and is central to this assessment. As requested by the sponsors, the assessment focused on identifying promising and strategic interventions that could be implemented to further strengthen AMS in food-producing animals in Canada, to mitigate the risk of AMR to human and animal health.

This project spanned a 14-month period (Jan 2024- Mar 2025), and was completed under the guidance of a Chair and a thirteen-member Canadian expert panel representing diverse expertise in AMR/AMU. The assessment was informed by:

1. A review of evidence in the published and grey literature
2. International case studies of policy (and practice) initiatives across 8 jurisdictions
3. A cross-Canadian engagement that included Canadian key informant interviews, virtual engagement sessions, and consumer focus groups

Key Findings: Topic Areas

Fifteen key findings were identified across 6 topic areas. “Key findings” refer to significant or important evidence derived from the academic literature reviews, international case studies, and Cross-Canadian engagement. These included:

- The current state of knowledge of AMR in food-producing animals and transmission of AMR to humans (Ch. 2)
- Antimicrobial stewardship in food-producing animals (Ch. 3)
- Governance, policy, and regulatory approaches to support AMS (Ch. 4)
- Farm-level interventions to reduce the need for AMU (Ch. 5)
- Surveillance of AMR and AMU in food-producing animals (Ch. 6)
- Impacts of interventions to reduce AMU on AMR (Ch. 7)
- AMR awareness and education in consumers (Ch. 8)

Detailed key findings are addressed under each respective chapter. Relevant gaps, including key gaps (i.e. gaps in knowledge, regulations, Federal-Provincial-Territorial (FPT) jurisdictional issues, and practice as compared to other countries) were also identified for each topic area.

All of the key findings align with the actions identified in the PCAP. The greatest areas of alignment are under the surveillance pillar of the PCAP, followed by the stewardship pillar, and the infection prevention and control pillar.

Key findings fell under four major interconnected thematic areas:

1. ***Leadership, coordination, and political commitment***
    - There is strong evidence from other jurisdictions that leadership and political commitment at the highest levels of government are essential to motivate all individuals and organizations involved in food animal production to reduce the use of antimicrobials to where benefits are clear and substantial and exceed the risks. Effective coordination is also critical.

2. ***Supporting veterinarians and producers in keeping animals healthy***
    - Preventing and controlling infections is crucial to reducing AMU. Biosecurity and evidence-based livestock management practices, effective vaccines and alternative products, and validated AMU decision-making tools are essential for keeping animals healthy so that they require fewer antimicrobials.

3. *Embracing antimicrobial stewardship*
    - The 5R's of AMS encompasses all of the principles that are needed: responsibility to improve antimicrobial drug use, reducing, refining, and replacing AMU when possible, and reviewing the impact of changes on a continuous basis. Antimicrobial stewardship is a helpful framework to bring government, industry sectors, veterinarians and producers together to work collaboratively through a holistic approach to address AMS.
4. *Enhancing surveillance and measurement of AMR in pathogens of veterinary interest and measurement of AMU in food-producing animals to meaningfully evaluate and document our successes and failures*
    - An essential cross-cutting theme is that "we cannot manage what we cannot measure." Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) is an important enabler to Canada's efforts to monitor AMR; however, there are major gaps that would need to be addressed to provide a clearer picture of where we are in Canada with AMR in pathogens of interest to animal health.

Promising and strategic interventions to further strengthen antimicrobial stewardship in food-producing animals in Canada

The expert panel developed five strategic interventions that could strengthen AMS based on the fifteen key findings. These actions to support change are not mutually exclusive; individually, each could bring about meaningful change, and collectively they could have a profound impact. Each addresses one or more of the thematic areas identified above; these are put forward for consideration with supporting evidence and potential consequences in Chapter 9. These interventions form the basis of the steps that could be taken to enhance AMS in food-producing animals in Canada.

Strategic intervention 1: Identify a governance structure to lead and coordinate implementation of the PCAP for food-producing animals

- AMR is a complex issue with many involved parties; a full consensus on pathways forward may not always be achievable. Thus, there is a clear and compelling need for a dedicated governance structure including leadership and resources to fully coordinate and implement the next steps required to operationalize the PCAP.

Strategic intervention 2: Adopt farm-level AMU data collection and benchmarking

- Countries with strong AMS frameworks use farm-level AMU data as a key component in their overall approach. Without measurement of AMU, it is not possible to determine why some farms / veterinarians / commodity groups / production sectors / or countries use more antimicrobials than others. Without measurement, it is impossible to evaluate whether AMS efforts are effective, or to monitor and document progress.

Strategic intervention 3: Make antimicrobial stewardship the standard of practice for veterinarians

- Expansion of the veterinary standard of practice to specifically include AMS, including benchmarking and restricting the use of category I antimicrobials in food-producing animals, would be an important part of a "made-in-Canada approach" to address AMS. This would ensure antimicrobials are used only when the benefits clearly outweigh the risks.

Strategic intervention 4: Restrict the use of Category I antimicrobials in food-producing animals

- Québec has successfully restricted the use of Category I antimicrobials in food-producing animals, leading to reductions in their use. Adopting restrictions for Category I use nationally would enhance AMS.
- Several specific opportunities would enable reductions in the use of Category I antimicrobials.

    1. **Preventive uses:**
    - Ban the use of all Category I antimicrobials for systemic / injectable or oral use for preventive purposes in food-producing animals.
    - Implement a ban on blanket dry cow therapy with ceftiofur in dairy cows with a move to selective dry cow therapy, wherein treatment with ceftiofur would need to be explicitly justified.

    2. **Therapeutic uses:**
    - Ban the extra-label drug use of Category I antimicrobials for disease treatment in food-producing animals without laboratory evidence that no other treatment option will be effective.
    - Require a written justification based on clinical or laboratory evidence and a written farm-level protocol for use of all category I antimicrobials already licensed for treatment of specific conditions in food-producing animals.

Strategic intervention 5: Support relevant targeted research to enhance knowledge on application and efficacy of strategies and products to keep animals healthy

- Countries that have implemented AMS programs and policies have enhanced biosecurity, effective vaccine programs, and access to effective alternative products. However, there is limited evidence for effectiveness of these strategies and products under current commercial conditions in Canada (Ch. 5). Additional research that prioritizes promising biosecurity measures, vaccines, and alternative products, with rigorous replication of studies, is essential for building an evidence-based foundation to support effective AMS.

Do we need to set targets in Canada? Jurisdictional case studies have shown that setting targets and tracking progress using mandatory on-farm benchmarking data are effective at reducing AMU. However, based on our engagement activities, it is anticipated that there would be considerable resistance to setting reduction targets from many involved parties in Canada at this time. The ultimate goal is not meeting a set target, but rather is to reduce the use of antimicrobials to where benefits are demonstrably clear and substantial and exceed the risk.

Conclusion

In the face of the ongoing global threat of AMR to human and animal health, the incentives and motivation for change are clear. There will be no substantial new antimicrobials introduced into food-producing animal agriculture in the foreseeable future. If AMS is to improve for food-producing animal agriculture, a long-term commitment to action is required. This requires the sustained leadership of politicians, veterinarians, organized veterinary medicine, food-producing animal producers and their organizations, regulatory agencies, consumers, and food-producing animal product retailers, and a more effective and focused system of managing this commitment. The promising and strategic interventions outlined above could help bridge the key gaps identified through this assessment, ensure that antimicrobials are preserved as a precious resource for generations to come and used where the benefits are clear and substantial.

Table of Contents

List of Tables and Figures

Tables

Figures

Acronyms

AHC: Animal Health Canada
AMR: Antimicrobial resistance
AMS: Antimicrobial stewardship
AMU: Antimicrobial use
ARG: Antimicrobial resistance genes
BRD: Bovine respiratory disease
CAHSS: Canadian Animal Health Surveillance System
CIPARS: Canadian Integrated Program for Antimicrobial Resistance Surveillance
CVMA: Canadian Veterinary Medical Association
E. coli: *Escherichia coli*
ELDU: Extra-label drug use
FPT: Federal-Provincial-Territorial
HGT: Horizontal gene transfer
IPC: Infection prevention and control
KTT: Knowledge translation and transfer
Vet-LIRN: Veterinary Laboratory Investigation and Response Network
MDR: Multidrug resistance
mg/kg: milligrams per kilogram
MIA: Medically important antimicrobials
MRSA: Methicillin-resistant *Staphylococcus aureus*
PCAP: Pan-Canadian Action Plan, referring to the *Pan-Canadian Action Plan on Antimicrobial Resistance*
PCUca: Population correction unit Canadian average
RUMA: Responsible Use of Medicines in Agriculture Alliance
SAVI: Stewardship of Antimicrobials by Veterinarians Initiative
VASR: Veterinary Antimicrobial Sales Reporting
WGS: Whole-genome sequencing
WHO: World Health Organization

CAHS
ACSS

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 1:

Overall approach

Introduction

Antimicrobial resistance (AMR) is a threat to global public health and animal health, including food-producing animals. AMR has a substantial socio-economic impact in Canada:

- In 2018, nearly 15 people per day were estimated to have died in Canada due to AMR infections, with a cost to the health care system of $1.4 billion.
- The impact on Gross Domestic Production (GDP) was an estimated $2.0 billion (PHAC, 2023a).
- The cost to food-producing animal producers attributed to animal disease and death from AMR infections is not known; however, a 2019 report by an expert panel for the Canadian Council of Academies concluded that if AMR in animals continued to increase at the current rate, by 2050 the cumulative loss to Canada's GDP was estimated to be $388 billion (Council of Canadian Academies, 2019).

The Canadian Academy of Health Sciences (CAHS), with financial support from the Canadian Food Inspection Agency (CFIA) and the Public Health Agency of Canada (PHAC), conducted the present assessment on Antimicrobial Resistance (AMR) and Antimicrobial Use (AMU) in food-producing animals in Canada. This assessment is intended to support the *Pan-Canadian Action Plan on Antimicrobial Resistance* (hereafter, "PCAP"), a shared Federal-Provincial-Territorial (FPT) commitment to address AMR across 5 pillars and 10 priority actions.

1.1 The Charge

This assessment focuses on identifying promising and strategic interventions that can be implemented to further strengthen the prudent use of antimicrobials in food-producing animals in Canada and to mitigate the risk of AMR to human health. The specific charge to the CAHS from the project sponsors (CFIA and PHAC) was as follows:

Given that it is well understood that the overuse and misuse of antimicrobials drives AMR, what are the promising and strategic interventions that can be implemented to further strengthen the prudent use of antimicrobials in food-producing animals in Canada, to mitigate the risk of AMR to human health?

Additional questions posed included:

- What is the current state of knowledge on: AMR in animal pathogens, the extent of transmission of AMR pathogens from animals to humans, and the importance of AMU on animal health and/or productivity?
- What interventions to reduce AMU in food-producing animals have already been implemented by different Canadian agricultural industry groups, as well as FPT governments?

- What additional interventions could be implemented in the future?
- Which elements of international action plans and strategies have most effectively reduced AMU in food-producing animals? Could any of these practices be implemented in the Canadian context?

1.1.1 Species scope

Food-producing animals that are within the scope of this assessment include: beef cattle, dairy cattle, swine and poultry, small ruminants, and aquaculture (limited to farmed finfish). The species to be included were selected by the sponsor.

This assessment is focused on AMU in food-producing animals in Canada. It is important to acknowledge the complexity of AMR through a One Health lens. Thus, this work is undertaken with the understanding that AMU in humans and companion animals is also a major contributing factor to AMR, but is out of scope in this assessment.

1.1.2 Timeline

The timeline for the assessment spanned January 2024 (project start), to March 2025 (launch of final report).

1.2 Antimicrobial Stewardship (AMS) as a Framework to addressing AMR/AMU

Antimicrobial stewardship (AMS) focuses on all the factors that would result in less use of antimicrobials and, therefore, limit resistance (Chapter 3). The complexity of factors affecting the effectiveness of AMU, and of AMR and its epidemiology, means that effective AMS requires multiple approaches. Key elements in successful national veterinary AMS programs in food-producing animals identified in the different country case studies are the integration of leadership, commitment, coordination, surveillance of AMR and AMU, regulation, measurement towards clear goals, benchmarking, education and training. Given that we consider that such an AMS focus could be the backbone of a national approach addressing AMR in food-producing animals, we

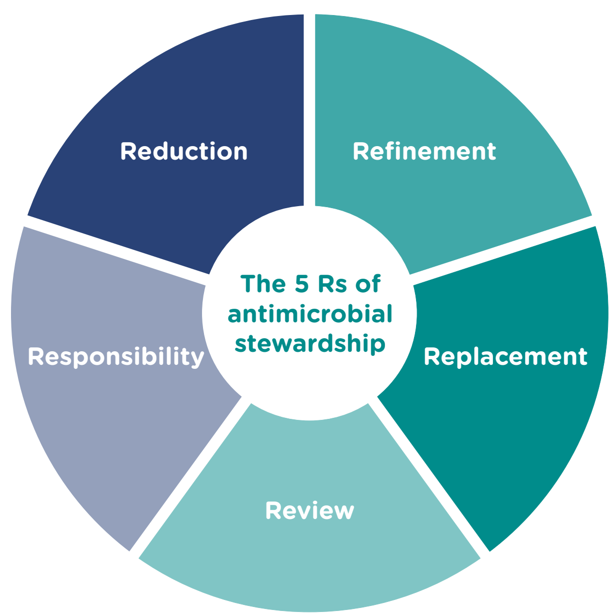


Figure 1-1. The 5R's of antimicrobial stewardship (Figure taken from ACER Consulting Limited, 2018)

suggest that adoption of a 5R's approach (Figure 1-1) of responsibility, reduction, replacement, refinement, and review, described in Chapter 3, is a holistic and potentially unifying framework for the evolution of improved AMS and its measurement in food-producing animals. It is applicable across all actors involved with AMU (governments, regulators, veterinarians, and producers) because it allows a potentially complex process to become both practical and effective.

1.3 Classification of Antimicrobials

Antimicrobials have different classifications nationally and at the WHO level. Throughout this report, reference will be made to categories of antimicrobials as they are classified by Health Canada (see Table 1-1).

Table 1-1. Health Canada's categorization of importance of antimicrobial drugs for human medicine used in risk assessment for use in food-producing animals (Health Canada, 2009)

Category	Preferred option for treatment of serious human infections	Examples of drugs used in treatment of bacterial infections in food-producing animals
I-Very High Importance	These antimicrobials are considered of very high importance in human medicine as they meet the criteria of being essential for the treatment of serious bacterial infections and limited or no availability of alternative antimicrobials for effective treatment in case of emergence of resistance to these agents.	Cephalosporins – third generation; fluoroquinolones; penicillin-β-lactamase inhibitor combinations; polymyxins
II-High Importance	Antimicrobials in this category consist of those that can be used to treat a variety of infections including serious infections and for which alternatives are generally available. Bacteria resistant to drugs of this category are generally susceptible to Category I drugs which could be used as the alternatives.	Aminoglycosides (except topical agents); cephalosporins – first and second generations; lincosamides; macrolides; penicillins; trimethoprim/ sulfamethoxazole
III-Medium Importance	Antimicrobials in this category are used for treatment of bacterial infections for which alternatives are generally available. Infections caused by bacteria resistant to these drugs can, in general, be treated by Category II or I antimicrobials.	Aminocyclitols; aminoglycosides (topical agents); bacitracins; nitrofurans; phenicols; sulphonamides; tetracyclines
IV-Low Importance	Antimicrobials in this category are currently not used in human medicine.	Flavophospholipols; ionophores

In some instances, this report also makes reference to WHO's Medically Important Antimicrobial (MIA) List, previously known as the WHO Critically Important Antimicrobials List for Human Medicine (World Health Organization, 2024a).

1.4 The CAHS Approach

The Assessment was informed by three distinct areas of work, with Chair and Expert Panel oversight:

1. Evidence-based review of academic and "grey" literature
2. Case studies of policy (and practice) initiatives across 8 international jurisdictions, including a review of international policy documents, grey literature, and interviews with key informants
3. Cross-Canadian engagement, including:
    a. Canadian key informant interviews with individuals and organizations, including industry organizations, veterinary professionals, and FPT governments.
    b. Virtual engagement sessions (with a broader group of the same categories of participants as stated in part "a").
    c. Surveys with Canadian key actors (with a broader group of the same categories of participants as stated in part "a").
    d. Opportunity for written document submissions.
    e. Focus groups with Canadian consumers, primarily those who consume products derived from food-producing animals, but also those who do not.

These three areas of work were integrated to develop key findings to respond to the charge from the sponsor (Figure 1-2). "Key findings" refer to significant or important evidence derived from the literature review, international case studies, and Cross-Canadian engagement.

The purpose of this assessment was to respond to the sponsor's charge in a meaningful way considering multiple forms of evidence. The goal was to provide a contextually relevant understanding of the issues together with some suggestions for pathways forward. The evidence considered included published literature (prioritizing the strongest forms of research evidence), and also grey literature regarding relevant initiatives in other jurisdictions, together with perspectives of relevant key informants/interested parties, as well as the public.

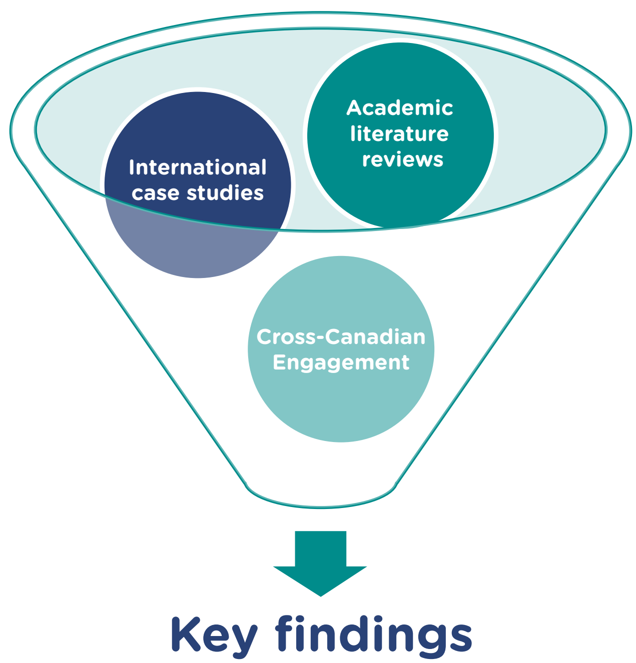


Figure 1-2. The CAHS approach of integrating literature review, international case studies, and cross-Canadian engagement to develop key findings

The elements of the CAHS approach are outlined in detail below, and in Appendix 1 .

1.4.1 Academic Literature Review

A structured and targeted literature review was conducted, focusing on systematic reviews, meta-analyses, scoping reviews, and narrative reviews (2013-2023). This approach was selected to accommodate the large breadth of areas to be informed by this assessment as part of the sponsor's request, and to identify the strongest evidence available in a limited time. Systematic reviews were generally given the greatest weight (Appendix 1). Thus, where available, evidence from systematic reviews and meta-analyses or network meta-analyses are presented.

Systematic reviews involve a structured approach to document the identification and selection of the articles included in the review and include a consideration of the risk of bias for the included studies. Meta-analysis statistically combines the results from multiple studies comparing one intervention to another ("pairwise") to calculate a summary effect size. Pairwise meta-analysis is an extension of meta-analysis that allows an estimation of the comparative efficacy of more than two interventions. The results of meta-analyses provide an average estimate of the effectiveness of an intervention, which may not be applicable across the diversity of farm settings. However, the systematic approach reduces the probability that the studies included in the review are a biased subsample of the literature. Single research studies do not provide as high a level of evidence as systematic reviews and meta-analysis, as systematic reviews summarize the full body of research.

Despite the major changes occurring in AMU for food-producing animal production in intensive agriculture globally, the number of systematic reviews and meta-analyses was relatively scant. Where systematic reviews were not available, or for research questions not readily summarized by a systematic review approach, selected narrative reviews and original studies were used to supplement the findings. Over 600 articles were included as part of the assessment. Original research studies were incorporated to supplement areas where literature reviews were not available to address a specific issue.

1.4.2 International Case Studies

Eight international case studies were conducted from Australia, Denmark, the European Union, France, Germany, the Netherlands, the United Kingdom, and the United States.

These jurisdictions were selected by the sponsor (n=4) and Expert Panel (n=4) for their jurisdictional relevance to Canada in terms of their approach to governance, and for their activities to address AMR/AMU in food-producing animals that would enable the Expert Panel to respond to the primary question in the Charge.

The methodology for the international case studies included both a review of the grey literature and interviews, with a total of 23 key informants from across the jurisdictions included. Over 330 individual references were cited across all international case studies. Two-page summaries of each international case study are included in Appendix 2.

1.4.3 Cross-Canada Engagement

The following cross-Canada engagement was also conducted:

- Two virtual engagement sessions, engaging a total of 107 participants
- Interviews with 33 Canadian key informants
- Two rounds of focus groups (8 focus groups with a total of 69 participants) with Canadian consumers
- Two rounds of written surveys with a total of 102 survey participants
- Written policy documents, guidelines, and/or ongoing initiative submissions from 7 organizations

Details on the methods and demographics for these rounds of engagement are discussed in Appendix 1.

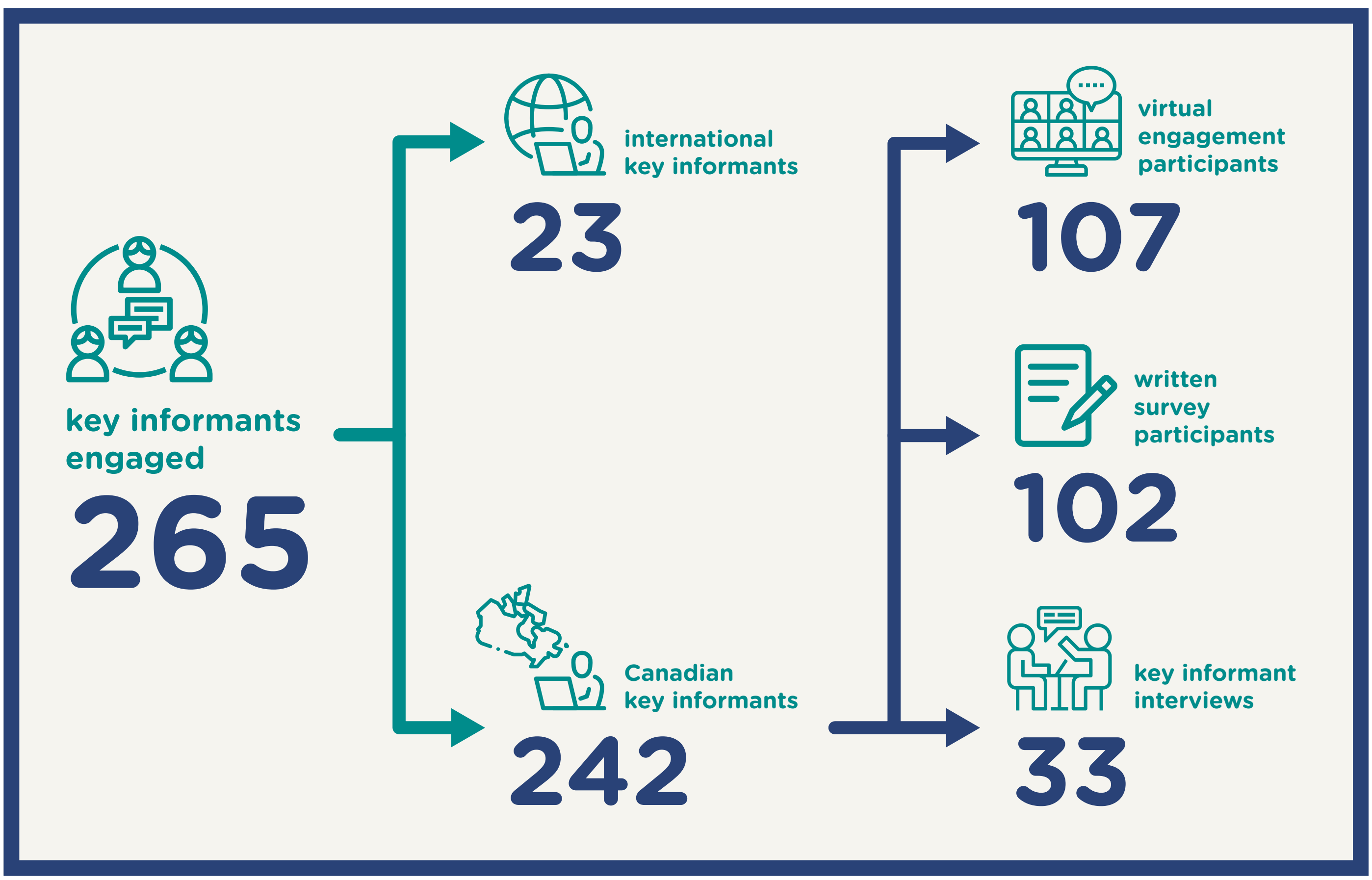


Figure 1-3. Summary of the number of key informants engaged through various modalities for the assessment on AMR/AMU in food-producing animals

1.4.4 Expert Panel and Task Group Meetings

Expert panel. Expert Panel members were selected from among the CAHS fellows and other individuals with expertise in the field to collectively provide both depth and breadth of expertise to inform the issue of AMR/AMU in food-producing animals. The 13 Expert Panel members met a total of 10 times as a panel to discuss key issues and aspects related to the assessment. Panel discussions were moderated by a neutral Chair.

Task groups. Task groups were formed to identify and discuss key findings in key content areas. Key content areas were identified as part of this assessment based on an analysis of the project charter. These content areas also constitute the main chapter titles of this assessment; they include:

- Current state of knowledge of AMR in food-producing animals and transmission of AMR to humans (Ch. 2)
- Antimicrobial Stewardship in Food-Producing Animals (Ch. 3)
- Governance, policy, and regulatory approaches to support antimicrobial stewardship (Ch. 4)
- Farm-level interventions to reduce the need for AMU (Ch. 5)
- Surveillance of AMR and AMU in food-producing animals (Ch. 6)
- Impacts of interventions to reduce AMU on AMR (Ch. 7)
- AMR awareness and education in consumers (Ch. 8)

Six task groups were formed to identify and discuss key findings in these content areas. Task group members were selected by the Chair from among the 13 Expert Panel members based on expressed areas of expertise and interest, with 3 to 5 Expert Panel members in each task group. A lead was appointed for each of the task groups; the lead or Chair facilitated task group discussions. Any conflicting interpretations of the evidence were discussed within the task groups and, if consensus could not be reached, these issues were brought forward by the task group lead for discussion

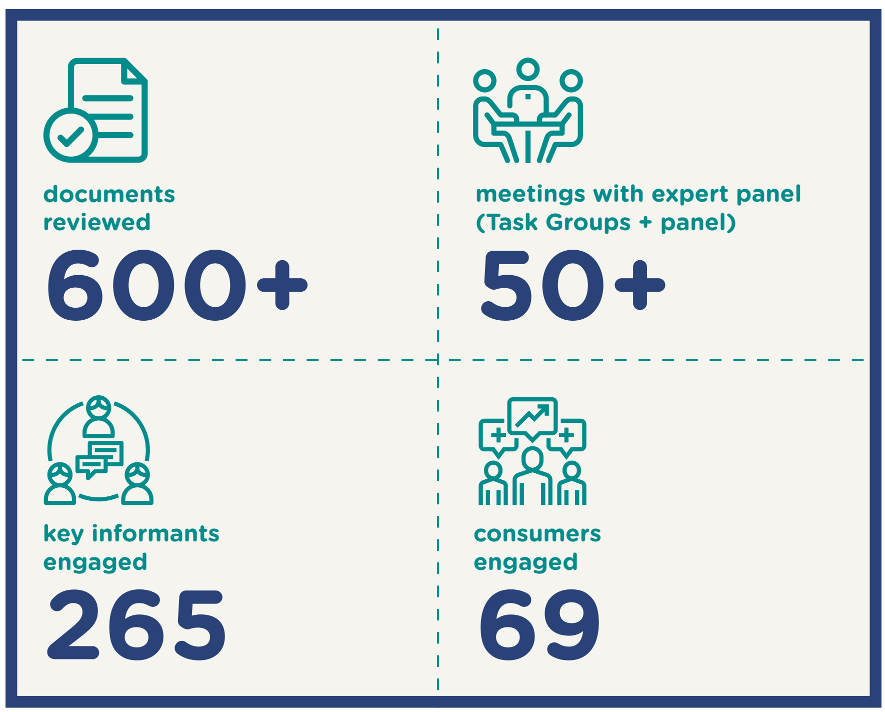


Figure 1-4. Summary of metrics for activities contributing to the development of key findings

by the full panel. An additional task group was established to discuss "unresolved issues" that were identified as relevant and important by panel members, and to assist with the integration of these issues into the assessment.

1.4.5 Identification of Key Findings and Key Gaps and Strategic Interventions

Key findings were identified under each of the content areas based task group discussions of the evidence provided from the review of the scientific literature, international case studies, and input from the cross-Canada engagement. Relevant gaps (i.e. gaps in knowledge, regulations, FPT jurisdictional issues, and practice as compared to other countries) were also identified using a similar process to correspond to each key finding.

All key findings were subject to review and critical analysis by the Expert Panel. Contentious issues were first discussed at the task group level. When a task group lead and/or Chair felt that broader input was required, the issue was taken to a full panel meeting for discussion. Pre-panel surveys were used to involve the Expert Panel in prioritizing key findings for discussion at panel meetings. All key findings and key gaps were presented for discussion at panel meetings and agreed by consensus of the panel members.

Key findings and key gaps are outlined in the blue boxes under each respective chapter. Specific areas of potential alignment of key findings with the actions identified as part of the PCAP are indicated in blue boxes, after the key gaps.

In the final chapter (Ch. 9), the Expert Panel integrated the key findings and key gaps from the previous chapters to identify and present promising and strategic interventions to further strengthen AMS in food-producing animals in Canada. The strategic interventions were developed based on collective consideration and critical appraisal of all of the key findings and key gaps through several iterative Expert Panel discussions. Strategic interventions were discussed at the panel level until consensus was reached. Disagreements were handled through panel member votes, and where appropriate, discussion moderated by the neutral chair.

1.4.6 Peer Review

This work was peer-reviewed by two independent expert peer reviewers; peer review feedback was anonymized for the Chair and Expert Panel, i.e. the names of the reviewers were not revealed to the panel during incorporation of comments and reviews were not attributed to individual reviewers at any point.

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 2:

Current State of Knowledge of Antimicrobial Resistance in Food-Producing Animals and Transmission of Antimicrobial Resistance to Humans

Introduction

Antimicrobial resistance (AMR) is a profound threat to human and animal health, driven by intricate transmission pathways and interconnections between humans, animals, and the environment. Central to the AMR dialogue are important questions regarding the role of human activities—including the methods used in modern food-producing animal production—in promoting its emergence. This crisis not only endangers both animal and human health but also jeopardizes our capacity to maintain sustainable food production practices, both now and in the future. These pressing concerns underscore the urgent need for enhanced antimicrobial stewardship (AMS) and strategic efforts to address the impacts of AMR.

To address these issues, this chapter focuses on three main areas: 1. How AMR emerges, how this emergence is related to antimicrobial use (AMU) in food-producing animals, and where AMR organisms are found, 2. Routes of potential transmission of AMR from animals to humans, including direct contact with food-producing animals, food-borne transmission, and the environment, and 3. AMR in animal pathogens, and the extent to which it is problematic now and in the future across the major commodity groups.

2.1 What is Antimicrobial Resistance and How Does it Emerge?

What is Antimicrobial Resistance?

"Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. AMR occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death. As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others."

(World Health Organization, 2024b)

The emergence of AMR is complex. This assessment is limited to AMR in bacteria. Bacterial resistance is either natural or acquired; natural resistance is intrinsic to the organism and is present irrespective of exposure to antimicrobials. Acquired resistance is the development of resistance genes or traits through genetic mutation and/or transmission of resistance genes through the process of horizontal gene transfer (HGT) among bacteria. Acquired resistance is selected for and accelerated by exposure to antimicrobials at the population level.

There are many ways by which HGT occurs, with the end result being the transfer of AMR genes (ARGs) from one organism to another (Partridge et al., 2018; Despotovic et al., 2023). This transfer can cross bacterial species boundaries (Tóth et al., 2021). Importantly, while most antimicrobial resistant bacteria are not identified as a direct cause of human disease, they can still pose a risk for transfer of ARGs to human-adapted strains of the same species, genus, or other genera (Economou & Gousia, 2015). Some animal pathogens, accompanied by their resistance genes, can cause disease in humans (and vice versa), or can transfer their resistance genes to human pathogens or their microbiota. The epidemiology of AMR is highly dynamic, with an extensive and expanding reservoir of ARGs in the microbiomes of humans and animals attributable to exposure to antimicrobial drugs (Zamudio et al., 2024; Kim & Cha, 2021; Martiny et al., 2024).

ARGs can be found in pristine environments and are 'normal' (Kim et al., 2022; Van Goethem et al., 2018), but AMU is the major selective pressure for development, acquisition, maintenance and spread of bacterial ARGs within food-producing animals. While eliminating or reducing the use of antimicrobials will not fully eliminate AMR, reducing AMU reduces the selection pressure to acquire and maintain resistance and thus could help to reduce AMR over time. Chapter 7 (Impacts of interventions to reduce AMU) discusses some of the evidence to support this.

How is the emergence of AMR related to food-producing animals?

In Canada, the total amount of antimicrobials sold for use in food-producing animals is 1.5 times that sold for use in humans, on a mg per kg biomass basis (PHAC, 2023b; PHAC, 2024a). AMU practices in food-producing animal production include therapeutic treatment of sick animals to protect animal health and welfare, prophylactic treatment of healthy animals to prevent disease, and metaphylactic use to limit disease spread at the group level, where the group includes both sick and healthy animals. Collectively, AMU administration to food-producing animals at individual and group levels in feed, water, or by injection contributes to selection pressure for AMR.

Where are antimicrobial resistant organisms found?

Antimicrobial-resistant bacteria may occur within many different "reservoirs", including people, food, the environment (e.g. soil, water), animals (Chatterjee et al., 2018), plants, and crops. Maintenance and transmission of AMR is influenced by numerous factors that cut across sectors, including trade, travel, human and animal migration, the outputs of health care systems, and more. Animal agriculture, similar to hospitals and human sewage, is a source of waste that contributes to environmental reservoirs of ARGs and resistant bacteria. Thus, transmission of AMR, and use of antimicrobials in food-producing animals needs to be considered as part of the wider, One Health context. The concept of One Health is a fundamental principle to support strategies and actions that promote AMS to address AMR and acknowledge this complexity.

2.2 Transmission of AMR from Animals to Humans

As the AMR problem spans humans, animals, plants, crops and the environment (soil, water, and air), questions addressing how AMR is transmitted among these domains, the direction of transmission, the importance of that transmission and, if important, what can be done to mitigate transmission need to be answered. This section explores the evidence that is relevant to answering these questions.

There are a variety of routes through which AMR may spread among different elements of the One Health spectrum. Figure 2-1 illustrates this complex 'web' of interaction.

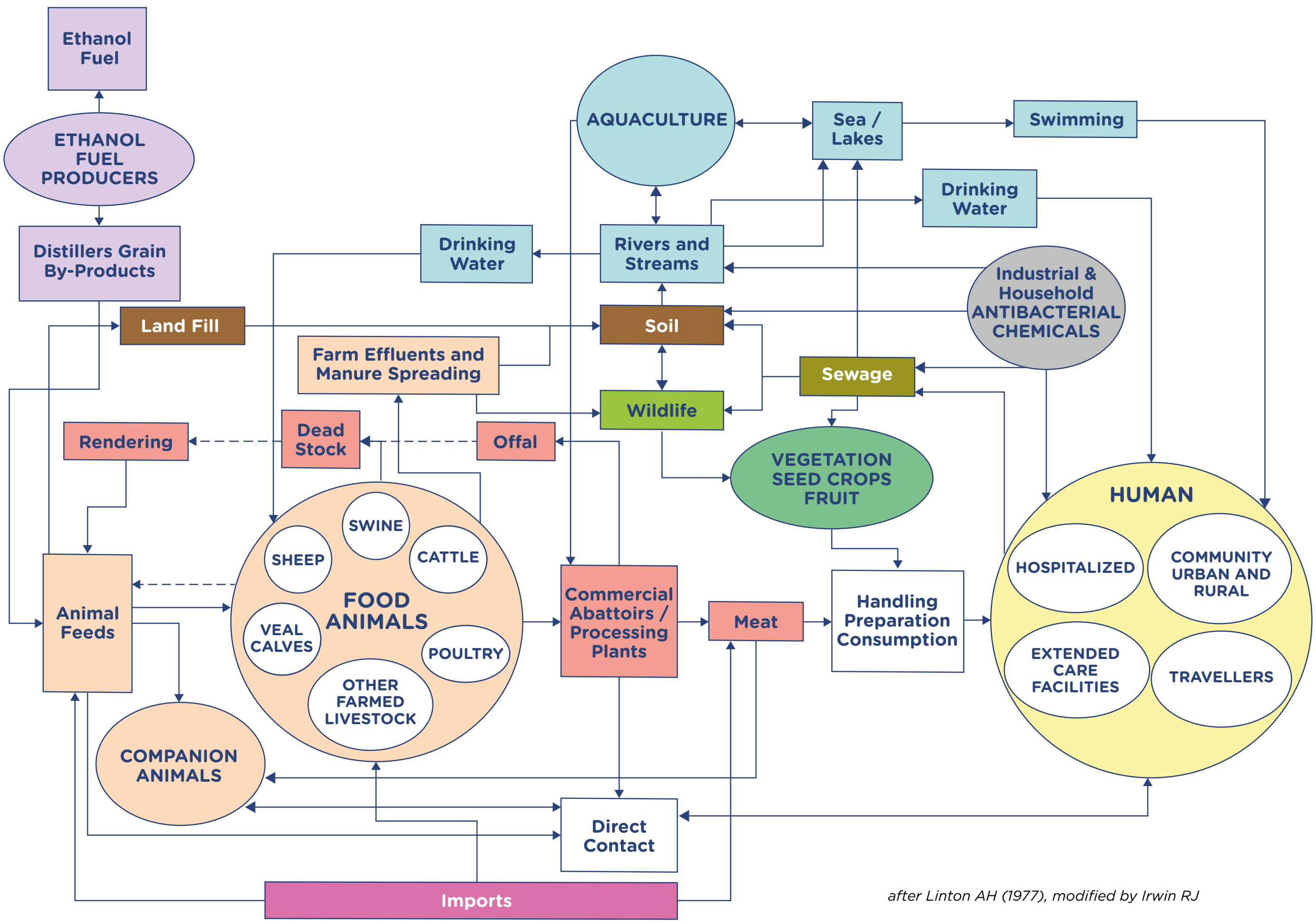


Figure 2-1. Epidemiology of AMR. This is a schematic representation of the potential transmission routes for resistant bacteria and resistance genes across multiple ecological compartments. The circles, and circles in the circles, represent different and, to some extent, self-contained ecological compartments, with the rectangles representing transmission routes. The size of the circles does not represent the relative importance of AMR within these compartments (PHAC, 2024b)

In the context of food-producing animals, the three main routes of AMR transmission between animals and humans are: 1. direct contact of humans with food-producing animals, 2. humans consuming and/or handling contaminated food-producing animal products, and 3. humans being in contact with environmental reservoirs such as commercial farming operations (Despotovic et al., 2023), as addressed in the sections below.

Direct contact of humans with food-producing animals. Humans, including producers, veterinarians, butchers, and slaughterhouse workers working in direct contact with food-producing animals are at increased risk of acquiring antimicrobial-resistant bacteria. Human to animal transmission is also possible. A systematic review and meta-analysis of 37 studies reported that livestock workers and veterinarians had an odds ratio of 9.8 for livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) compared to individuals with close proximity to animals but with no direct contact. Swine workers had the highest odds ratio (OR=15.4), followed by cattle workers (OR=11.6), veterinarians (OR=7.6), poultry workers (OR=5.7), and slaughterhouse workers (OR=4.7) (Chen & Wu, 2021). Based on three studies evaluating the odds of infection, livestock workers had an odds ratio of 3.4 compared to individuals without direct contact with animals. A UK-based systematic review identified 45 studies involving AMR transmission in the context of direct human contact with food-producing animals. It found evidence of transmission of AMR from food-producing animals to humans (in 8 studies), evidence of transmission between animals and humans with no direction specified (in 25 studies), and 12 studies that did not support transmission (Muloi et al., 2018). Due to high heterogeneity among the studies in methodological approach, animal species, antibiotics evaluated, and quality of evidence, no meta-analysis was conducted to quantify the results. Thus, direct animal to human transmission of AMR occurs, and further evaluation of risks and impacts is warranted.

Foodborne transmission. Foodborne transmission is an important route through which AMR has the potential for direct impact on the general human population via contaminated food derived from animal products (Chatterjee et al., 2018). Some antimicrobial resistant organisms, such as fluoroquinolone-resistant non-typhoidal *Salmonella* are considered as pathogens of "high priority" by the World Health Organization (World Health Organization, 2024c). Non-typhoidal *Salmonella* are also associated with a high health care burden in Canada (Glass-Kaastra, 2022). *Salmonella enterica* serovar Heidelberg is found in some chicken meat products and poses a public health risk in Canada (Collineau et al., 2020). Historical surveillance evidence in Canada has suggested a very strong association between ceftiofur use in chickens and third-generation cephalosporin resistance in *Salmonella* Heidelberg and generic *Escherichia coli* from chicken and humans (Dutil et al., 2010, Figure 2-2). Some modeling work has also attributed a proportion of cases of infection with a ceftiofur-resistant strain to prior human antibiotic consumption (Otto et al., 2014), a recognized risk factor for human salmonellosis generally, but noted that the source of the organism was still from contaminated poultry products.

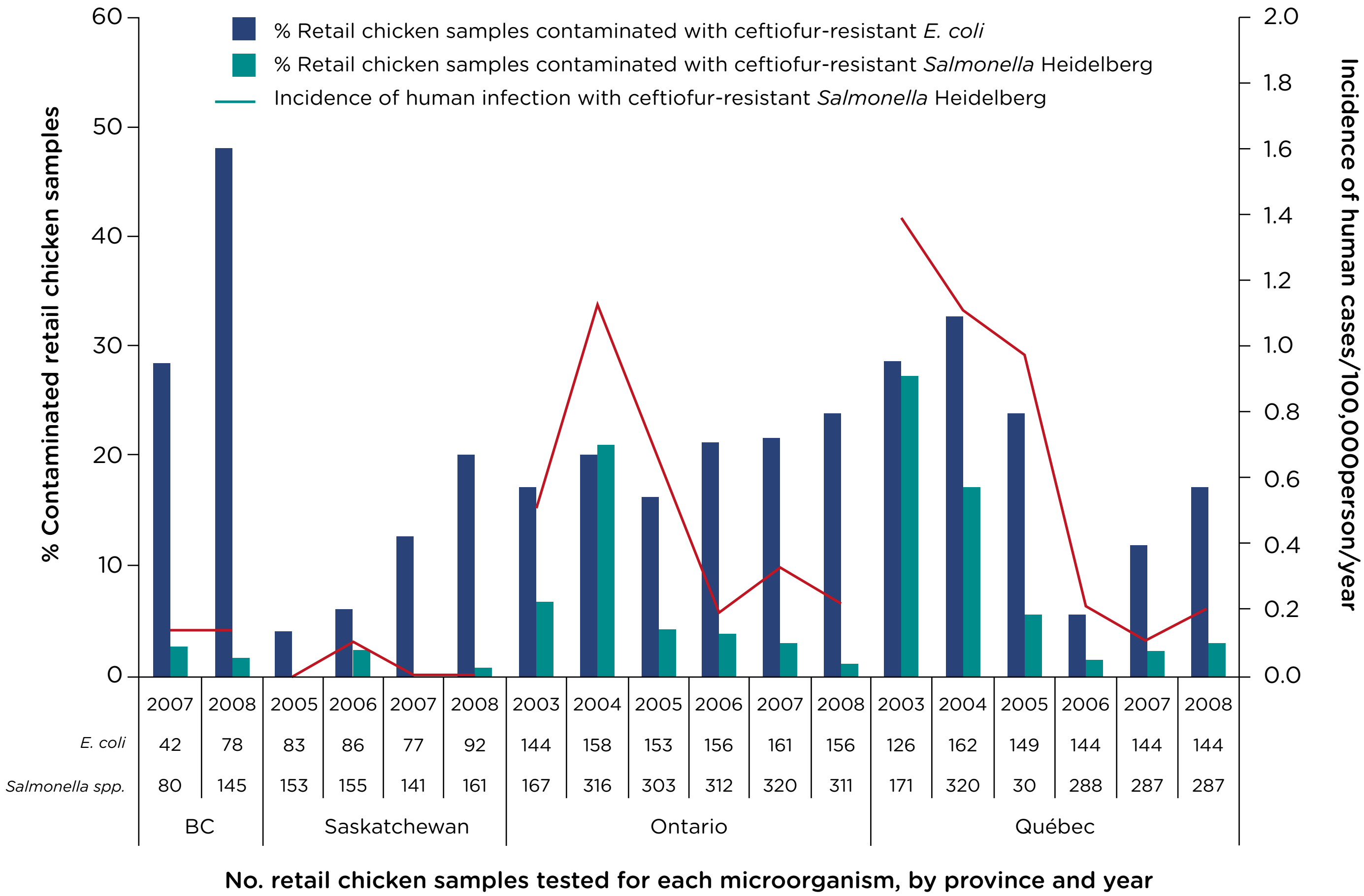


Figure 2-2. Prevalence of retail chicken contaminated with ceftiofur-resistant *Escherichia coli* and *Salmonella enterica serovar Heidelberg* and incidence of human infections from ceftiofur-resistant *Salmonella Heidelberg* in Canada (Dutil et al., 2010)

The greatest opportunity to minimize the risk of transmission of AMR organisms to humans from animal-derived foods is during and post-harvest. One source of foodborne contamination is fecal contamination in processing plants (e.g., of antimicrobial resistant strains of *E. coli*), as illustrated in the Figure 2-2. However, it is important to note that in this example, generic *E. coli* represents contamination of food products but is not necessarily a human or animal pathogen. This happens when animals entering processing plants are shedding resistant bacteria in their feces, or are otherwise contaminated with antimicrobial resistant bacteria. It is especially problematic with poultry at the processing plant. Contamination may spread to packaging and other aspects of food processing.

Sidenote: Surveillance of foodborne pathogens. While there are multiple examples of AMR in foodborne pathogen surveillance in humans, food, and other sources, in Canada and most other parts of the world, these pathogen isolates are not uniformly tested for antimicrobial susceptibility. A particularly good example of a country with a system in place to track the movement of resistant bacteria, including numerous resistant non-pathogens and their resistance genes into the human population through foodborne routes, is Denmark. Denmark uses DANMAP, a government-backed program with four key elements: 1. robust laboratory testing systems, 2. well-designed surveys, 3. reliable data registers, and 4. a strong foundation of trust and transparency among all participants. DANMAP tracks resistance in various bacteria and contexts, including foodborne zoonotic bacteria across the entire food chain to check for resistance in pathogens that affect both animals and humans (Statens Serum Institut, 2023).

Chapter 7 describes some excellent examples of the reduction in AMR in indicator bacteria associated with reductions in AMU in food-producing animals from Canada and other jurisdictions.

Environmental transmission from food-producing animal sources. The environment is the third part of the One Health paradigm of AMR. Antimicrobial resistant organisms can reside in environmental reservoirs including those potentially linked to animal agriculture, such as ground/surface water, as well as soil and related manured environments. The environment, in particular water (e.g. wastewater), can be important for two major AMR-related processes (Bengtsson-Palme et al., 2023). First, the environment is a means of dissemination of antimicrobial resistant bacteria among humans, among animals, or between animals and humans. Second, the environment can act as a reservoir that can promote the evolution of AMR.

There is considerable evidence for the dissemination of AMR in the farm environment when antimicrobial drugs are used (Bueno et al., 2017, 2018; Scicchitano et al., 2024). Two systematic reviews conducted by Bueno et al. evaluated studies investigating the strength or magnitude of the effect between an agricultural point source(s) and the frequency or concentration of AMR bacteria (Bueno et al., 2018) or resistance genes (Bueno et al., 2017) in the surrounding environment (mostly surface water). In open aquaculture settings, both bacterial and gene abundance studies identified transmission of AMR (Bueno et al., 2017, 2018). In poultry and swine, studies had mixed findings, with evidence of AMR transmission of some, but not all of the AMR bacteria analyzed. For beef cattle, there was also some evidence of transmission of AMR genes downstream. No evidence was found for transmission among dairy cattle, although that does not exclude the possibility of such transmission (Bueno et al., 2017).

Interventions to mitigate the spread of AMR across the One Health spectrum have also been evaluated. A UK-led team conducted a systematic review including 104 articles from 39 countries evaluating interventions intended to reduce the spread of AMR across the One Health spectrum in agricultural settings. Studies on ARG mitigation interventions applied to manure or wastewater from farms reported reductions in spread or transmission of AMR (Pinto Jimenez et al., 2023). Interventions focused at the farm-level, rather than societal- or community-level had the best outcomes for limiting the spread of antimicrobial resistant organisms. However, a gap was identified in the implementation and evaluation of “structural interventions” to prevent AMR transmission in agricultural communities (Pinto Jimenez et al., 2023). The term ”structural intervention” is one that is used in public health to refer to “interventions that work by altering the context within which health is produced or reproduced” (Blankenship & Mersen, 2000).

A global review of bioaerosols downwind of confined animal feeding operations included studies identifying MRSA and other antibiotic resistant bacteria in aerosols downwind of swine operations and MRSA in aerosols downwind of poultry operations (Kumar et al., 2024). The human or animal health impacts were not evaluated. Recently, a large-scale project evaluating the potential for airborne movement and transmission of antimicrobial resistant organisms and genes through aerosols is being conducted in Canada. The project components are described in George et al., (2022), although results from this project are still pending.

Key finding 1

Antimicrobial resistant bacteria and their resistance genes in food-producing animals can transmit to humans through food-producing animal products, direct contact with food-producing animals, and the environment.

- AMR in foodborne bacteria presents one route of transmission (Farm-to-Fork) of AMR to humans through bacterial contamination of products that reach consumers.
- Direct transmission to individuals who interact with food-producing animals is also important.
- There is considerable evidence for the dissemination of AMR in the environment of farms.
- While the scale of the transmission of AMR from food-producing animals to humans is unclear, the evidence is compelling that it occurs.

2.2.1 Gaps

Gaps exist across public health, academic, commodities, and animal health sectors with limited molecular tracking of AMR strains and of illnesses caused by AMR bacterial species in food-producing animals. Important knowledge gaps need to be addressed to support routine environmental monitoring of AMR, including lack of knowledge of background levels of environmental AMR, definition of “high-risk” environments for transmission, poor understanding of the concentrations of antimicrobials and other chemical agents, other environmental drivers such as anoxic sediments under fish farms or in manure lagoons that promote resistance selection, and limited options for detecting all relevant resistance genes.

Furthermore, the lack of knowledge about the importance and scale of the transmission via the respective routes is also limiting. Without information about background levels of environmental AMR, it is difficult to understand the importance of the contributions of human activities to this phenomenon. A consensus on the definition of “high-risk” environments for transmission is also important to mobilize action, but has not yet been adopted. Nevertheless, these gaps do not have to hinder immediate action to promote AMS in food-producing animals.

Key gap 1

There is limited knowledge on how AMR transmission occurs and the importance and scale of the transmission via the potential respective routes.

- Knowledge gaps need to be addressed to support the use of environmental monitoring of AMR on a large scale.

Related Action in the Pan-Canadian Action Plan

- Under the Surveillance pillar: “Expand sources, coverage and integration of AMR and AMU surveillance data, including the use of modern laboratory technologies and standardized reporting, to help monitor AMR/AMU across One Health sectors, with specific focus on improving data from the environment; transmission pathways between sectors; and population groups disproportionately impacted by AMR and inappropriate AMU.”
- Under the Infection Prevention and Control (IPC) pillar: “Support the increased implementation of enhanced IPC, biosecurity, and food safety protocols across the agriculture and agri-food sectors, prioritizing sound animal husbandry, access to veterinary care, and access to additional health and nutritional aids to promote animal health.”
- Under the Research and Innovation pillar: “Develop a One Health, national research strategy for combating AMR across all action plan pillars.”

2.3 Antimicrobial Resistance in Food-Producing Animal Pathogens

In food-producing animals, AMR may occur in: 1. bacteria that specifically impact the health of animals (animal pathogens), 2. non-pathogenic, commensal bacteria that may or may not be harmful if transmitted to humans; and 3. zoonotic bacteria that may cause disease in both animals and humans (Caneschi et al., 2023). The following section will specifically discuss the problem of AMR in the first category, food-producing animal pathogens.

What is an animal pathogen?

Animal pathogens refers to a variety of organisms, such as bacteria, fungi, helminths, protozoa, and viruses, that cause disease in animals. Resistance to drugs used to treat these diseases has been noted in many of these organisms; here we focus on bacterial pathogens.

The development and spread of AMR in food-producing animal pathogens are important problems for animal agriculture. Antimicrobials in all food-producing animal groups are becoming less effective over time. While some pathogens do not readily develop resistance, other important pathogens have acquired resistance, and in many cases, also spread resistance to susceptible related pathogens through mobile genetic resistance elements (Schwarz et al., 2018). There is outstanding, world-class science being done in Canada by several research groups to address the development and genetic basis of resistance in farm animal pathogens.

Resistance data for important animal pathogens in the major Canadian farmed animal groups are not nationally collected or available in a systematic way. Where available, Canadian AMR data parallel resistance findings from animal health diagnostic laboratories in Europe and the United States. CIPARS data are valuable for showing trends in generic *E. coli* as an indicator and in *Salmonella* obtained through surveillance, but these are not pathogens of animals (with the exception of some non-typhoidal *Salmonella* serovars). Some industry-funded data on BRD pathogens in feedlot cattle have also been recently reported in collaboration with CIPARS (Canadian Feedlot AMU/AMR Surveillance Program, n.d.).

One approach to understanding the burden of acquired resistance in food-producing animal pathogens in Canada is to examine reports of resistance in these pathogens obtained from animal health diagnostic laboratories. These reports are not routinely shared among all laboratories or summarized nationally. A pilot Canadian study by AMRNet-Vet could incorporate this data, but the limitations must be acknowledged. A criticism of diagnostic data is that it is not representative of food-producing animal pathogens in general, as samples are typically submitted from animals that have not responded to treatment and only from a very select subset of herds, and there is no population denominator against which these data can be compared. Nevertheless, identifying resistant pathogens in diagnostic samples is one way to monitor the emergence of resistance, of ARGs, and of more virulent strains of these resistant pathogens.

Beef cattle. Beef cattle have the third highest use of antimicrobials among the major food-producing animals in Canada in mg/kg biomass (trailing closely behind poultry) (PHAC, 2024a). Based on Veterinary Antimicrobial Sales Reporting (VASR) 2023 data, tetracyclines accounted for 75% of the total volume of medically important antimicrobials (MIAs) being sold for use in beef cattle. Most in-feed AMU (tetracycline, tylosin) as described here were directed toward prevention and control of liver abscesses (Brault et al., 2019). In Canadian feedlot beef cattle, bovine respiratory disease (BRD) is the most common cause of disease and mortality, as well as a common reason for injectable AMU (Brault et al., 2019). There is evidence of AMR in common bacterial BRD pathogens, including for products used for metaphylaxis. A large cross-sectional study of 2,824 cattle at entry to 10 Canadian feedlots, representing protocols used in >80% of the Canadian feedlot industry, investigated the epidemiology of AMR in bacteria most consistently associated with BRD (Andrés-Lasheras et al., 2021; Andrés-Lasheras et al., 2022). The isolate-level prevalence of many types of AMR were significantly higher at arrival in feedlot calves of dairy origin than in beef calves (Figure 2-3 below). Oxytetracycline was the most frequent resistance across all Pasteurellaceae. The finding that *Mycoplasma bovis* exhibited high macrolide MICs was consistent with other studies (Cai et al., 2019; Jelinski et al., 2020).

Research from Saskatchewan supports the previous finding that AMR in BRD pathogens is limited on arrival for beef calves, then varies based on days on feed (Abi Younes, Campbell, Otto et al., 2024); however, there is little data describing any type of temporal trends over time. The numbers of BRD isolates collected and tested for AMR in collaboration with CIPARS described below (Canadian Feedlot AMU/AMR Surveillance Program, 2023) have not been sufficient to date to consistently and effectively evaluate trends over time.

Currently, the Canadian Feedlot Antimicrobial Use and Antimicrobial Resistance Surveillance Program (CFAASP) data collected for 2019 to 2022 and reported with the CIPARS feedlot initiative suggest very high susceptibility (92%) at arrival to the antibiotics most commonly used for BRD treatment (Canadian Animal Health Surveillance System, 2023). Resistance to florfenicol, fluoroquinolones, and 3rd-generation cephalosporins was very low. Data from CFAASP reported very low levels of AMR to macrolides and tetracyclines on arrival, but this increased 14-30 days into the feeding period (Canadian Animal Health Surveillance System, 2023).

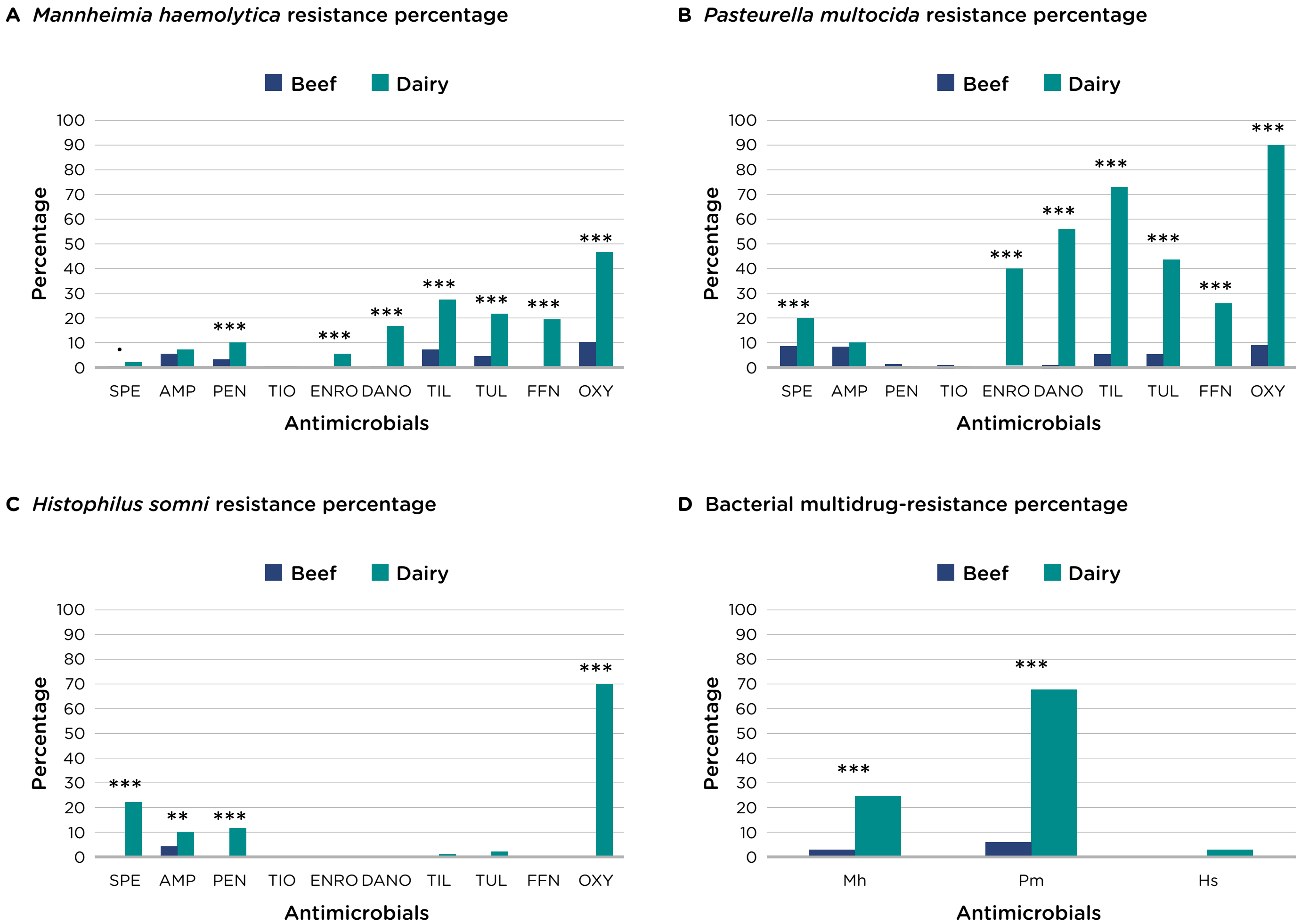


Figure 2-3. Antimicrobial resistance percentages of the BRD-bacterial isolates recovered from beef and dairy-type cattle at feedlot arrival. The asterisks represent the statistical test significance levels as follows: "." 0.1, "**" 0.01, "***" 0.001. Multidrug resistance was defined as resistance to 3 or more different antimicrobial classes (Andrés-Lasheras et al., 2021).

The treatment data collected as part of the CFAASP initiative to date cannot be linked for analysis to AMR. However, the increase in AMR for some BRD pathogens early in the feeding period reported by Canadian Feedlot AMU/AMR Surveillance Program (2023) is consistent with other studies, including one in western Canada showing an increase in tulathromycin resistance associated with tulathromycin metaphylaxis (Younes et al., 2024a). While AMR is one of the reasons for treatment failure, the issue of treatment failure is far more complex than AMR alone (Booker, 2021; Booker & Lubbers, 2020).

Integrative and conjugative resistance elements (ICE) have gained increasing notoriety in BRD *Pasteurellaceae* as they have the potential to play a critical role in the dissemination of multiple AMR genes (Beker et al., 2018; Klima et al., 2020). While ICE appears to be important in *Pasteurellacea*, identification of AMR in *M. bovis* is typically based on genetic point mutations (Waldner, Kinnear et al., 2022).

Dairy cattle. Dairy cattle have the fourth highest use of antimicrobials among the major food-producing animals in Canada in mg/kg biomass (PHAC, 2024a). Mastitis is the most common reason for AMU for both prevention ("dry cow treatment") or treatment of active disease. Data on AMR in dairy cattle pathogens other than those causing mastitis are fragmentary or unavailable. The 5 bacterial species most frequently involved in mastitis are *E. coli*, *Streptococcus uberis, Streptococcus dysgalactiae*, *Staph. aureus*, and *Klebsiella pneumoniae*. Antimicrobial drugs are not indicated for use in the treatment of *E. coli* mastitis because antimicrobials available for treatment of mastitis are not effective against Gram-negative bacteria, clinical disease is related to endotoxin produced by the bacteria, and the organism is quickly cleared by the body so antimicrobials are ineffective and unnecessary. Only for severe *E. coli* mastitis, parenteral treatment with fluoroquinolones or third- or fourth-generation cephalosporins is recommended (Suojala et al., 2013). A review of AMR in mastitis submissions to veterinary diagnostic laboratories from 2011-2022 in North America (including Canada) demonstrated that resistance to common antimicrobial drugs, even to drugs that have been used in dairy farms for mastitis management for many years, remains low, with prevalence of resistance below 5% for most mastitis pathogens and most antimicrobials (Sweeney et al., 2024). Global analyses support this conclusion. The difference from BRD pathogens in beef cattle may relate to how antimicrobials are used, systemically for BRD versus via the intramammary route for mastitis (Otto et al., 2024; Nobrega et al., 2018).

Although bacterial infectious disease is not uncommon in cattle, notably in calves, there is little recent published data addressing the occurrence of AMR in dairy cattle for non-mastitis pathogens of veterinary interest in Canada. A study with diagnostic and post-mortem samples from calves ≤ 2-months-old submitted to the Animal Health Laboratory in Guelph, Canada between 2007 and 2020 evaluated AMR in *E. coli* (n=434 samples) and *Salmonella* (n=378). Most *E. coli* isolates (91%) and *Salmonella* isolates (97%) were resistant to at least one antimicrobial (Uyama, Renaud et al., 2022). The lack of systematic collection and analysis of AMR in dairy cattle pathogens, attributed to logistical difficulties and cost, limits analysis of the impact of interventions to reduce and improve the use of antimicrobials in dairy cattle on AMR. Indirect analysis, however, using generic indicator bacteria such as *E. coli*, may be a reasonable surrogate. For example, a recent study of 87 farms using manure from calves and cows and the manure pit, evaluated the impact of the 2019 regulation by Québec of the use of high priority MIAs. There was a significant decline in the proportion of Multidrug resistant (MDR) *E. coli* two years after the restrictions compared to two years before (de Lagarde et al., 2022).

Poultry. Poultry have the second highest use of antimicrobials among the major food-producing animals in Canada in mg/kg biomass (PHAC, 2024a). AMR in avian pathogenic *E. coli* (APEC) is a major problem for the poultry industry. There is limited choice of approved antimicrobials effective for the treatment of infection by APEC, so some treatments involve extra-label drug use (ELDU) (Agunos et al., 2012). A study of APEC isolated in Ontario in 2016 showed MDR (to 3 or more classes of antimicrobials) in 46% of isolates (Varga et al., 2018). Resistance was present to ceftiofur (15%) and to trimethoprim-sulphamethoxazole (18%). The number of antimicrobial drugs to which an isolate was resistant increased significantly with the presence of certain virulence genes. The prevention of necrotic enteritis, a very important broiler disease, involves extensive use of antimicrobials, notably bacitracin as well as of Category IV ionophore antimicrobials. Although *C. perfringens* from Canadian chickens remain highly susceptible to antimicrobials such as penicillin and erythromycin, resistance to the commonly used bacitracin is widespread due to the presence of an acquired bacitracin resistance gene. In summary, data on AMR in Canadian poultry pathogens are limited, but suggest there is variable antimicrobial susceptibility among common pathogens. Most notably, AMR is particularly problematic for APEC, as is the case globally (Nhung et al., 2017).

Swine. Swine have the highest use of antimicrobials among the major food-producing animals in Canada on a mg/kg biomass basis (PHAC, 2024a). As noted for other major food-producing animal species, data giving an overview of AMR in the pathogens that impact swine in Canada is limited. For enterotoxigenic *E. coli*, which causes neonatal and post-weaning diarrhea, the spread of mobile AMR determinants combined with the decrease in the available antimicrobials is a global problem. Multidrug resistance is common in swine clinical isolates in Ontario, with resistance to tetracycline and ampicillin consistently high (>50%) (Kadykalo et al., 2018). Swine dysentery associated with *Brachyspira hyodysenteriae* and *Brachyspira hampsonii* re-emerged in the late 2000's. Canadian studies have documented resistance of some clinical *Brachyspira* isolates to pleuromutilin, macrolide, and lincomycin antimicrobials used in their control (Kulathunga et al., 2023).

Predominant respiratory pathogens in swine, *Actinobacillus pleuropneumoniae*, *Bordetella bronchiseptica*, *Pasteurella multocida*, and *Streptococcus suis*, isolated by diagnostic laboratories in specimens from diseased pigs in the United States and Canada, maintained high rates of susceptibility to most veterinary antimicrobials (Sweeney et al., 2022). The authors commented that management practices common in modern pig farming (appropriate manure management, age segregation, all-in all-out management, and multi-site production) may all have contributed to a lower occurrence of disease among swine and the observed overall high level of antimicrobial susceptibility. *Glaesserella parasuis* is the cause of meningitis and polyserositis in young pigs (Glasser's disease). A reduction in AMU in swine in Germany in 2013 was followed by a significant decline in AMR prevalence in *G. parasuis* (Wiencek et al., 2022). For example, tetracycline resistance was 100% between 2006-2013 but declined to 72% between 2014-2021. A striking characteristic of a wide range of swine pathogens is the extremely widespread resistance to tetracyclines (Aarestrup et al., 2008). There is almost universal resistance of swine pathogens to tetracyclines reported after many decades of use.

Finfish Aquaculture. Aquaculture has the lowest use of antimicrobials among the major food-producing animals in Canada in mg/kg biomass (PHAC, 2024a). Despite being highly regulated in terms of management, disease, and AMU reporting, there is no AMR monitoring from bacterial isolates or pathogens from farmed finfish in Canada that is publicly available or available to national surveillance. The only data currently available in Canada are from two historical collections of bacterial isolates obtained from submissions to regional diagnostic laboratories; one from the east and one from the west coast. Historic data from the BC farmed salmonid submissions included 1,237 unique bacterial isolates from finfish spanning 2007-2018 and tested for susceptibility to florfenicol (FLOR), oxytetracycline (OXY), trimethoprim-sulfadiazine (SXT), and triple-sulfa (TRI) composed of sulphamerazine, sulphathiazole, and sulfadiazine (de Jongh, 2024). These mirror the common drugs approved for use in finfish in Canada (FLOR, OXY, and SXT). The isolates included a diverse collection of 44 bacterial genera, with the most common reported species including *Aeromonas salmonicida*, *Aliivibrio wodanis*, *Yersinia ruckeri*, *Vibrio tapetis*, *Vibrio splendidus*, *Aeromonas sobria*, *Vibrio anguillarum*, and *Vibrio ordalii*. Resistance to FLOR or OXY were non-existent or at very low levels in most of these commonly reported species, with exceptions being *A. salmonicida* (FLOR resistance 18%, OXY resistance 22%) and *A. sobria* (OXY resistance 24%). Resistance to TRI and SXT were variable across these species and higher in some cases. Care must be taken when interpreting these data as the numbers of isolates by species were low (most <50) with little to no ability to examine trends of AMR over time.

The east coast data were reported in a recent study from farmed salmonids in Atlantic Canada that included susceptibility data for 2000-2021 (Ojasanya et al. 2022). This study reported similar levels of FLOR resistance in *Aeromonas salmonicida* (FLOR 12% in atypical and 28% in typical) but higher levels of OXY resistance (96% atypical and 59% typical) as compared to the west coast. Resistance in *Y. ruckeri*, the most common isolate in their dataset, and in *Vibrio anguillarum* was also very low to non-existent for all antimicrobials tested. This study identified different commonly reported bacterial species: *Pseudomonas fluorescens*, *Edwardsiella piscicida*, *Flavobacterium columnare*, *Aliivibrio salmonicida*, *Aeromonas hydrophila*, and *Flavobacterium psychrophilum*. With the exception of *P. fluorescens* (97.9%) and

F. psychrophilum (12.5%), all were completely susceptible to FLOR and had variable susceptibility to OXY and SXT. The study authors presented annual resistance levels by species and drug, but the results require cautious interpretation due to the small sample sizes. This study also tested susceptibility to the fluoroquinolone, enrofloxacin, but only identified one resistant *F. psychrophilum* isolate.

Generally, these studies illustrate low levels of AMR to drugs approved for use in bacterial isolates from farmed salmonid submissions on the east and west coast of Canada, particularly in species that are known finfish pathogens, such as *Aeromonas salmonicida* and *Y. ruckeri* (de Jongh, 2024; Ojasanya et al. 2022). Some of the “high” levels of resistance need to be considered with caution. In some cases, there is still very little knowledge of the intrinsic resistance for drugs and organisms. For example, there is limited literature on the AMR of *P. fluorescens*, which is understood to be a species complex and for which there is a poor understanding of intrinsic resistance (Silverio et al., 2022). The finding of 98% FLOR resistance in the 47 *P. fluorescens* isolates may not be cause for concern, as it could be intrinsic.

Resistance data for important animal pathogens in the major Canadian farmed animal groups are not nationally collected or available in a systematic way. Available data are often fragmented or are focused on the most important disease problems. Nevertheless, the evidence shows that AMR in farm animals is a current and increasing problem. There are opportunities now, however, to introduce or strengthen programs and practices to limit future negative impacts. AMR is present, although variable across the different commodity groups. There is some evidence that antimicrobials in food-producing animal groups are becoming less effective over time, in some cases very seriously so. No new antimicrobials will likely be introduced for animal agriculture in the future. Because of experience with AMR and the current trajectory of continuing evolution and spread of resistance genes in different bacterial populations, the evidence shows that preservation of the efficacy of antimicrobials in food-producing animals through improved AMS is essential both for animal health and in reducing agriculture’s contribution to AMR more generally.

Key finding 2

Development and spread of AMR in animal pathogens are important problems for animal agriculture. Antimicrobials in many commodity groups have become less effective over time because of AMR.

- Multi-drug resistance is common and very important in poultry and swine pathogenic *E. coli*, and indeed globally in intensively reared animals.
- In Canadian feedlot beef cattle, there is evidence of AMR in common bacterial respiratory pathogens, including to products used for metaphylaxis. However, surveillance data suggest there is high susceptibility to the antimicrobials most commonly used in treatment protocols for high risk calves as they enter feedlots.
- In Canadian dairy cows, resistance to common antimicrobial drugs used for mastitis pathogens continues to remain low, even to drugs that have been used in the dairy industry for mastitis management for many years, because of the unique nature of the efficacy of intramammary antimicrobials in the closed environment of the udder.
- Data on AMR in dairy cattle pathogens other than those causing mastitis are fragmentary or unavailable.
- Limited data on AMR in Canadian poultry pathogens suggest that there is variable antimicrobial susceptibility among common pathogens, and that AMR can be a problem.
- Data on AMR in swine pathogens in Canada suggests that there is still widespread susceptibility to most recently introduced antimicrobials; resistance to tetracyclines is, however, ubiquitous.
- Reducing AMU can generally be expected to reduce AMR. Although the relationship is likely not direct due to the complexity of AMR, measuring AMU is logistically a more efficient way to assess the impact of improvements in AMS than directly measuring AMR.

2.3.1 Gaps

Resistance data for important animal pathogens in the major Canadian farmed animal groups are not nationally collected or available in a systematic way. The availability and accessibility of systematically collected data for animal pathogens from the major commodity groups would allow Canada to monitor the impact of AMS efforts on the resistance levels in important animal pathogens, and position commodity groups to take and promote appropriate measures to curb resistance.

These challenges include the logistics of collecting the data, ensuring standardized methodology across the different animal health laboratories, assessment of the "representativeness" of the data, the ability to store selected isolates for further molecular study, agreement of which pathogens should be monitored and on which resistances are of special concern, and a lack of incentive to develop such a systematic program. The challenges are surmountable and can be addressed using Promising and Strategic Intervention 1 in Ch. 9.

Meanwhile, the relationship between AMR in food-producing animal pathogens and clinical outcomes of treatment (i.e., treatment success or failure) is poorly understood. Systematic data collection that includes information on animal health outcomes in addition to AMR/AMU will be valuable to mobilize stewardship actions in this area.

Key gap 2

The lack of systematic collection and analysis of AMR data in important animal pathogens means that it is not possible to evaluate the impact of future improved AMS in food-producing animals on AMR in pathogens.

- There is no systematic data collection describing AMR in important animal pathogens from the major Canadian commodity groups.
- There is incomplete understanding of the relationship between AMR in food-producing animals and clinical outcomes of infections in those animals.

Related Actions in the Pan-Canadian Action Plan

- Under the Surveillance pillar: "Expand sources, coverage and integration of AMR and AMU surveillance data, including the use of modern laboratory technologies and standardized reporting, to help monitor AMR/AMU across One Health sectors, with specific focus on improving data from the environment; transmission pathways between sectors; and population groups disproportionately impacted by AMR and inappropriate AMU."
- Under the Stewardship pillar: "Foster understanding of the risks of AMR and the importance of appropriate use of antimicrobials in humans and animals amongst the public, patients and producers through awareness/education campaigns, feedback mechanisms and policy and regulatory initiatives."
- Under the IPC pillar: "Support the increased implementation of enhanced IPC, biosecurity, and food safety protocols across the agriculture and agri-food sectors, prioritizing sound animal husbandry, access to veterinary care, and access to additional health and nutritional aids to promote animal health."

CAHS
ACSS
Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 3:

Antimicrobial Stewardship (AMS) in Food-Producing Animals

Introduction

Antimicrobial stewardship (AMS) is an essential component of national approaches to AMR/AMU. This chapter will start with an overview of AMS, then review the 5R's Framework for Antimicrobial Stewardship. The CAHS evaluation of the case studies from the 8 different countries show that key elements in successful national veterinary AMS programs in food-producing animals are the integration of leadership, commitment, coordination, surveillance of AMR and AMU, regulation, measurement towards clear goals, benchmarking (discussed in Ch. 7), education and training. Canada currently does not have all of these elements. Because of their role in prescribing the use of antimicrobials in animals, veterinarians in Canada are ideally positioned to be drivers for the development and implementation of AMS programs. Thus, the final section of this chapter reviews literature on facilitators and barriers to AMS for both veterinarians and producers.

3.1 What is Antimicrobial Stewardship?

Antimicrobial Stewardship (AMS): A One Health definition

"A concept relevant to and applicable by all (individuals, communities, and institutions) [scope and scale], aiming at using and prescribing antimicrobials in humans, animals and the environment in a way that ensures the availability of antimicrobials for individuals in the present day, as well as preserving antimicrobial effectiveness for current and future populations [collective and temporal responsibility]. The operationalisation of stewardship includes considerations of whether antimicrobials should be used, the ways in which antimicrobials are used, as well as the broader context within which these decisions are made [contextual contingency]." (Hibbard et al., 2024)

Antimicrobial stewardship is the term increasingly embraced globally that replaces the older terms "prudent use" or "judicious use". Antimicrobial stewardship focuses on all the factors that would result in **less use** of antimicrobials and, therefore, limit AMR. For example, infection prevention and control (commonly described in food animal veterinary medicine as biosecurity), improved immunization, or enhanced animal management protocols would not be considered as "prudent use", but are important examples of the different AMS elements focused on preventing AMR, in part through reduction of the need for AMU. We discuss these further in Chapter 5. Antimicrobial Stewardship also prioritizes appropriate use in terms of using drugs in ways that minimize the emergence of resistance. These include giving the right drug to the right patient(s), for the right reasons, for the right period of time, and by the right route and dosage. Antimicrobial stewardship thus embraces the multifaceted approaches required to sustain the efficacy of antimicrobials and to minimize the emergence and spread of resistance. The complexity of factors affecting the effectiveness of AMU, and of AMR and its epidemiology, means that effective AMS requires multiple approaches, which are not fully captured in the concept of prudent use. Despite efforts of commodity groups in implementing stewardship programs and conducting research and outreach activities (discussed in Ch. 4), fostering a culture of stewardship across all producers remains a challenge. However, developing the culture of stewardship across governments and practicing veterinarians is also an obvious challenge. The success of any AMS initiative relies in part on leadership, governance and a commitment to change (also discussed further in Ch. 4).

Given that AMS is the backbone of a national approach addressing AMR, it is important to take a look at what such a framework might look like, especially at the national level.

3.2 The 5R's Framework for Antimicrobial Stewardship

A holistic framework is helpful for the evolution of improved AMS and its measurement in food-producing animals. The 5R's approach (Figure 1-1), which provides such a useful framework, is of responsibility, reduction, replacement, refinement, and review (Lloyd & Page, 2018; Page et al., 2014; Speksnijder et al., 2025). A few examples from a recent textbook describe, under these headings, how this approach could be used internationally, nationally or locally (Speksnijder et al., 2025) (see Table 3-1). For example, under Responsibility, one statement is that "national commitment to the regulation and monitoring of the use of antimicrobials in food-producing animals" is essential.

The 5R's approach has already been implemented in Canada at the local level through the Farmed Animal Antimicrobial Stewardship (FAAST) initiative in Ontario. FAAST is a collaborative effort between the Ontario Veterinary Medical Association, government, academic, and industry partners (OMVA, 2024). FAAST aims to educate farm animal owners and their veterinarians on the use and application of this approach. At the farm-level, the implementation of the 5R's framework depends on the establishment of a valid veterinary client user-relationship. Through this relationship, a veterinarian develops an AMS plan with a producer while considering ways that use of antimicrobials can be reduced, replaced, and refined, its implementation can be monitored, and treatment plans are reviewed and refined on a periodic basis.

At the national level, the 5R's framework for AMS provides a systematic and comprehensive approach to AMS planning, implementation and monitoring, to allow a potentially complex process to be both practical and effective (Lloyd & Page, 2018; Page et al., 2014; Weese et al., 2013). Table 3-1 provides a generic example of what a 5R's approach to AMS could look like at a national level, with a few selected examples from Speksnijder et al. (2025).

Table 3-1. A generic example of what a 5R's approach to AMS could look like at a national level (Speksnijder et al., 2025). These are single sample examples from a longer Table.

Responsibility	National commitment to the regulation and monitoring of the use of antimicrobials in food-producing animals.
Reduction	National targeted commitment to reduction and improved use of antimicrobials in food-producing animals. National policies and standards are pursued by livestock commodities and implemented using farm-level practices.
Replacement	Alternatives to using antimicrobial drugs should be pursued wherever possible and where there is sound evidence of safety and effectiveness. Supportive therapies in many instances can abate the need for antimicrobial treatment.
Refinement	Antimicrobials that are important for treating refractory or serious infections in humans should be used sparingly in animals and only after careful consideration. The WHO high priority medically important antimicrobials (MIAs) are a highly important target for reduction of use in food-producing animals; these would require laboratory validation before use.
Review	A critical aspect of the "5Rs" of good stewardship is that continuous improvement is fundamental to good stewardship. Stewardship actions are evaluated and documented regularly. Potential benefits of introducing new interventions should be evaluated. The goal should be the best possible practice of AMS.

Note: The above table is intended to provide examples of the 5R's of AMS at the national level, but the role of P/T jurisdiction policies on AMS are discussed in Chapter 4, as well as later in this Chapter.

3.3 National Antimicrobial Stewardship (AMS) Programs: International Case Studies

The key elements in successful national veterinary AMS programs in food-producing animals are the integration of the elements of leadership and commitment, coordination, surveillance of AMR and AMU, regulation, measurement towards clear goals, benchmarking, education and training. Figure 3-1 shows elements of successful national veterinary AMS programs, some of the most successful examples of which are described in the international case studies (Appendix 2).

Figure 3-1. Elements of national veterinary antimicrobial stewardship programs in food-producing animals (adapted from Speksnijder et al., 2025)

Different aspects of international initiatives to improve AMU in food-producing animals are described below, derived from two of the 8 international case studies in Appendix 2.

Australia. Australia is a good example of a jurisdiction that utilizes the 5R's framework for AMS at the national level; the country has done well at reducing AMU and has low levels of AMR present in key bacterial species such as *E. coli* and *Salmonella* (Trott et al., 2024). Australia takes a collaborative, national, cross-sectoral approach to AMS in food-producing animals. The Australian red meat, dairy, pork and poultry industries have all collaborated on the development of the Animal Industries' Antimicrobial Stewardship RD&E Strategy (AIAS)(Animal Industries' Antimicrobial Stewardship RDE Strategy, 2021), the goal of which is to:

"Create a collaborative mechanism for animal industries to identify common research, development and extension (RD&E) priorities for the effective monitoring of AMU and surveillance of AMR to inform stewardship actions that meet Australia's animal health and market access needs, without impacting food safety or human health." (Animal Industries' Antimicrobial Stewardship RDE Strategy, 2021).

As part of this initiative, Australian and state/territory governments work closely with the food-producing animal industries through the work of Animal Health Australia (AHA) and the Australian Veterinary Association (AVA) toward the implementation of good AMS principles for Australian veterinarians.

An Australian key informant believed that implementing co-designed strategies and partnerships in the context of AMS is essential for success. It is important to find the people who are enthusiastic and can bring their industries along on the journey, as results will be reaped much faster and in a much simpler and less controversial way, compared to regulating:

"Having open conversations and creating comfort around discussing AMR/AMU is critical. This is difficult due to sensitivities, as people's livelihoods are involved, but creating space for this conversation is useful. It is particularly important for the livestock sector to own the conversation, in the interest of the industry and its participants."
- Key Informant, Australia

The United Kingdom. The UK Veterinary School's Council sub-group on Antimicrobial Resistance & Food Industry Initiative on Antimicrobials recently published "A New Vision for Responsible Antibiotic Use Through Data Safeguarding and Optimisation in the UK Farm Livestock Sectors" (UK Veterinary Schools Council, 2024). The UK livestock sectors collaborate through the Responsible Use of Medicines in Agriculture Alliance (RUMA), which is outlined as a case study highlight, below.

Case Study Highlight

The UK's Responsible Use of Medicines in Agriculture Alliance (RUMA): A national Antimicrobial Stewardship Initiative

The UK provides an excellent example of cross-sectoral collaborative industry leadership in AMS in the livestock sectors. RUMA covers multiple food-producing animal sectors, including beef, dairy, sheep, pigs, laying hens, poultry, salmon, and trout.

The RUMA is a not-for-profit cross-sectoral Alliance of 26 organizations representing supply chains from farm to fork. The organization provides leadership to the UK's commodity groups by encouraging efforts to improve the responsible use of veterinary medicines while ensuring animal health and welfare (Responsible Use of Medicines in Agriculture Alliance, 2022). RUMA is funded using members' annual fees, government grants, and profit from a biennial conference first held in 2015.

"As little as possible, as much as necessary"

RUMA functions on the basis of the principle that antibiotics should be used "as little as possible, as much as necessary". The initiative provides evidence-based information to promote the livestock industry's responsible use of medicines. While the focus is on AMR as well as supporting the message of responsible use, it is more broadly committed to supporting a One Health strategy.

Although RUMA is only one component of the UK approach, the most recent RUMA Report showed decreased sales in cattle, sheep, pigs, and maintenance of low AMU in layer and broiler poultry. Overall, the UK reduced antibiotic sales by 59% since 2014, to 25.7 mg/kg (Responsible Use of Medicines in Agriculture Alliance, 2023).

3.4 Veterinarians as Drivers of AMS

Veterinarians have an essential role to play in AMS and are key actors in stewardship programs. This section briefly explores potential barriers and facilitators of antimicrobial stewardship by producers and veterinarians at the farm-level in North America and Europe. Not all the initiatives described here, and in the Chapter 4 overview of Canadian AMS initiatives to improve AMU in food-producing animals, incorporate the full range of the different elements of effective AMS programs in food-producing animals (Figure 3.1). A comprehensive AMS approach involves integration of the multiple different elements of leadership and commitment, coordination, surveillance of AMR and AMU, regulation, measurement towards clear goals, benchmarking, education and training.

3.4.1 Literature on Facilitators and Barriers to AMS

In a systematic review of factors influencing AMU behaviour in producers and veterinarians, McKernan et al. (2021) examined 103 studies published between 2002 and 2020 across 48 countries. Fifteen of the studies were conducted in North America, and 47 in Europe. Several factors were associated with better stewardship practices, such as younger age of producers, and education of both veterinarians and producers. In some countries (US, UK), affiliation with assurance schemes or herd health plans associated with training opportunities improved compliance with antimicrobial stewardship recommendations. Many barriers were identified to AMS, such as misconceptions about the consequences of imprudent AMU, perceived labour requirements, financial constraints, lack of access to resources, and feelings of uncertainty.

In addition, Gozdzielewska et al. (2020) conducted a scoping review of approaches for improving AMS in livestock producers and veterinarians. The review included 52 studies, 45 of which were studies of facilitators and barriers of AMU in antimicrobial prescribing. Evidence for effective interventions was limited due to the quality of the studies; however, evidence supported the important role of attitudes and education as potential barriers or facilitators to AMS. Most of the studies included in the review were conducted in Europe, predominantly in high-income countries, with only seven studies in low- or middle-income countries.

The Yellow Card scheme implemented in Denmark in 2010 required that pig farms using twice the average quantity of antimicrobials received a government order to reduce AMU below a threshold in 9 months (see section 7.2.3). Danish swine producers who had reduced their AMU by at least 10% following implementation of the yellow card scheme (n=179) and their veterinarians (n=58) were surveyed in 2012-2013 to collect information on approaches they perceived to be the most helpful in reducing AMU (Dupont et al., 2017). Approaches frequently perceived as contributing to reductions in AMU included an increased use of vaccines (52% of producers; 35% of veterinarians), less use of group medication (44% of producers; 58% of veterinarians) and staff education (22% of producers; 26% of veterinarians). Less than 20% of both producers and veterinarians perceived that shorter treatments, smaller doses, or changes in antimicrobial products were factors in their reduction of AMU.

In Canada, an online survey and focus group of dairy cattle veterinarians and dairy producers also identified facilitators and barriers of change (Cobo-Angel et al., 2021). The findings of this study confirm many of the same barriers and facilitators identified in the reviews mentioned above. Barriers and facilitators identified in all these studies are presented in Table 3-2. These findings are corroborated by virtual engagement findings and international case studies.

Table 3-2. Barriers and facilitators of farm-level antimicrobial stewardship (AMS) for veterinarians and producers, with examples from the Canadian dairy sector (Cobo-Angel et al., 2021)

	Barriers to AMS	Facilitators to AMS
Veterinarians	• Questioning the scientific link between AMU and AMR • Blaming human medicine as the [only/sole] cause of AMR • Delayed timing of results for diagnostic testing to inform AMU • Stewardship training on AMR/AMU being delivered in technical language that is difficult to understand	• High veterinary knowledge on AMR/AMU • Concern about AMR • Sense of responsibility for promoting AMS • Having sufficient information to discuss the role of AMU on AMR with the producer • Improved diagnosis of diseases requiring AMU (e.g. mastitis) • Improved vaccination protocols
Producers	• Cost of interventions to reduce disease burden • Habit of treating the animals without veterinary consultation • Low awareness of AMR implications in dairy farming • Low adoption of preventative measures to reduce diseases • Knowledge on AMR/AMU being communicated in technical language that is difficult to understand	• Access to grants to improve the farm facilities to have better ventilation, calf housing, and animal welfare • Affiliation with assurance schemes or herd health programs • Use of alternative interventions to refine AMU (e.g. AMU reduction via selective dry cow therapy) • Better herd management (e.g. better culling protocols for animals with recurrent infections)

Some factors associated with AMS are discussed further, below.

Education. The quality of education of veterinarians on AMR and AMS has been identified as a key facilitator to AMS (McKernan et al., 2021; Cobo-Angel et al., 2023; Gozdzielewska et al. 2020). Conversely, lack of knowledge was a barrier, with some veterinarians stating in their responses that they "do not have enough information to discuss the role of AMU in dairy cattle on AMR." This underscores the importance of AMR and AMS content being incorporated in veterinary training programs. In the human medical literature, however, a review of 48 articles concluded that it is unclear whether early education of physicians on AMS influences physician behavior or results in lowered AMR rates (Silverberg et al., 2017). AMS programs as part of required continuing education (CE) for maintaining professional veterinary licensure may help reinforce the implementation of AMS principles.

Attitudes. Positive attitudes towards AMU reduction and AMS are a key facilitator in implementing AMS (Gozdzielewska et al., 2020; McKernan et al., 2021). McKernan et al. (2021) reported that in Canada and New Zealand, although producers "were concerned about AMR", less than half of them considered AMR when deciding on treatments (McKernan et al., 2021). In contrast, in a 2020 survey of 142 cow-calf producers in Canada, 97 (67%) of producers indicated the issue of AMR was of high importance to both the industry and to them personally (Fossen et al., 2023). Almost half of producers reported concerns that AMR development had impacted their AMU decisions. Likewise, concern about AMR and feeling responsible for reducing AMU on dairy farms was associated with good stewardship practices among Canadian dairy veterinarians (Cobo-Angel et al., 2023).

Conversely, Canadian veterinarians not as actively involved in AMS espoused an attitude of blame towards human medicine for AMR, or questioned the scientific link between AMU and the emergence of AMR in human pathogens (Cobo-Angel et al., 2023). This finding is not limited to Canada; some US, Australian, Dutch and UK producers doubted the link between AMU in agriculture and AMR as well as the associated risks to human health (McKernan et al., 2021).

To address these issues, McKernan et al. (2021) have suggested "a carefully considered, evidence-based approach," based on behaviour change theory, when designing on-farm interventions/strategies to bring about sustained AMU behaviour change. The authors indicate that AMS strategies should also encourage incremental behaviour change so that producers and veterinarians feel capable of implementing AMS practices (McKernan et al., 2021).

Commodity groups are important partners in this process. For example, the Canadian Beef Cattle Research Council identifies a variety of different drivers that may motivate livestock producers to adopt AMS practices, such as:

- Slowing or minimizing AMR, especially for producers who have had a relative hospitalized with an intractable infection
- Maintaining consumer confidence
- Ensuring the continued effectiveness of antimicrobials to treat cattle diseases
- Cost savings they could see from improved disease prevention practices in calves (e.g., nutrition, vaccination and husbandry practices) and less money spent on antimicrobials

These factors are not unique to the beef cattle sector, and emphasize that improved AMS requires a diverse range of messages for these different audiences.

Regan et al. (2023) build on the existing knowledge of behavioral drivers of change and propose a number of interventions to improve AMS among farmers and/or veterinarians. These include message framing, One Health awareness campaigns, specialised communications training, on-farm visual prompts and tools, social support strategies, and AMU monitoring.

Provincial veterinary medical regulators also have an essential role in creating a 'culture of stewardship', and setting expectations for veterinary practitioners to implement important AMS principles such as those in the 5R's framework. Professional regulators may support stewardship in many ways in addition to continuing education, such as establishing an "AMS champion" or "train the trainer" stewardship programs to change attitudes and practices, one clinical practice at a time. This is important in light of the finding that a veterinarian's prescribing behaviour is influenced by peer veterinarians, particularly through influential relationships (Gozdzielewska et al., 2020; McKernan et al., 2021).

3.4.2 The Canadian Veterinary Medical Association's (CVMA) SAVI Tool

The CVMA has made some important efforts in AMS, and has staff who have been recognized internationally for their work in this area (World Veterinary Association, 2024). CVMA has Guidelines for Veterinary Antimicrobial Use, which CVMA members can access (Canadian Veterinary Medical Association, 2024a). They have also developed the Veterinary Oversight of Antimicrobial Use: A Pan-Canadian Framework of Professional Standards for Veterinarians (Canadian Veterinary Medical Association, 2024b).

The Stewardship of Antimicrobials by Veterinarians Initiative (SAVI), is an excellent example and is a starting point to enable additional tools for AMS to be rolled out. The initiative is driven and managed by Canadian veterinarians and "aims to provide veterinary professionals with the knowledge and tools necessary to make informed decisions on AMU in a wide range of species." The initiative is supported by the government of Canada and the Canadian Agricultural Partnership (Stewardship of Antimicrobials by Veterinarians Initiative, 2024).

As part of the SAVI initiative, the CVMA, the University of Calgary, and Firstline Clinical (TM) have launched the CVMA Guidelines for Veterinary Antimicrobial Use on Firstline, an innovative tool designed by the AMR – One Health Consortium and CVMA to assist Canadian veterinarians in making sound, evidence-based prescribing decisions. Firstline (there is a human medicine version as well) delivers the current CVMA guidelines to veterinarians at point of care. The app allows Canadian veterinarians who are members of CVMA to access species-specific options for AMU that incorporate the latest AMS guidance.

Key finding 3

Well coordinated and integrated national AMS programs are essential to address AMR/AMU and require substantial and dedicated investment.

- International case studies have demonstrated that key elements in any successful national veterinary AMS program in food-producing animals are leadership, commitment, coordination, sustained resources, surveillance of AMR and AMU, regulation, measurement towards clear targets, benchmarking, education and training, infection prevention and control/ biosecurity, and resources.
- The 5R's Framework for AMR Stewardship is useful within the context of a national strategy to guide stewardship efforts.
- Adopting a broad-ranging stewardship approach to addressing AMR in food-producing animals would be a highly integrating way of focusing the national effort.
- Positive attitudes towards AMS, training, cost savings, positive impact on management, and availability of alternatives have been identified in the literature as potential facilitators to AMS.
- In Canada, the Canadian Veterinary Medical Association's SAVI is a starting point enabler to allow for additional tools for AMS to be rolled out.

3.5 Gaps in Antimicrobial Stewardship

The main gap in stewardship in Canada is the current lack of coordination of efforts to improve AMS in food-producing animals taking a broad stewardship approach incorporating the different elements described earlier. A national stewardship program could address this gap through the use of the 5R's antimicrobial stewardship framework, as illustrated in sections 3.2 and 3.3 of this chapter. Other gaps remaining in operationalizing AMS are outlined below.

Application of knowledge of behavioural drivers of change. Behavioral drivers of change are very important considerations to increase and improve AMS. Commodity groups and veterinary associations need to work together to identify behavioral drivers of change in those sectors and target on-farm stewardship initiatives accordingly. Some interventions informed by the current understanding of behavioral drivers of changes are discussed by Regan et al. (2023).

Workforce. The CAHS virtual engagement highlighted access to veterinary services as an issue (CAHS Virtual Engagement Finding, Round 1; CAHS Written Survey, Round 1). Access to veterinary services is an essential prerequisite to support stewardship initiatives and the shortage of veterinarians has been a barrier in Canada that impacts all commodity groups. This shortage results in veterinarians stretched beyond capacity with limited time for participating in AMS initiatives, and rural areas not having access to veterinary care.

Federal-provincial-territorial initiatives such as the Sustainable Canadian Agricultural Partnership initiative, a jointly funded initiative between the Government of Canada and provinces, are an important way to support access to veterinary care. As part of this initiative, the governments of Canada and Manitoba recently announced funding for Manitoba to assist rural clinics in modernizing their equipment to support the recruitment and retention of veterinarians in rural areas (Government of Canada, 2023a). The governments of Canada and Ontario also jointly invested through the same initiative to give Ontario producers improved access to veterinary services (Government of Canada, 2023b).

Veterinarians' capacity to discuss AMS. Veterinarians are ideally positioned to be the leaders in AMS, but there are limited individuals available to fill this gap. Veterinary practitioners have limited time or mandate to discuss AMS. Currently there is not a strong business case for them to implement AMS with their clients. There have been calls to expand the role of veterinary technicians in supporting certain aspects of veterinary practices, such as obtaining data to evaluate AMS, and it is possible that AMS could benefit from this. Making AMS a standard of veterinary practice, as suggested in the Promising and Strategic Intervention 3, supported by farm-level measurement of AMU and benchmarking (Promising and Strategic Intervention 2) would be major initiatives to address this gap.

Limited access to stewardship tools/resources. There are indications that many veterinarians in Canada are not aware of or cannot access CVMA's guidelines (SAVI) or the FirstLine Stewardship App as non-members. SAVI and its tools are accessible only to members of the CVMA, which does not include all veterinary professionals in Canada as membership is not a requirement in all provinces and territories. As a result, many non-member veterinarians in Canada may not be aware of or cannot access CVMA's guidelines (SAVI) or the FirstLine Stewardship App. While these are excellent resources, limiting access to members-only is a barrier for all veterinarians to access them.

Because of the importance of stewardship approaches, comprehensive resources are now increasingly widely available (Dowling et al., 2025) and could readily be developed into educational programs, as for example have been done in Quebec by OMVQ.

Limited awareness of stewardship tools/resources. Communication is also a critical component of AMS to increase awareness among veterinarians of the tools that are available. CFIA's animal health public opinion research from 2024 has shown that "awareness of the CVMA FirstLine app was very low", and only one veterinarian who was interviewed reported "having used it and being somewhat familiar with it" (Earnscliffe Strategy Group, 2024). This also underscores the importance of Canada having a coherent, effective, measurable, well coordinated national plan for AMS in animal health that can evaluate the effectiveness of AMS initiatives.

Key gap 3

There is currently a lack of coordination of efforts to improve AMS in food-producing animals in Canada.

- There is a need for better understanding and application of knowledge of the drivers for behavioral change to increase and improve AMS.
- Veterinarians have limited time or requirements to discuss AMS. Veterinarians are ideally positioned to be the leaders, but there are limited individuals available to fill this gap.
- There is limited access to, and awareness of, stewardship tools like SAVI that are targeted to veterinarians.
- In some regions there is a lack of access to veterinary services.

Related action in the Pan-Canadian Action Plan

- Under the Stewardship Pillar: "Develop, implement and promote guidelines/standards for appropriate AMU in humans and animals through policy and regulatory initiatives, monitoring and educational interventions/ accreditation requirements for health professionals and prescribers."

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 4:

Antimicrobial Resistance, Risk Governance, Policy, and Regulatory Approaches to Support Antimicrobial Stewardship

Introduction

Improved antimicrobial stewardship (AMS) includes governance and regulatory approaches targeted at addressing AMR/AMU (Chapter 3). Canada has taken some steps forward in operationalizing the Pan-Canadian Action Plan (PCAP), but critical elements are currently missing from this framework to support an effective governance approach to AMS.

This chapter provides a discussion of the Canadian approach to AMR governance, policy, and regulatory approaches to support stewardship, in particular at the Federal-Provincial-Territorial (FPT) levels. Commodity groups and other industry groups' activities and influences are also discussed in the context of creating a culture of stewardship. The key elements of a national framework for AMS are discussed, in the context of some key Canadian and international initiatives in the area of stewardship.

The Office of the Auditor General's 2023 assessment of the Pan-Canadian Action Plan on Antimicrobial Resistance (PCAP) was that it "did not cover many important elements—such as concrete deliverables, timelines, and details about who is accountable for each action and that, without these key elements, it is unlikely that the plan will result in meaningful actions and produce desired outcomes" (Office of the Auditor General, 2023). The Office of the Auditor General (2023) concluded that "the PCAP was incomplete and that, without specific accountabilities, deliverables, timelines, and measurable outcomes, there is a risk that action among federal, provincial, and territorial governments to tackle AMR will be delayed, poorly coordinated, and not comprehensive" (Office of the Auditor General, 2023). This is the reason the panel focuses on leadership, political commitment and coordination as the first Promising and Strategic Intervention. Chapter 9 outlines Promising and Strategic Interventions to address some of the deficiencies in the PCAP identified by the Auditor General.

4.1 Existing Provincial and Commodity Group Initiatives

Due to the nature of AMR as a 'wicked' problem, and given the interconnectedness of animals, humans, plants/crops and the environment, it is critical for a One Health framework to be the integrating factor at the core of any AMR governance model to support AMS. As described in the PCAP, the approach to assessing the risk of AMR to human and animal health requires re-framing the issues as a wider societal problem, creating a need for a multi-level as well as multi- and cross-sectoral governance framework.

There are numerous efforts towards better AMU in food-producing animals across Canadian jurisdictions and commodity groups. This section highlights some prior and existing initiatives and collaborations in place within the provinces and livestock, poultry, and aquaculture industries (including commodity groups, pharmaceutical companies, and other industry organizations).

4.1.1 Activities at the Provincial-Territorial Level

Despite the consensus that AMR is a threat to the health and welfare of animals and humans, specific provincial government policies and activities vary widely, as does the capacity, funding, and resources designated to address AMR.

Partnerships between governments and industry (livestock, poultry, and veterinary) manifest in different ways in the various provincial-territorial systems, but are important for supporting AMR/AMU initiatives, especially related to surveillance, education and outreach, and research. There are also many examples of collaboration within governments between animal health and human health departments. Table 4-1 outlines some of the provincial-territorial activities and programs that support efforts to address antimicrobial stewardship in Canada Many of these activities were mentioned by key informants as examples of activities that could support AMS, but most were not specifically designed or funded as AMS activities.

Table 4-1. Activities and/or programs of Canadian provincial and territorial governments related to understanding and/or improving AMU in food-producing animals

Province	Activities/programs
Newfoundland and Labrador	Regional veterinary service, meat and dairy inspection programs, farm monitoring, research, animal health laboratory, education and outreach (Government of Newfoundland and Labrador, 2024)
Prince Edward Island	Research funding, collaboration with human health and veterinary colleges and university, subsidized testing, education (Government of Prince Edward Island, 2023)
Nova Scotia	Livestock health program, collaboration between human and animal health sectors, sales data, animal health laboratory, and support commodity group initiatives and programs (Government of Nova Scotia, 2021)
New Brunswick	Provincial veterinary services, provincial veterinary laboratory, sales data (Government of New Brunswick, 2024)
Québec	Education of veterinarians and producers, policy on health promotion promotes collaboration with human and animal health, funding, strategy for animal welfare, sales data, surveillance (Gouvernement du Québec, 2024)
Ontario	Education and awareness of producers and veterinarians, feed companies and pharmaceutical representatives, including survey of licensed livestock medicines outlets; surveillance, stewardship, research, and national collaboration (Government of Ontario, 2024). Farmed Animal Antimicrobial Stewardship initiative (FAAST): education and communication, research, collaboration (Ontario Veterinary Medical Association, 2024)
Manitoba	Collaboration with industry and human health, provincial veterinary health laboratory, surveillance, funding, data sharing, and education (Government of Manitoba, 2024)

Province	Activities/programs
Saskatchewan	Surveillance and diagnostics programs, education, funding, research, Prairie Diagnostic Services (Government of Saskatchewan, 2024)
Alberta	One Health AMR Framework for Action released (Government of Alberta, 2024); AMR - One Health Consortium, a pan-provincial interdisciplinary One Health collaboration on AMR funded in part by the Government of Alberta's MIF fund (University of Calgary, 2024)
British Columbia	One Health collaborations between human and animal health, research including pilot projects, funding, subsidized testing, surveillance, laboratory system and labour capacity development (Government of British Columia, 2024; Radke, 2023; British Columbia Society for the Prevention of Cruelty to Animals, 2024a; British Columbia Society for the Prevention of Cruelty to Animals, 2024b)
Northwest Territories	No AMR/AMU activities identified for food-producing animals
Nunavut	No commercial food-producing animals raised in this territory
Yukon	No AMR/AMU activities identified for food-producing animals

4.1.2 Activities of Commodity Groups and Industry on AMR/AMU

Examples of AMR/AMU initiatives led by commodity groups and other industry organizations are outlined below.

4.1.2.1 Commodity Groups

Findings from our international case studies (Australia, EU, France, The Netherlands - Appendix 2) indicate that it is essential that the animal agricultural industries are committed and engaged in improving AMS in food-producing animals to ensure widespread adoption and action by members of those industries.

Currently, all major commodity groups in Canada are engaged in some level of activity to address the issue of AMR, ranging from publicly acknowledging the issue to promoting stewardship-related initiatives and guidelines to reduce AMU. Across national commodity groups, there are several common elements to their policies and activities:

- Participation in surveillance activities - membership and participation in Canadian Animal Health Surveillance System (CAHSS) AMR/AMU network, Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) programs, and Animal Health Canada (AHC) Working Group
- Stewardship-related activities - establishment of Quality Assurance (QA) programs for most commodities encouraging the collection of data and promoting infection control and biosecurity

- Communications to producers and consumers about AMR and AMU through policy statements or website content

A number of examples of these types of activities are noted below and referenced with respect to the Canadian commodity groups.

Voluntary changes that make big impacts on stewardship. An example of leadership in a commodity group resulting in tangible change can be seen with the Chicken Farmers of Canada (CFC). In response to CIPARS data and a CBC Marketplace program (Canadian Broadcasting Corporation, Feb 10, 2011) which reported a high level of AMR in Canadian chicken products, the CFC voluntarily withdrew the prophylactic use of Category I antimicrobials from poultry operations in 2014. Their AMU strategy further eliminated the preventative use of Category II antimicrobials by the end of 2018 (Chicken Farmers of Canada, 2024a). This was associated with reduced AMR in indicator *E. coli* and non-typhoidal *Salmonella* from retail chicken meat, discussed in detail further in Chapter 7. Following the voluntary ban by the Chicken Farmers of Canada on extra-label use of ceftiofur in poultry in 2014, there was a marked decline in ceftiofur-resistant *E. coli* in broiler chickens and in broiler chicken retail products (Figure 4-1).

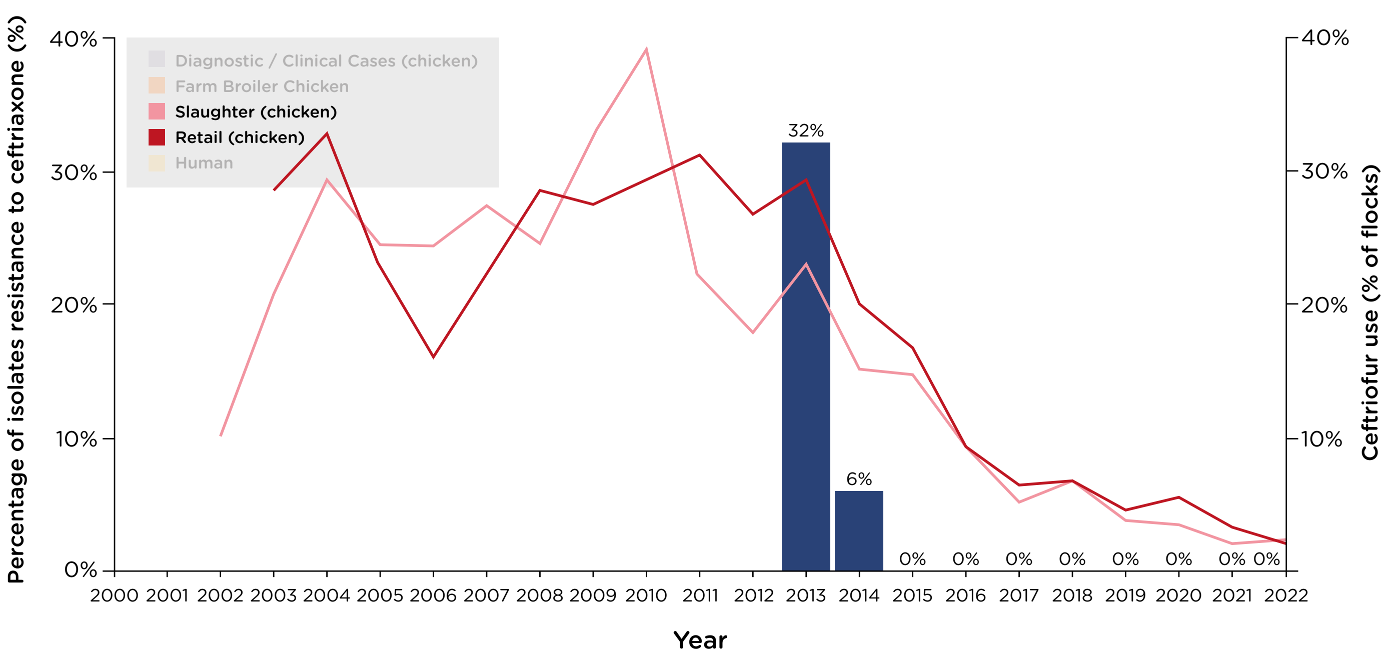


Figure 4-1. Temporal trends in Canada of ceftriaxone-resistant *Escherichia coli* in broiler chickens (PHAC, 2024c). The grey bar indicates use of cefiofur in broilers flocks from 2013 to 2022.

In addition, CIPARS data from 2013-2022 showed not only a decline in ceftriaxone (ceftiofur) resistant *E. coli*, but a rise in pan-susceptible *E. coli* and a decline in MDR *E. coli* in chicken (Figure 4-2) (PHAC, 2024c). Taking a leadership role in implementing such mandatory changes is possible in supply managed commodity groups.

The Chicken Farmers of Canada had also put forward the objective to eliminate preventative use of Category III antimicrobials (Chicken Farmers of Canada, 2024a), but decided not to move forward with it after review (CAHS Key Informant Interview).

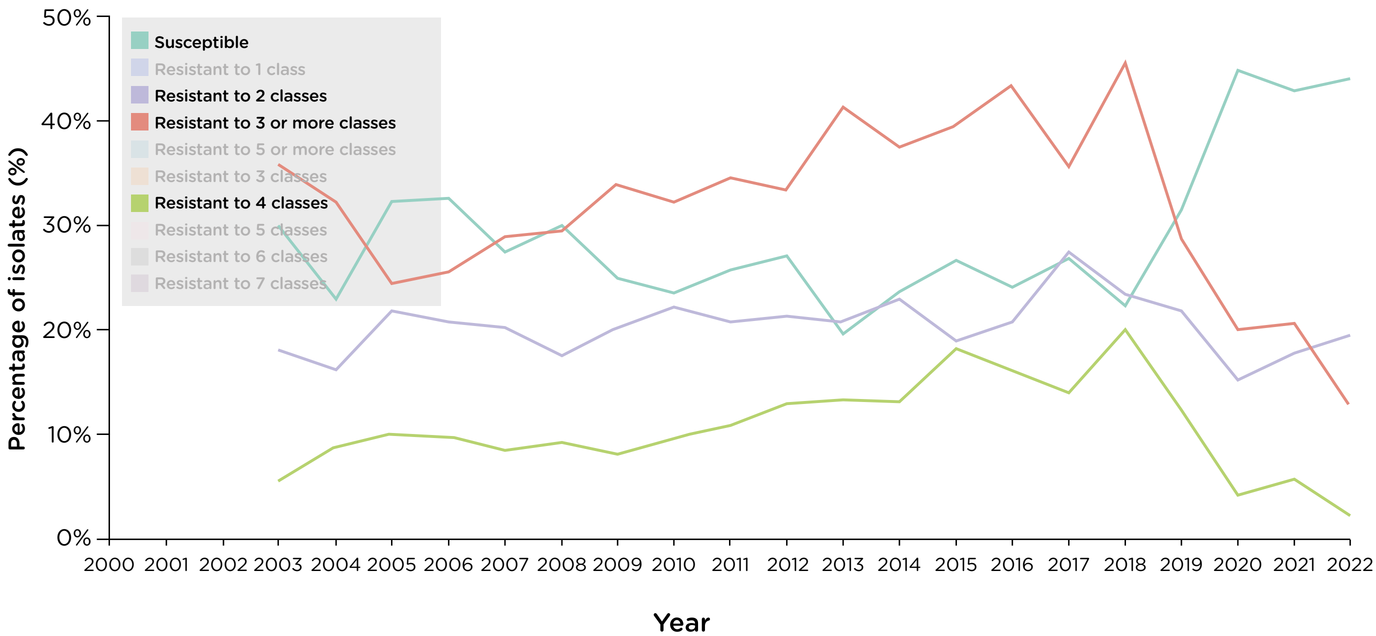


Figure 4-2. Temporal trends in Canada of multiclass-resistant indicator *Escherichia coli* from chicken meat at retail isolates (PHAC, 2024c)

There is a common understanding among Canada's major commodity groups and the veterinarians serving these groups that antimicrobials are necessary for maintaining animal health and welfare, supporting environmental and economic sustainability, and protecting food safety (CAHS Virtual Engagement Finding; Canadian key informant interviews). Most commodity groups also recognize the importance of reducing the need for AMU through an AMS approach including disease prevention, reducing unnecessary use, and using antimicrobials of less importance to human health whenever appropriate (CAHS Virtual Engagement Finding; Canadian key informant interviews). Furthermore, the major commodity groups clearly communicated that national efforts should be on "appropriate use", rather than simply "reduction" of total amount used (CAHS Virtual Engagement Finding). These terms are common wording used in human medicine as well (Okonkwo et al., 2024). However, "appropriate use" is not readily measurable. Appropriate use must happen within an overarching stewardship framework aimed at responsibility, reduction, replacement, refinement and review (as discussed in Chapter 3) with clear and measurable goals or outcomes, as well as guidance on how to actually evaluate whether the use is "appropriate" (as discussed in Chapter 7, Impacts of interventions to reduce AMU).

AMR/AMU Strategies and other activities. Animal Health Canada (AHC) provides a detailed accounting of the organization-specific AMR programs, policies, and activities implemented by AHC members. At a minimum, AHC members have programs, policies, and activities in place to improve animal health and welfare through adoption and implementation of best infection prevention and control practices, which in turn will help to reduce AMU. This represents the core foundational pillar to most organizations' AMR response. Recommendations, requirements, and best practices for producers are often structured under organizational quality assurance programs, which often contain food safety and biosecurity modules (Table 4-2).

Table 4-2. Examples of quality assurance programs in the major commodity groups

Commodity group	National Quality Assurance Program or other Initiative	Mandatory or Voluntary	AMU addressed (yes/no)
Dairy cattle	proAction Program (Dairy Farmers of Canada, n.d.-a)	Mandatory	Yes
Beef cattle	The Verified Beef Production Plus (VBP+) program (Verified Beef Production Plus, 2021) The Canadian Feedlot Audit guide (National Cattle Feeders Association, 2023)	Voluntary	Yes
Poultry	On-Farm Food Safety Manual (Chicken Farmers of Canada, 2021)	Mandatory	Yes
Swine	Canadian Pork Excellence standards and identification include three components: -PigTRACE -PigSAFE -PigCARE (Canada Pork, 2025)	Voluntary; Currently required by federally inspected slaughter facilities (Agriculture and Agri-Food Canada 2021), which slaughter approximately 96% of Canadian production	Yes. Drug Use Policy includes information on AMR and AMS
Aquaculture	Canada's Quality Management Program Canadian Shellfish Sanitation Program (Canadian Aquaculture Industry Alliance, 2023)	Mandatory	No

*In addition to the QA programs listed here, there is also a code of practice for all food-animal species (National Farm Animal Care Council, 2025).

With respect to AMR/AMU-specific policies/activities, most organizations describe a commitment to acting on the growing threat of AMR through supporting surveillance, responsible stewardship, and research (Table 4-3). AMR/AMU is recognized as a risk to market access and industry sustainability. Several organizations also underscore their public statements with the importance of AMR from a global One Health perspective.

Table 4-3. Antimicrobial stewardship-related publications of Canadian commodity group organizations

Organization	Program, Policy, and/or Activities
Canadian Cattle Association	Global Roundtable for Sustainable Beef Statement on Antimicrobial Stewardship (Canadian Cattle Association, 2024) Canadian Beef Research & Technology Transfer Strategy, beef research on AMR/AMU (Beef Cattle Research Council, 2021) Verified Beef Production Plus with sector specific, producer driven programs for on-farm food safety and biosecurity delivered under the Beef Cattle Research Council (Verified Beef Protection Plus, 2024) Webpages with an overview of issues outline programs and policies (e.g. Beef Cattle Research Council, 2019a) and Fact sheets on website (e.g. Beef Cattle Research Council, 2016a) and numerous lay summaries of completed research projects (on website and routinely distributed in producer publications)
National Cattle Feeders Association	No available full statement on AMR/AMU, some CIPARS sheets about AMR/AMU hosted on website (Canadian Cattle Feeders, 2015)
Dairy Farmers of Canada	ProAction food safety webpage (Dairy Farmers of Canada, n.d.-b) and how and when we use antibiotics webpage (Dairy Farmers of Canada, 2020) Dairy research about AMR/AMU (Dairy Farmers of Canada, 2024) AMU-related guidance documents for reducing AMU in adult cattle and youngstock, and guidelines for navigating AMU/AMR, and stewardship, shared via the Canadian Association of Bovine Veterinarians
Canadian Pork Council	Vaccine and Drug Use Policy, New Rules for the Access and Use of Veterinary Drugs, summary of AMR issue on their website (Canadian Pork Council, 2024)
Chicken Farmers of Canada	The Antimicrobial Use Reduction Strategy Booklet, Responsible AMU Strategy (Includes some outcomes) (Chicken Farmers of Canada, 2024b)
Turkey Farmers of Canada	Responsible Antimicrobial Use in the Chicken and Turkey Sectors, Turkey producers of Canada On-Farm Programs (mentions Flock Care Program online which is access-restricted) (Turkey Farmers of Canada, 2024)

Organization	Program, Policy, and/or Activities
Canadian Hatching Egg Producers	None identified (Canadian Hatching Egg Producers, 2024)
Egg Farmers of Canada	Sustainability Report 2019 mentions participation in Pan-Canadian Action Plan and similar initiatives; nothing run by Egg Farmers of Canada (Egg Farmers of Canada, 2019)
Canadian Veal Association	None identified
Canadian Sheep Federation	Flock Health, FAAST sheets (Canadian Sheep Federation, 2024)
National Sheep Network	Mentions AMR/AMU on the page but has no specifics or documents (National Sheep Network, 2024)
Canadian Aquaculture Industry Alliance	No documents. The website has the statement: "Treatment products must be authorized for sale by Health Canada and prescribed by a licensed veterinarian. Farmers work to minimize therapeutic use; it is estimated that fewer than 5 percent of farmed fish are treated with antibiotics." (Canadian Aquaculture Industry Alliance, 2024)
Animal Nutrition Association of Canada	Factsheets on the sales and dispensing of antimicrobials (Animal Nutrition Association of Canada, 2024)

Examples of actions in support of improved AMU by two important Canadian commodity groups are highlighted below.

Commodity Group Highlight:

ProAction Quality Assurance Program for Canadian Dairy Cattle

ProAction is an excellent example of a quality assurance initiative that includes significant elements of antimicrobial stewardship. The program is mandatory for all Canadian dairy farms and has 82 verifiable requirements through on-farm validations.

Validations are carried out in person, on each farm, at least once every two years by trained professionals independent of the producer. Assessors are trained and re-trained every six months to evaluate herds. During the alternate year, farms are required to complete a self-declaration, and a random sample of 5% of the farms are selected for on-farm validations after they submit self-declarations.

Six modules are included: Milk quality, Food safety, Animal care, Livestock traceability, Biosecurity, and Environment. The traceability module includes requirements for dairy producers to report their animal movement data to DairyTrace.

How does proAction address AMU?

The program ensures that dairy producers take proactive actions to ensure:

- Antibiotics are administered only by trained personnel
- Prescriptions are documented on-farm in permanent records
- Treatments are administered according to the label or as prescribed by veterinarians
- All treatments are recorded to respect milk withdrawal times and animals that are sold are kept on the farm until the meat withdrawal times are respected
- Treated cows are visually identified so their milk is discarded until deemed safe
- Antibiotics are kept at their proper storage temperature and conditions

As part of ProAction, corrective actions may be required, with a specific timeframe to implement them.

Commodity Group Highlight:

Beef Cattle Sector's Policy Statement on Antimicrobial Stewardship

The Canadian beef industry recognizes the importance of maintaining the efficacy of antimicrobials for human and animal health, and seeks to minimize the development of AMR. Thus, the Canadian Cattle Association has published the following official statement on antimicrobial stewardship in 2019:

This statement is intended to help cattle producers and veterinarians maintain herd health and welfare, economic viability, industry competitiveness and sustainability, public health, and consumer confidence. Canadian beef cattle producers, veterinary profession and value chain partners work together to:

- *Establish a valid Veterinarian-Client-Patient relationship (VCPR), and develop and regularly review a herd health plan including applicable preventative measures to refine, reduce and where possible replace the use of antimicrobials.*
- *Prioritize the welfare of animals within the confines of a valid VCPR, focusing on good animal husbandry and vaccinations to prevent common infectious diseases. Treat as few animals as possible when required, but as many as necessary for effective disease control.*
- *Ensure those administering antimicrobials are appropriately trained and competent in correctly following prescription and label instructions.*
- *Ensure legal compliance in administration of antimicrobials with drug indication, dose, route, frequency, duration, withdrawal period, and storage, as per prescriptions/label directions and health protocols from a veterinarian.*
- *Dispose of all expired antimicrobials safely in accordance with relevant regulations;*
- *Keep treatment records that include the date, disease diagnosis, antimicrobial product name, dosage, route of administration, treatment outcomes when attainable, and any pertinent diagnostic test results.*
- *Adopt a tiered approach to AMU: use effective antimicrobials of the lowest importance in human medicine as the first choice and those of highest importance in human medicine as the last choice, provided doing so does not delay effective treatment or compromise animal health and welfare.*

Commodity Group Highlight:

- *Not use licensed antimicrobials that Health Canada categorized as Very High Importance in human medicine unless no other antimicrobials licensed for use in cattle would achieve the desired animal health, welfare and food safety outcomes.*
- *Not use any antimicrobials other than ionophores to improve feed efficiency.*

(Canadian Cattle Association, 2024)

Research initiatives. Most Canadian commodity organizations are involved at various levels in collaborative research on AMU and AMR. One example of a sector that has been proactive in this area is the Canadian beef cattle sector. The beef cattle sector started funding studies using the 1990-2004 Canada-Alberta Beef Industry Development Fund. The Beef Cattle Research Council was established in 1998 as the research arm of the Canadian Cattle Association and coordinates the most recent activity through the National Beef Antimicrobial Research Strategy (2023-28, and previously, 2018-23), which identifies priority research and surveillance outcomes for AMU, AMR, and alternatives for the Canadian beef industry.

Several major projects have been conducted by the beef cattle sector during the past two decades involving CIPARS, AAFC, industry, and Canadian and US animal health and human health researchers. In 2007, a project led by CIPARS developed a framework to track AMU and AMR in commercial feedlot cattle to facilitate the incorporation of the feedlot sector into CIPARS's on-farm surveillance network. New genomic tools were used to explore the potential that humans may be exposed to AMR bacteria or AMR genes transmitted from cattle environments via water or beef. Ultimately, these projects contributed to CIPARS obtaining sufficient funding to add a feedlot component to their joint CFAASP on-farm surveillance program in 2019. Since 2014, numerous on-farm projects have also been funded to examine AMU and AMR within the Canadian cow-calf industry as an extension of regional and then later national surveillance programs co-funded with AAFC.

4.1.2.2 Other Industry Groups

Other industry organizations, such as pharmaceutical companies, multinational fast food chains, and vertically integrated producers can also influence AMU practices.

One example was an initiative by Canadian pharmaceutical industry groups to voluntarily remove growth promotion claims from drug product labels, as part of a joint activity with Health Canada. In 2014, the Canadian Animal Health Institute (CAHI) issued a statement of their intent to work with the Veterinary Drugs Directorate (VDD), Health Canada to remove growth promotion claims on drug products containing medically important antimicrobials (MIAs) (Canadian Animal Health Institute, 2014). This included in-feed medications for use in food-producing animals. Growth promotion claims were removed as part of the actions to promote responsible use of MIAs in 2018; as a result, MIAs in food producing animals are only to be used to treat or prevent diseases (Health Canada, 2024a).

Another initiative that CAHI participated in, which is unique to Canada, was the voluntary provision of CAHI data on volumes of antimicrobials distributed for sale in Canada prior to the 2017-18 regulations; these regulations require manufacturers/importers to provide this data. CAHI data were important additions to CIPARS and another example of industry-government collaboration/cooperation.

An indirect example of industry influence exerted at the opposite end of the food supply chain is seen in A&W's "Raised without the use of antibiotics" campaign, and McDonald's Canada's "raised without antibiotics important to human medicine" policy. In the latter case, McDonald's asserts that producers who supply chicken for its menu will continue to "responsibly use ionophores", a type of antimicrobial not used for humans. McDonald's also has a "Global vision for the use of antibiotic stewardship in food-producing animals", and as part of that, "is committed to reducing the need for antibiotics, and has a preference for raw materials [..] supplied through progressive farming practices including the Responsible Use of Antibiotics" (Global Quality Systems and Global Strategic Sourcing Food, 2017). These campaigns indirectly influence AMU in food-producing animals by promoting greater public attention and emphasis on the prudent use of antimicrobials in the food-producing animal production sectors.

4.2 Federal-Provincial-Territorial Regulatory and Policy Considerations

Canadian governments have taken a collaborative approach to working with industry partners to institute change, ranging from the development of the PCAP, which is a culmination of decades of engagement efforts to develop policy in the area of AMR, to instituting policy and regulatory changes and supporting industry activities to enhance AMS. The PCAP is the basis of Canada's 5-year commitment to address AMR. It outlines five key pillars of action: Research and Innovation, Surveillance, Infection Prevention and Control, Stewardship, and Leadership, with ten actions collectively identified under these pillars. Released in June 2023, the PCAP provides the basis for a coordinated response to AMR/AMU. One of the key actions is to build on existing One Health AMR governance in support of action plan implementation (PHAC, 2023a). Although important, the PCAP is only an initial step towards action, and after its release in June 2023 no steps have been made towards reduction of AMU in Canada.

However, Canada lags behind some other developed countries despite these initiatives and having many of the above elements in place. For example, between 2017-2023, TrACSS data shows that Canada has lagged behind the G7 countries in developing a national surveillance system for AMR, raising awareness and understanding of AMR risks and response, and the development of a national AMR action plan. Specific to the veterinary sector, Canada lagged in training and education on AMR in the veterinary sector, catching up between 2021-2023 (Food and Agriculture Organization of the United Nations, United Nations Environment Programme, World Health Organization, & World Organization for Animal Health, n.d.). In the period preceding that, a Canada-wide environmental scan of policies to address AMR between 2008 and 2018 suggested that Canadian AMR efforts were “disjointed and inadequate, given the urgency of this public health threat”, and that federal and provincial governments have “mostly refrained from using more powerful policy tools, including regulation, legislation and fiscal measures” (Van Katwyk et al., 2020).

In 2021, two models of governance of the One Health AMR response were proposed in a PHAC-commissioned report entitled “Strengthening Governance of the Antimicrobial Resistance Response Across One Health in Canada”. These include: the AMR Network model, and the AMR Centre model. The AMR Network model considers the AMR ecosystem in Canada as complex in terms of the diversity of actors and the range of actions required, and does not have one centre of control. The AMR Centre model adopts a classic top-down approach where one organization makes meaningful changes in defined priority areas, utilizing its own resources and strong partnerships with leading institutions and experts (Morris et al., 2021). To date, the expert panel is unaware of any actions to implement either of the two models or the recommendations provided in this report.

International case studies (Appendix 2; Chapter 3) show that critical elements of successful governance frameworks to harmonize national efforts to reduce AMR include political leadership, collaboration, coordination, integrated multi- and cross-sectoral approaches, clear delineation of responsibility for given actions, accountability, and sufficient resources to implement them. An example discussed below as a case study that highlights this is that of France. The French case study suggested that a harmonized national governance framework with strong leadership allowed multiple stakeholders to align with FPT departments and agencies responsible for addressing the issue of AMR, had clear delineation of responsibilities for given actions, and had sufficient resources to implement those actions.

International key informant (KI) interviews from other jurisdictions also made it clear that the livestock industry, government agencies and departments of health and agriculture, as well as veterinary sectors also need to work together, especially pertaining to the development of policies and interventions. While FPT departments and agencies, veterinarians and livestock groups were actively engaged in developing the PCAP, the only identified, current designated infrastructure for continued collaboration and shared governance is Animal Health Canada.

Case study highlight:

France’s Écoantibio Plan: An Approach to Key Actor Involvement

A successful participatory approach taken in France is seen through the governance of the Écoantibio plans. The Écoantibio plan was created as part of the country’s national action plan in the context of AMR/AMU in animals, including food-producing animals, with Écoantibio 1 (2012-2017), Écoantibio 2 (2017-2021), and more recently Écoantibio 3 plan (2023-2028). Each plan built on the successes of the previous ones.

An evaluation of the first two plans reported substantial progress towards reduced AMU, reduced AMR in some bacteria, and changes in practice among professionals. The successes were rapid and significant with the first plan and continued with the second plan, albeit at a slower pace. Identified shortcomings included research into new antimicrobials, education of the general public, development of rapid diagnostic tests, and evaluation of the social, environmental, and economic impacts of the plans (Laugier & Guillaume, 2022).

The following objectives are defined as part of the Écoantibio 3 plan:

- Maintain the dynamic of reducing current levels of exposure to antibiotics by maintaining the current levels of exposure of livestock to antibiotics and by setting a specific target of reducing dogs and cats' exposure to antibiotics by 15% by 5 years
- Preserve the therapeutic arsenal in animals
- Strengthen the prevention of diseases that lead to the use of antimicrobials and antiparasitics
- Promote the proper use of antimicrobials and antiparasitics at the animal and herd level
- Better understanding of antimicrobial and antiparasitic resistance
- Encourage the commitment of sectors, professionals, and citizens on antibiotic resistance

The Écoantibio 3 has 25 actions, categorized under five axes (Ministere de l’Agriculture et de la Souverainete Alimentaire, 2023):

- Prevention against the appearance and spread of antimicrobial and antiparasitic resistance in livestock and companion animals
- Training, awareness and commitment in the field of antimicrobial and antiparasitic resistance in animal health, in a "One Health" dynamic
- Research and monitoring of antimicrobial and antiparasitic resistance in animal health

Case study highlight:

- Maintaining, improving and developing a therapeutic arsenal favourable to the proper use of antimicrobials and the optimization of animal health prescription practices
- Fight against antimicrobial and antiparasitic resistance in animal health, from the territorial to the international level

These plans were associated with tight governance, supervision, support, and involvement across various sectors. According to two French key informants who were jointly interviewed, the governance of these plans was a key element to their success. The plans were not just documents, but were associated with tight governance, meetings, supervision, support, and involved all the key actors around the table. This coordination of key actors was conducted by the ministry. The approach was original; it was not just the ministry that unfolded its plan, but the ministry involved the key actors in piloting various actions in the plan. This is still evident in the EcoAntibio 3 plan today. The Ministry of Agriculture delegates responsibilities to each key actor to pilot the action, which has the virtue of involving them. From a participatory perspective, one key informant found this to be a very strong approach.

Key finding 4

Critical elements of successful governance frameworks to harmonize national efforts to reduce AMR include political (public and private sector) leadership, collaboration, coordination, regulation, integrated multi- and cross-sectoral approaches, clear delineation of responsibility for given actions, accountability, and sufficient resources to implement them.

- The Office of the Auditor General's (2023) assessment was that the current Pan-Canadian Action Plan is incomplete and does not cover many important elements that will result in meaningful actions and produce desired outcomes.
- Canada lags behind some other developed countries although it has some of the elements in place to be successful.
- The federal agencies involved in food-producing animal AMR/AMU, provincial veterinary medical regulators, and provincial agencies involved in food-producing animal AMU must work together to improve AMS in food-producing animals in Canada.
- From international key informant (KI) interviews, it is clear that the livestock industry, government agencies and departments of health and agriculture, as well as veterinary sectors need to continue to work together beyond the creation of the PCAP, especially pertaining to the development of policies and interventions.
- Policy/program evaluations are critical elements of good governance and are necessary to demonstrate the impact of given actions.

4.3 Gaps in Political Commitment and Leadership

Canada has some of the elements in place to guide the systems and agencies involved in addressing the issue of AMR, but other critical elements are still missing. Political commitment and leadership on AMS in food-producing animals are required to provide a mandate to appropriate federal agencies and departments, adequate and sustainable resources, and coordination of national efforts on antimicrobial stewardship.

As noted earlier, the Office of the Auditor General's (2023) assessment was that the Pan-Canadian Action Plan on Antimicrobial Resistance (PCAP) "did not cover many important elements—such as concrete deliverables, timelines, and details about who is accountable for each action and that, without these key elements, it is unlikely that the plan will result in meaningful actions and produce desired outcomes" (Office of the Auditor General, 2023).

The Office of the Auditor General concluded that "the PCAP was incomplete and that, without specific accountabilities, deliverables, timelines, and measurable outcomes, there is a risk that action among federal, provincial, and territorial governments to tackle AMR will be delayed, poorly coordinated, and not comprehensive" (Office of the Auditor General, 2023). Our suggested Promising and Strategic Interventions (Ch. 9) address some of the deficiencies in the PCAP that were identified, and is the reason that we focus on the critical elements of leadership, political commitment and coordination as the first Promising and Strategic Intervention.

In October 2023, Animal Health Canada (AHC; formerly the National Farmed Animal Health and Welfare Council) and Agriculture and Agri-Food Canada began a project to develop the leadership and plan for the implementation of the PCAP for AMR in animal health. This partnership was undertaken in consideration of AHC's mandate to establish a harmonized and integrated approach to the management of broad animal health and welfare program issues and to provide scientific, strategic, and policy advice and recommendations on animal health and welfare. However, Animal Health Canada was not created to support this type of activity (implementation of the animal health component of the PCAP) and currently has limited infrastructure (space, staff, etc) to accomplish this.

Leadership of the national action plan for the animal sector

Key provincial and federal participants from government, industry, and across different commodity groups agree on the need for one entity to lead with the support of all key actors, and the need for a collaborative approach. The European experience suggests that the government is often not the best entity to be the sole leader of such initiatives, and that producer and veterinarian associations can play a significant role in educating and implementing better management practices, supported by government funding (Key Informant Interview, Italy/EU). This is also addressed in a report commissioned by PHAC, where two models of governance for a One Health AMR response were proposed, a network model without one centre of control and a centre model where one organization makes changes in defined priority areas, with strong partnerships with other organizations and experts (Morris et al., 2021) .

Canada has multiple FPT governance structures that are already in place and other existing networks working to implement PCAP, and the year 1 progress report for the PCAP shows progress in a number of important areas (PHAC, 2024d). However, there is no one entity leading the way and holding all stakeholders accountable with respect to implementing PCAP actions specific to animal health, resulting in paralysis of movement and of commitment to improve, and lack of focused leadership.

In 2023, the Office of the Auditor General reported that "the federal government did not do enough to address the growing resistance to antimicrobial drugs, such as antibiotics, to help safeguard the health of Canadians" (Office of the Auditor General, 2023). For example, the PCAP did not cover many important elements, such as specific deliverables, timelines, and assignment of accountability for each action. According to the report, this makes it "unlikely that the plan will result in meaningful actions and produce desired outcomes" (Office of the Auditor General, 2023).

Furthermore, the Auditor General report also found Canada to be lagging in coordinated efforts from all levels of government and stakeholders. The report proposed that PHAC, Health Canada, CFIA, and AAFC should engage with federal, provincial, and territorial partners and stakeholders to complete, execute, and monitor the Pan Canadian Action Plan on Antimicrobial Resistance (Office of the Auditor General, 2023).

While Health Canada had strengthened its oversight by implementing regulatory and policy changes to preserve the effectiveness of antimicrobials, the Auditor General found that the department had not assessed whether the changes it had implemented were working as intended to preserve the effectiveness of antimicrobials. Furthermore, the report proposed that Health Canada should finalize its review of veterinary antimicrobials with unspecified or prolonged durations of use and prioritize product label changes (Office of the Auditor General, 2023).

While there is agreement that AHC has the commodity industry network required for bringing the animal health sectors together, there is concern that AHC does not currently have long-term stable resources to lead this task (CAHS Virtual Engagement Finding). Concerns were also expressed as to whether AHC currently has the connections with the human health counterparts that would be necessary for a true One Health approach, or whether the organization may be too siloed for the task. There is concern among the Panel that delegating this sole animal health leadership responsibility to AHC removes some of the onus on governments to provide resources and be part of the required leadership to motivate and sustain change.

AAFC recently announced funding of approximately $13 million to AHC, including $3,534,174 over five years (2023-2028) to the CAHSS division to focus on "building resilient animal health surveillance through a One Health lens" (Government of Canada, 2024). While this is applauded, this is mostly project-based funding directed at achieving short-term outcomes. Long-term base funding is required to sustain animal health surveillance through a One Health lens and set up an effective leadership structure to address all of the animal health components of the PCAP.

Clear objectives and goals. A national approach requires clear objectives and goals developed collaboratively by government and industries, and a time-frame, so the effectiveness of the PCAP can be evaluated independently to assess achievement of specific short and long-term goals. This is supported by evidence from several international case studies, including the United Kingdom, and the Netherlands, that illustrate that jurisdictions that have been most successful at reducing AMU have done so in the context of clear targets. This issue is discussed further in Chapter 7.

Key gap 4

Political commitment and willing leadership across public and private sectors on antimicrobial stewardship in food-producing animals is required in Canada to mandate and coordinate national efforts.

- An integrated multi-sectoral approach is currently missing in the context of the Pan-Canadian Action Plan (PCAP), particularly interagency coordination.
- The work of the different federal agencies involved in food-producing animal AMU currently appears to be siloed, and not part of a coordinated effort in Canada.
- There is significant provincial/territorial responsibility for areas of antimicrobial governance relevant to stewardship. However, the commitment to improved AMS in food-producing animals varies between provinces and is siloed both between and within provinces and with the federal government.
- While Animal Health Canada (AHC) could act as a facilitator to bring many animal sectors together, the organization is siloed from activities occurring in human health, which can present barriers to a cross-sectoral approach. AHC currently lacks sufficient resources and infrastructure to act as a hub for implementation of the required AMR/AMU activities for food-producing animals.
- The lack of a single organization to lead and coordinate Canada's approach across animal and human health, along with a lack of adequate and sustained resources, continues to be a barrier to progress in Canada. This need was clearly supported by the international case studies.

Related action in the Pan-Canadian Action Plan

- Under the Leadership pillar: "Working closely with the FPT AMR Steering Committee, First Nations, Inuit and Métis partners* and other partners across sectors to develop an effective network of networks approach for supporting the successful implementation of the action plan, building on best practices and evidence."

* At the time of this report, the voices of Canada's Indigenous partners with respect to AMU and AMR in food-producing animals were not available to the CAHS panel.

4.4 Regulatory and Other Policy Approaches in Canada on AMU

Regulations have been an important and effective tool for AMS in Canada. These include regulations related to both the licensing of antimicrobials (and other products) and regulatory approaches related to the AMU. This section highlights changes to AMU in Canada since 2017, as well as providing comparisons to other countries included in the international case studies.

As compared to some other jurisdictions (except the US) considered in this review, Canada takes a less stringent stance on specific regulations impacting AMU in food-producing animals. Appendix 2 provides a summary of all international case studies, including findings from review of the published and grey literature, and interviews with international key informants.

4.4.1 Prescription-only Status for Veterinary Antimicrobials

The federal government has made important changes to the oversight and use of MIAs in Canada during the last six years. In 2017/2018, several regulatory and policy changes resulted in all MIAs for veterinary use requiring a veterinary prescription for access, as well as removing growth promotion claims from all such products. In addition, restrictions were put in place to: 1. prevent/prohibit the own use importation of MIAs, 2. add a requirement for good manufacturing practices for importation and use of active pharmaceutical ingredients of MIAs, 3. add a requirement to hold a Health Canada issued Establishment License for anyone importing a MIA, and 4. add a requirement to annually report sales (manufacturing, importation, and compounding) data for antimicrobials destined for use in animals in Canada. There was no change to the prescription status of category IV antimicrobials, such as ionophores and coccidiostats, as they are not used in human medicine as antimicrobials.

While most antimicrobials used in food animal medicine have required prescriptions before 2018, these changes did affect veterinary oversight of older MIA classes such as most penicillins, tetracyclines, and sulfonamides that were previously available for direct purchase. It is important to note that while these classes did not require a prescription before 2018, there were many commonly used product formulations, particularly injectables, that were only available through veterinarians as a voluntary measure by some pharmaceutical companies. The biggest impact of the 2018 change to prescription only status for all MIAs was associated with the in-feed and in-water MIAs; for example, the need for a prescription for tetracycline use given its importance in disease prevention and control in the swine and feedlot industries. As discussed in section 4.5.2 of this chapter, veterinarians can authorize the extra-label use of antimicrobial products under certain conditions.

Regulations are most successful when based on sound science and applied in the context of collaborative engagement with commodity groups, veterinary groups, and producers. To bring about the changes in 2017/2018, Health Canada had very effective ongoing engagement and communication with the Canadian Food Inspection Agency, the Public Health Agency of Canada, provincial and territorial partners (Ministries of Agriculture and veterinary licensing bodies), Canadian Veterinary Medical Association (representing veterinarians), Animal Nutrition Association of Canada (representing animal health nutritionists as well as feed mills), Canadian Animal Health Institute (representing drug manufacturers), and national commodity group organizations (Health Canada, 2024b).

4.4.2 Restriction of Category I Antimicrobials

The EU and a number of other countries have designated antimicrobials or groups of antimicrobials as reserved for the treatment of certain infections in humans. In the EU, a list of 18 Category A (avoid) antibiotics, 18 antivirals, and one anti-protozoal are restricted for use in human medicine (European Union, 2022). While Canada does not explicitly state that Category I drugs are reserved for use in humans, almost all of the drugs listed by the EU as "Avoid" (exception virginiamycin) are not licensed for use in food-producing animals in Canada. Category I antimicrobials which are licensed for use in animals in Canada would be designated in the EU as "Restrict".

With regards to the use of Category I antimicrobials in Canada, Québec has provided leadership in this area to align with international policies not allowing the use of third-generation cephalosporins and fluoroquinolones (which are Category I antimicrobials) for preventative purposes in food-producing animals and limiting the use of these antimicrobials for treatment (McCubbin et al., 2021). There are no label indications for the preventative use of these drugs in food-producing animals in Canada with exception of 3rd-generation cephalosporins for blanket dry cow treatments (i.e., treatment of all mammary glands of all cows at the time of dry-off) in dairy cattle. Extra label drug use regulations provide a potential opportunity for exceptions for the use of Category I drugs for prevention, such as was reported for the use of ceftiofur (a 3rd generation cephalosporin) in suckling pigs to prevent respiratory disease (PHAC 2022a). This product is labeled for treatment of respiratory disease in swine. Further discussion on the use of Category I antimicrobials in Canada is included in section 4.5.3.

Regulations do not need to be government based, and can be industry based, as in the actions of the Chicken Farmers of Canada where the elimination of the preventive use of Category I and II antimicrobial drugs is mandatory and enforced with annual audits (Chicken Farmers of Canada, 2025).

4.4.3 Removal of Labeling of Growth Promotion Use of Antimicrobials in Feed

Although Canada has not explicitly banned the growth promotion use of all antimicrobials, Canada has removed growth promotion label claims for MIAs. However, it is important to note that antimicrobials (e.g. monensin, lasalocid) that are in Category IV (i.e. low importance to human medicine) in the Canadian classification system are not classified as antimicrobials in some jurisdictions. International comparisons, therefore, need to take this into consideration.

The impact of restricting the use of antimicrobials for prevention and growth promotion can be illustrated by the example of avoparcin in the EU. Avoparcin was used both for disease prevention and growth promotion prior to being banned in the EU in 1997 due to concerns about its role in the emergence of vancomycin resistance. Following that ban, there was a decrease in the prevalence of vancomycin-resistant enterococci (VRE) in food-producing animals (Aarestrup et al., 2001). Although this example shows the potential impact of restricting the use of antimicrobials, the relevance of the specific example is limited as avoparcin has never been licensed for use in food-producing animals in Canada, and CIPARS surveillance has not identified any VRE isolates from food-producing animals.

Key finding 5

Government and industry regulations have been important tools for AMU reduction in Canada and worldwide, and have been most successful when based on sound science and applied in the context of collaborative engagement with commodity groups, veterinary groups, and producers.

- The federal changes to the oversight and use of medically important antimicrobials (MIAs) in Canada in 2018, such that all MIAs for veterinary use required a veterinary prescription. Other jurisdictions examined in this report also have this minimum level of restriction including the EU.
- Québec has provided leadership in this area in not allowing the use of third generation cephalosporins and fluoroquinolones (which are Category I antimicrobials) for preventative purposes in food-producing animals and limiting the use of these antimicrobials for treatment.
- The changes made by the Chicken Farmers of Canada, which were implemented voluntarily, removed the use of Category I and Category II antimicrobials, while working closely with CIPARS and Health Canada.
- There is a need for movement towards international alignment for all aspects of the regulatory approval process, use, and labelling for veterinary products, including manufacturing, inspection, and approval.

4.5 Gaps: Unresolved Regulatory Issues Impacting Antimicrobial Stewardship in Canada

4.5.1 Goals for AMU Reductions

Targets for reduction in AMU have been implemented in some jurisdictions and have been followed by substantial reported decreases in the sale of antimicrobials as measured by the weight of active ingredient adjusted for biomass. For example, in 2020, the European Commission's Farm-to-Fork Strategy set the target of reducing sales of veterinary antimicrobials in the European Union (EU) by 50 percent by 2030, compared to 2018 levels (European Commission, 2020a; Canali et al., 2024). The process started in 2001 with the first Community Strategy against AMR, leading to the EU ban on the use of antibiotics as growth promoters in 2006, and the Action Plans against AMR of 2011 and 2017. Figure 4-3 shows the EU's progress towards AMU reduction targets between 2010-2022. Mandatory antimicrobial reduction targets have also been implemented in individual countries such as the Netherlands

(Speksnijder et al., 2014), and Denmark. Veterinary sales data on all EU member countries are available through the European Medicines Agency (2023).

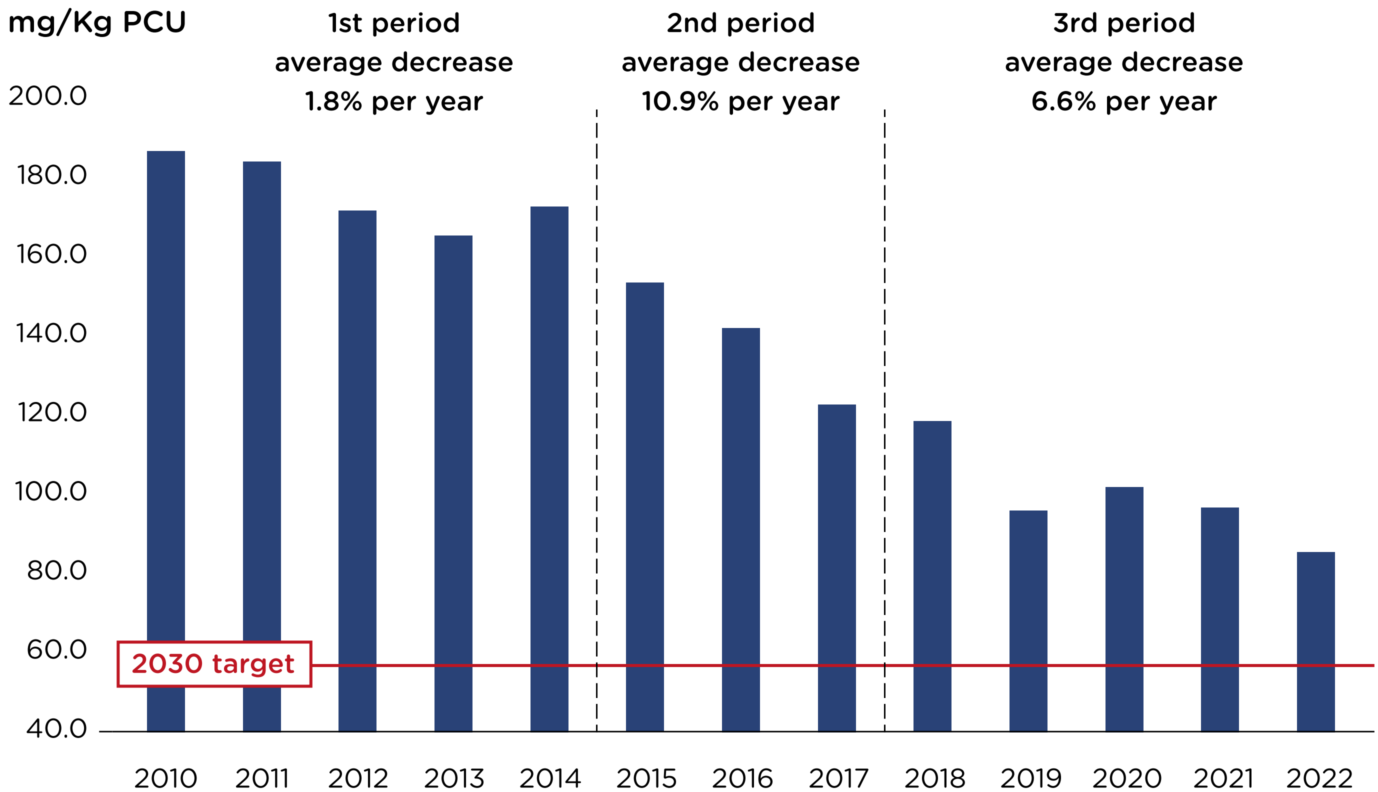


Figure 4-3. Total sales of veterinary antimicrobials in the 27 EU Member States in mg of active ingredients per kg PCU [Note: Sales in Bulgaria, Cyprus, Germany, Poland and Slovakia are accounted from 2011; sales in Luxembourg from 2012; in Croatia and Romania from 2014; in Greece from 2015; and in Malta from 2016] (Canali et al., 2024)

However, this regulatory approach has been controversial in other jurisdictions. Indeed, a proposed target to reduce AMU in agriculture by 30% was removed from the Sep. 26, 2024 United Nations political declarations following push-back from Canada, the USA, Australia, and New Zealand (Gilbert, 2024).

There are a number of issues related to AMU targets at the national or commodity group level. The first is that the word "targets" is off putting to many partners, due to the issues regarding the implementation of these targets in other jurisdictions, as heard in the virtual engagement sessions. It might be more appropriate to refer to AMU "goals" or "objectives" to differentiate the intended Canadian approach. Therefore, throughout this section, the word "goals" will be used. Setting SMART (Specific, Measurable, Achievable, Relevant, and Time-bound) goals requires objectives of those goals to be clearly defined and agreed by consensus of all relevant parties. In the EU, targets were based on an overall reduction in AMU based on weight of antibiotic used. However, it may be more appropriate to consider other objectives, such as reduction in specific classes of antimicrobials, reductions in specific types of use (for instance, reducing systemic use of antimicrobials in dairy calves may be more relevant than reducing intramammary use in terms of impact on AMR), reductions in AMR (for pathogens of importance to animals, indicator bacteria, and/or pathogens of concern to human health), and prevention of further increases in AMR (for specific bacteria-antimicrobial combinations).

A first step to determining AMU goals would be farm-level AMU data collection. In many commodity groups, this is already occurring. In dairy, to be compliant with proAction, all uses of antimicrobials must be recorded. In swine, Canadian Pork Excellence standards involve all individual animal AMU to be recorded for pigs after weaning, and many poultry and feedlot operations also record AMU. However, there are issues with consistency (within and across commodities) and potentially quality of the data, as well as logistical issues related to centrally accessing these data for goal setting and outcome evaluation. There are also issues related to the metrics used to measure AMU; for instance, goals related to total kg of AMU are not sufficient and can be misleading due to changes in the underlying animal populations, differences across the sectors and across drug classes and routes of administration, as well as quantitative differences in the efficacy of different classes of antimicrobials that have different levels of importance with respect to human medicine. Concerns have been expressed by producers, producer groups, and veterinarians as to who would have access to and store these data for goal setting and evaluations, how the data would be used, and whether or how industries or farms might be held accountable. Some commodities hold AMU data as highly confidential and proprietary when it comes to protocols. For example, one Canadian key informant suggested that "benchmarking is limited by confidentiality, data complexity." It also is important to recognize that the different commodity groups are at different stages of implementing AMS and have different logistical and management constraints for managing disease and recording use; thus goals will need to be sector-specific and stage-of- production-specific for some commodity groups.

Resolving these issues will require discussion amongst all relevant parties, and whatever approach ultimately is used will need to be tailored to the Canadian context. It is possible that a government entity might consider mandating goals (as was the case in Denmark and Netherlands). However, the details of how goals might vary across commodities and how any goals can best be achieved are ideally determined by industries. It also will be important to ensure that implementation of goals does not reduce competitiveness with the USA and other trading partners, particularly for non-supply managed industries.

4.5.2 Additional Regulatory Issues That Affect Licensing and Use of Antimicrobials

The following section outlines some unresolved regulatory issues around food-animal AMU. These include considerations unique to the Canadian context, including the structure of the different federal, provincial and territorial groups concerned with AMS in food-producing animals, and the current state of the science of optimal AMU and AMS.

Open-ended labels on antimicrobials that do not specify a duration of use. Health Canada has yet to require a change on the open-ended labels on antimicrobials that do not specify a duration of use. The continued use of "open-ended" prescriptions (i.e., no end date of administration) of antimicrobial drugs in food-producing animals is the subject of intense debate in the United States, and is no longer allowed in Europe. Unspecified duration of use of antimicrobials is not consistent with good stewardship practice and may lead to using antimicrobials for longer than is necessary (Davedow et al., 2020). It is encouraging to note that this important issue, identified also as a deficiency in the 2023 Auditor General's evaluation of Canada's response to AMR, is currently (as of November 2024) being addressed in a planned post-market re-evaluation of MIAs for veterinary use with unspecified or prolonged durations of use (Health Canada, 2024c).

The drug approval process in Canada and extra-label drug use (ELDU). Health Canada approves veterinary drugs based on the evaluation of safety (animal and human), efficacy and quality of veterinary drugs. The assessment includes considerations of potential AMR. Health Canada does not regulate the use of veterinary drugs, but determines what information is on the label. Veterinarians have the ability to use or prescribe drugs in an extra-label manner, known as ELDU. CgFARAD™ is the Canadian segment of the Global Food Animal Residue Avoidance Databank program and provides veterinarians with information on the withdrawal time before animals or animal products can enter the food chain (Chicken Farmers of Canada, 2024c) when the drug is used in a way that varies from the label. A CgFARAD™ recommendation must be obtained when drugs are used extra-label for all processed poultry and eggs. The annual newsletter summarizes requests for information by drug and species. As an example, there were no requests for extra-label use of category I drug ceftiofur in poultry from May 1, 2022 to April 30, 2023 and < 5 requests for extra label use of fluoroquinolones for treatment. The most common reasons for all ELDU requests for chickens were for coccidiosis and necrotic enteritis (CgFARAD, 2023).

All other CgFARAD™ requests are submitted on a voluntary basis by veterinarians, who are responsible for the withdrawal period or withholding time for extra-label use. Because of the high cost of getting a drug to the market in Canada, and the small size of the Canadian market with a low return on investment, there are very few antimicrobials approved for use in "minor species" such as sheep, and goats and therefore many antimicrobial drugs are used "extra-label" in these animals.

4.5.3 Federal-Provincial Jurisdictional Constraints on the use of Antimicrobial Drugs in Food-Producing Animals

Another significant issue that impacts AMS in Canada is the federal-provincial jurisdictional constraints and the role of the provincial veterinary regulators in the use of approved drugs.

Since the practice of veterinary medicine is a provincial regulatory responsibility, the actual use of approved antimicrobial drugs is determined by veterinarians, who are self regulated but under provincial authority.

The 2018 changes to require veterinary oversight of AMU in food-producing animals necessarily shifted a portion of the responsibility of AMS towards veterinary practitioners in terms of decision-making, requiring a robust veterinary-client-patient relationship (VCPR). Increased veterinary oversight is generally considered to improve responsible use of antimicrobials. However, there are concerns regarding veterinary antimicrobial oversight, particularly because of the potential for conflicts of interest inherent in the business distribution model of veterinary practice in Canada. In most countries, veterinarians are allowed to profit from pharmaceutical sales to clients as part of their total income.

Restricting the use of Category I antimicrobials. Another regulatory issue to be addressed is the use of MIAs in food-producing animals. The relevant drugs of current concern are the WHO list of Highest Priority Critically Important Antimicrobials (HPCIAs), and Canadian Category I antimicrobials, which includes 3rd generation cephalosporins (3GCs), fluoroquinolones, and polymyxins (colistin). The Government of Canada's categorization of the importance of antimicrobial drugs is presented in Chapter 1, Table 1-1.

In Europe, countries such as Belgium, Denmark, France and The Netherlands have regulations to limit the use of HPCIAs in food-producing animals (3rd and 4th generation cephalosporins, quinolones, and polymyxins) (although these do not include all Category I antimicrobials in Canada). This has resulted in a marked decline in their use. In Denmark the voluntary ban since 2013 on 3rd and 4th generation cephalosporins in swine has resulted in a significant decline in extended spectrum cephalosporinase producing indicator *E. coli* in swine and in pork products (Agersø & Aarestrup, 2013). Fourth generation cephalosporins have never been approved for use in food-producing animals in Canada and Canada requires AMR-specific warnings on antimicrobials belonging to Categories I, II, and III.

In February 2019, the Québec government introduced a new regulation to restrict the use of Category I antimicrobials in food-producing animals in the province (Roy et al., 2020). Québec's regulation has 2 components: i) the use of Category I antimicrobials in the treatment of disease, and ii) the use of Category I antimicrobials in the prevention of disease. Québec requires laboratory diagnostic evidence to support the use of these Category I drugs for therapeutic purposes. This means that treatment of a food-producing animal with a Category I antimicrobial is restricted to clinical cases that are not treatable with an antimicrobial of a lower importance category based on, for example, culture and susceptibility testing. For the prevention of disease, it is forbidden to administer a medication that belongs to Category I to an animal that will be used (or from which products will be used) as human food. This would impact dry cow therapy for dairy producers, but there are no other licensed uses of Category I products for prevention in livestock. Producers need a valid veterinary prescription and a completed veterinary justification form for every prescription of Category I antimicrobials. The application of the regulation by a veterinarian is examined during regular professional inspections performed by an inspector of the *Ordre des médecins vétérinaires du Québec* (OMVQ), the veterinary medical licensing board of Québec. Québec's approach to veterinary prescribing is presented as part of a case study highlight, below.

Québec's new regulation, the first of its type in Canada, was generally well-accepted by veterinarians and dairy producers, because they were well-prepared over a long period by several educational initiatives and because they saw the benefits and opportunities of improvement (Roy et al., 2020). The focus has shifted to the prevention of diseases and the use of more diagnostic tests and greater involvement of veterinarians in treatment decisions.

Analysis of antimicrobial sales of Category I antimicrobials in 3337 dairy herds in Québec in the year following implementation of the regulations, using the Vet-Expert software used by most dairy veterinarians in the province, indicated an average reduction of 19.6 defined course doses for cattle (DCDbovCA)/herd-year post-regulation from 26 DCDbovCA/herd-year pre-regulation (a 75% reduction in use). Importantly, there was no evidence of an increased use of other antimicrobials during this period. To put this in context with a garbage can survey (where drug containers placed in a central repository are inventoried) including other important dairy provinces for 2017-2020, 3rd generation cephalosporins (92% of herds) were the most commonly used antibiotics after penicillins (97% of herds) (Warder et al., 2023). Fluoroquinolone use was only reported in 6% of herds.

The changes in regulation in Québec are supported by a recent opinion survey of international experts using the Delphi approach on the use of MIA drugs in food-producing and companion animals (Sri et al., 2024). The consensus was that the use of high importance antimicrobials was appropriate if culture and sensitivity testing indicated the organism was resistant to low- and medium-rated antimicrobials so these agents could not be used for treatment. There was also agreement that a clear indication for this use and justification for antimicrobial choice must be recorded in the medical history, along with the dose rate, route of administration, the duration and the time point for review of the condition and associated antimicrobial therapy.

Taking action on Medically Important Antimicrobials: Québec's approach to veterinary prescribing

Québec takes a stringent approach to prescription of MIAs, in particular, Category I antimicrobials. As described by Roy et al. (2020) for dairy cattle, Category I antimicrobials can be prescribed to treat sick animals in 2 different situations:

1. When examined by a licensed veterinarian:

- If a licensed veterinarian concludes, based on the history of the animal or the herd, the physical examination with or without additional diagnostic tests such as milk culture or tracheal lavage, that only a Category I antimicrobial will cure the infection.
- Then, a prescription is made only for that animal and the required quantity of antimicrobial needed for that specific animal is dispensed.
- Furthermore, an official justification form is filled out by the veterinarian and provided to the dairy producer who must keep the form in his/her farm's records.

2. When not examined by a licensed veterinarian:

When a sick animal needs treatment but is not examined by a licensed veterinarian, the dairy producer can give the animal a Category I antimicrobial, but only in specific situations and only if restrictive criteria are fulfilled.

- First, a written protocol needs to be in place by the herd veterinarian.
- Second, the protocol that includes a Category I antimicrobial to treat a specific case scenario must be judged by the herd veterinarian as necessary based on the history of the animal or the herd, past physical examinations, or diagnostic tests previously performed on the herd.
- Third, the farm records need to be completed in a very comprehensive manner, thus allowing the veterinarian to monitor each dose of Category I antimicrobial that was administered to fill out a justification form.
- Finally, the protocol needs to be re-evaluated regularly to make sure it is still justified, with emphasis on infection prevention and control measures and improvement of herd management.

Restrictions on the use of Category I antimicrobial drugs in food-producing animals in Québec has significantly reduced their use. There is no consistent approach to improving the stewardship of HPCIA drugs in food-producing animals in the rest of Canada.

Regulatory barriers to accessing veterinary products. Regulations can also limit access to veterinary products, such as veterinary pharmaceuticals, animal vaccines and veterinary health products that help reduce AMU, and novel antimicrobials that are of lesser importance to human health. According to the CAHS virtual engagement sessions (rounds 1, 2), perceived government-level barriers for access to veterinary products include:

- Limited potential return on investment for veterinary products
- High fees for regulatory oversight of veterinary products
- Regulatory barriers for veterinary products

While there is a perception of regulatory and financial barriers related to access in the livestock production sectors, it is important to note that Canada accepts data generated in other countries when appropriate. The Canadian federal government is an active member of the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) with the United States, the United Kingdom, the European Union, Japan, Australia, New Zealand, South Africa and Switzerland. The purpose of this membership is to work together to adopt guidelines on the technical requirements for products to improve the generalizability of data generated, to speed up the rate of drug approvals internationally and to reduce the need for duplications of animal trials (Canadian Food Inspection Agency, 2022).

In addition to participating on VICH, Canada participates on international collaborative reviews for veterinary drugs, including with the United States, where the aim of the bilateral review is to reach regulatory decisions simultaneously between the countries and reduce the time difference of approvals between a larger market, like the United States, and a smaller market, like Canada.

In terms of veterinary biologics, such as animal vaccines, 90% of the vaccines used in Canada are imported from the United States (US), and Canadian data requirements are closely aligned with the US data requirements reducing regulatory burden on companies seeking authorization to use these products in Canadian livestock.

Key gap 5

Important changes are needed for Canada to make significant strides towards the goal of reducing AMU and improving AMS.

- Consensus around the objectives for specific goals related to AMU have not been articulated.
- Antimicrobials with prolonged or unspecified durations of use need to be assessed to determine if the labelled duration of use can be shortened and/or specified.
- There is no consistent approach in Canada to regulating the use of Category I antimicrobials in food-producing animals. An important area for regulatory review is the permitted uses of Category I antimicrobials such as third-generation cephalosporins (and fluoroquinolones) for preventive purposes, as was done in Québec.
- Harmonizing regulations on AMU across provinces and territories is important, particularly for permitted use of Category I antimicrobials.
- Medically important antimicrobials (MIAs) are available only with a veterinary prescription and veterinarians are regulated provincially-territorially by veterinary professional regulatory bodies.
- There is a need to identify ways to increase access to evidence-based veterinary products that may support a reduction in AMU.

Related action in the Pan-Canadian Action Plan

- Under the Stewardship Pillar: "Develop, implement and promote guidelines/standards for appropriate AMU in humans and animals through policy and regulatory initiatives, monitoring and educational interventions/accreditation requirements for health professionals and prescribers."

CAHS
ACSS

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 5:

Farm-Level Interventions to Reduce the Need for Antimicrobial Use

Introduction

Stewardship is the broad framework within which farm-level interventions are used to address antimicrobial use (AMU), as discussed in Chapter 3. In addition to having an antimicrobial stewardship (AMS) plan in place and reviewing that plan on a regular basis, three principles in the 5R Framework on Antimicrobial Stewardship involve the use of on-farm interventions; **reducing** the need for AMU to prevent disease (for example, through biosecurity and management, or the use of vaccines), **replacing** AMU where possible to reduce disease severity, manage and treat disease (for example, through the use of alternative products, vaccines, and biosecurity), and **refining** AMU prescribing and use practices (for example, through validated decision-making tools, drug categorization, and reduced duration of use). This chapter will specifically cover key findings in the areas of: 1. biosecurity and herd management; 2. vaccines; 3. alternative products; and 4. validated decision-making tools. While the use of these tools is integrated within herd health programs, each area is presented individually to allow for discussion of distinct issues related to each topic and to highlight the evidence for the effectiveness of specific tools, approaches, and products.

There is a vast literature related to farm-level interventions to reduce AMU, and this literature includes a wide range of methodological approaches; from expert testimonies to network meta-analyses to evaluate the comparative efficacy of interventions across multiple studies. Identifying and summarizing this literature would require resources beyond the scope of this assessment. Therefore, the examples that follow are meant to be illustrative, rather than exhaustive, and focus on selected diseases associated with high AMU. An effort was made to provide examples for farm-level interventions in major commodity groups within the scope of this assessment (swine, poultry, beef cattle, dairy cattle, and aquaculture) when possible. In addition, relevant evidence from the international case studies and perspectives and opinions expressed through the CAHS virtual engagement sessions and Canadian key informant interviews is included.

5.1 Biosecurity (Infection Prevention and Control) & Management

Biosecurity and management are the cornerstones of antimicrobial stewardship efforts by reducing the need for antimicrobials. Biosecurity is the term used in the food-producing animal sector to refer to what in human medicine is referred to as “infection prevention and control” measures. Biosecurity can be internal or external. The concept of **external biosecurity** refers to reducing the transmission of pathogens from sources off farm, while **internal biosecurity** refers to measures that occur inside the farm to minimize or preferentially stop the spread of infections (Makovska et al., 2024). Thus, the underlying concept in effective biosecurity is to prevent the transmission of infectious diseases between and within farms. This corresponds to 2 broad principles; separating susceptible animals from infectious animals and environments, and reducing infection pressure (Dewulf, 2019). In a ranking exercise involving 111 pig health experts from Belgium, Denmark, France, Germany, Sweden and Switzerland, internal and external biosecurity were ranked highest of 19 possible alternatives to antimicrobials for perceived effectiveness (Postma et al., 2015). Internal biosecurity also was ranked in the top five for return on investment.

5.1.1 Literature on Biosecurity and Management

There is a scarcity of systematic review articles evaluating biosecurity measures and AMU. This is not unexpected, as biosecurity protocols involve a collection of individual components and the effectiveness of individual components may vary among farms, depending on farm-level factors or differing disease pressures. Thus, many components of biosecurity programs are based on plausibility or industry defined best practices, rather than scientific evidence. However, there is value in knowing which components are most effective and cost-effective.

A recent scoping review provided a global overview of internal and external biosecurity practices described in pigs, poultry, and cattle (dairy and beef), respectively, as well as practices within those commodity groups that were associated with higher AMU (Dhaka et al., 2023). However, many of the biosecurity practices were not relevant to the Canadian context, and results were descriptive rather than providing evidence for claims of effectiveness.

There are narrative reviews and individual studies that provide some specific examples of biosecurity (internal and external) and management practices for individual species. Below, we provide examples within each of the commodity groups.

Feedlot Cattle. While most AMU in beef cattle is for liver abscess prevention, BRD accounts for most injectable AMU and histophilosis prevention accounts for some in-feed use (Brault et al., 2019). One observational study found that a greater degree of commingling of cattle from multiple sources was associated with higher antimicrobial use compared to animals experiencing lower degrees of commingling (Santinello et al., 2022). Commingling typically occurs during purchasing calves for placement in feedlots when calves are sold through auction. Mixing can be exacerbated in the case of presort auction sales where cattle from multiple sellers are combined in lots of consistent sex, weight and color prior to sale and transport. Finally, commingling happens again at the feedlot where cattle from multiple sources are assembled to create large pens with cattle matched on sex, arrival weight and often color. While commingling is recognized as a risk factor for stress impacting the immune system and pathogen transmission (Cooke, 2017), the scale of modern commercial feedlots requires managing large pens of age/weight-sex matched cattle that are difficult to assemble from individual cow-calf herds due to the limited size of most cow-calf operations. Thus, significant reduction in commingling is likely not a viable option to reduce BRD (and thus AMU) under the current industry structure.

Given the challenges of implementing external biosecurity in an open system with cattle sourced from multiple locations, disease prevention focuses on management (Groves, 2020), including nutritional management (Krehbiel, 2020).

Cow-calf. In a cross-sectional study of 89 western Canadian cow-calf herds, several management strategies to reduce infection pressure and contact rates were associated with lower incidence of diseases (BRD, calf diarrhea) that are often treated with antimicrobials. These internal biosecurity strategies included sorting cow-calf pairs out of the calving area, not having winter feeding and calving in one area, calving heifers in a lower-density area, and decreased number of times cow-calf pairs were gathered before turn-out to summer pasture (Waldner, Wilhelm et al., 2022). In a survey of 80 producers in western Canada, management strategies linked to external biosecurity risks on cow-calf farms associated with BRD outbreaks included purchasing more than 10 bulls, bringing unvaccinated animals into the herd, and use of community pasture (Wennekamp et al., 2021).

Veal Calves. The main potential control points for biosecurity and management interventions for veal relate to the transportation of very young animals, introduction of animals from multiple sources to a barn, stocking density, and housing conditions. In a non-randomized controlled trial, a combination of transporting calves directly from the dairy farm to the fattening facility instead of commingling in dealer trucks, a three-week quarantine in an individual hutch, followed by outdoor hutches in groups of less than 11 calves was associated with lower AMU and mortality compared to conventional calf fattening operations (Becker et al., 2020). A systematic review and meta-analysis of veal calves evaluated associations between inadequate transfer of passive immunity (resulting from inadequate colostrum intake in the perinatal period) and respiratory disease and diarrhea which are leading causes of AMU in veal calves (Abdallah et al., 2022). The authors reported that calves with failure of passive immunity had higher odds of diarrhea and bovine respiratory disease, although the association for the latter was non-significant when publication bias was corrected.

A randomized controlled trial in the Netherlands evaluated the impact of cleaning and disinfection together with an AMU reduction protocol which limited the conditions under which group treatments and antimicrobials could be used; the authors reported that an AMU reduction protocol reduced MRSA carriage in calves compared to no protocol, but cleaning and disinfection in addition to the reduced AMU protocol did not reduce MRSA carriage compared to controls (Dorado-Garcia et al., 2015).

Dairy Cows. Most AMU on dairy farms is for the treatment and prevention of mastitis (McCubbin et al., 2022). According to a recent scoping review, 27 studies (17 trials, 10 observational studies) have been conducted on modification of the dry cow period length to improve udder health (McMullen et al., 2021). Nine of the trials and 4 of the observational studies compared the incidence of clinical mastitis between groups with different dry cow period lengths, which could have relevance to AMU. However, none of the studies directly evaluated AMU as an outcome. Including AMU as a core outcome for studies on mastitis (or other diseases associated with AMU) would be helpful as producers and veterinarians strive to identify evidence-based approaches to reduce AMU.

A common management practice associated with AMU is intramammary infusion with antimicrobials in all quarters of all cows at the time of dry off (a.k.a. Blanket dry cow treatment). An alternative management practice is selective dry cow treatment, using algorithms to identify cows where AMU might be warranted (for example, those with an existing intramammary infection). A systematic review of 9 controlled trials reported no difference in the risk of intramammary infection (IMI) at calving between blanket treatment and selective treatment when internal teat sealants were used (Winder, Sargeant, Kelton et al., 2019). However, when teat sealants were not used, there was an increased risk of IMI. AMU was not evaluated as an outcome in this review. These results are consistent with a more recent systematic review of 12 controlled trials, where the authors found no difference in the risk of IMI at calving, as well as no difference in the risk of developing a new IMI during the dry period or the risk of clinical mastitis in early lactation, as long as internal teat sealants were used at dry off (Kabera et al., 2021).

Similarly, not all cows with clinical mastitis may benefit from treatment with antimicrobials. Cows that experience a non-severe Gram-negative mastitis from e.g. *Escherichia coli* and cows with clinical mastitis but culture-negative milk, do not need to be treated with antimicrobials. In a systematic review and meta-analysis, de Jong, Creytens et al. (2023) concluded that not treating these cows with antimicrobials does not negatively affect clinical and bacteriological cure rates of those clinical mastitis cases.

All calves must receive an adequate amount of colostrum in the neonatal period to ensure passive transfer of immunity. Without this, calves are at high risk for diseases (and therefore AMU). A scoping review identified 256 articles addressing colostrum management (Uyama, Kelton et al., 2022). However, the review focused on associations between colostrum quality, quantity, and timing of administration and outcomes related to the passive transfer of immunity, rather than disease incidence or AMU specifically. No systematic reviews evaluating colostrum management and AMU were identified. However, the association between passive immune transfer and calf morbidity and mortality is well established and, in the United States, there are consensus recommendations for colostrum intake at the calf and herd level (Lombard et al., 2020).

Broiler chickens. In a systematic review and network meta-analysis evaluating various components of litter management (61 trials), no differences were identified that impacted mortality, including litter types, floor types, or additives (Sargeant, Bergevin et al., 2019). Furthermore, no differences were noted with regard to mortality between the use of fresh vs. used litter (7 trials). However, there was considerable heterogeneity among the studies. With respect to foot pad lesions (15 trials), peat moss appeared to be better than straw. In another meta-analysis evaluating the effectiveness of litter treatments on body weight gain, feed conversion, and mortality of broilers (de Toledo et al., 2020; 26 studies), acidifiers applied to the litter, including aluminum sulfate, sodium bisulfate, potassium permanganate, aluminum chloride, ferrous sulfate, acidified clay, alum, and hydrochloric-citric phosphoric acid, were associated with lower pH, moisture, ammonia, pathogenic bacteria, and mortality.

Swine. Swine production in North America has experienced the emergence or spread of several diseases of high consequence to swine health, such as porcine respiratory disease complex (PRDC) and porcine epidemic diarrhea (PED). Biosecurity is important both to reduce the risk of disease introduction and also to prevent or reduce transmission within infected herds. Although no systematic reviews on the efficacy of swine biosecurity practices were identified, a narrative review of swine biosecurity practices, with an emphasis on control of *Salmonella* spp., provided an overview of external and internal biosecurity practices (Andres & Davies, 2015). Some recommendations, such as distancing between farms, are only possible during new barn construction. Other external biosecurity practices included controlling access of vehicles and personnel, selecting replacement animals from farms with similar or higher health status, and isolating replacement animals, if feasible. Internal biosecurity recommendations included all-in all-out animal flow, pest control, and cleaning and disinfection. The authors noted that not all recommendations were directly supported by peer-reviewed studies and thus need to be considered as “best practices” to prevent disease, rather than evidence-based recommendations.

Another narrative review also described recommendations for biosecurity related to reducing risk when external sources of semen or replacement animals were used, implementing barrier measures for people and vehicles entering the premises, and layout of farm buildings to limit possible transmission from feed and other suppliers (Alarcón et al., 2021). Boeters et al. (2023) conducted a systematic review evaluating the impact of interventions relevant to endemic respiratory disease in pigs. Of the 35 studies included in the review which evaluated interventions, most (24/35) identified a positive economic impact following the application of the intervention, with 3 and 4 studies reporting a negative impact and a neutral impact, respectively. Most (24/35) of the interventions studied were vaccines, however, using management strategies such as nursery depopulation (n = 2 studies) and not mixing litters after weaning (n = 1) were also associated with lower levels of respiratory disease in pigs.

Aquaculture. A recent review of best practices for biosecurity and disease management for marine aquaculture in waters in the U.S. found that common features for disease management and biosecurity for shellfish, finfish, and seaweed/macroalgae include appropriate stock selection, incoming water quality and security, quarantine, disinfection and decontamination, health and pathogen surveillance, and environmental monitoring (Rhodes et al., 2023). In addition, each aquaculture sector has its own set of specific biosecurity needs (Rhodes et al., 2023).

Maulu et al. (2021) completed a systematic review of 126 studies that evaluated the prevention and control of streptococcus in tilapia culture, many of the principles of which may be similar among different pathogens. Water quality, including iron, osmotic strength, dissolved oxygen pH, salinity, and temperature, as well as poor farm management practices, including poor nutrition, high stocking density, and overfeeding were associated with fish stress, making the fish more vulnerable to disease. Dissolved oxygen is a critical component to water quality as it is often the first limiting factor for fish growth and welfare. Rapid temperature changes can also lead to increased disease. Specific to streptococcus, high salinity, high ammonia, and very high water clarity can increase susceptibility to infection (Maulu et al., 2021).

Biosecurity in aquaculture can be negatively impacted by region-specific issues in the US, such as hurricanes, petroleum pollution, harmful algal blooms, wildfires, and pesticides (Rhodes et al., 2023). A review done in the UK identified these and other issues which pose challenges for the design and implementation of biosecurity strategies and protocols in aquaculture, including using healthy seed, emergency preparedness and response, diagnostics, microbial management at the production level, disease and pathogen surveillance, trade in aquatic species, policies and regulatory framework, welfare, research and technology development, AMR, non-conventional ways of pathogen transfer, and Progressive Management Pathway (Subasinghe et al., 2023). Conversely, the potential negative environmental impacts of biosecurity interventions also need to be considered (Aly & Fathi, 2024). Innovative technologies such as sensors and artificial intelligence can improve biosecurity efficiency (Aly & Fathi, 2024) and potentially mitigate some of these impacts.

5.1.2 Biosecurity: Canadian Perspectives

Biosecurity programs have long been an important component of farm management across all Canadian commodity groups. Canadian commodity groups, government organizations, and veterinary regulatory bodies are interested in continually improving biosecurity and management practices and are actively working towards this goal. Animal Health Canada has created an excellent online resource for identifying biosecurity resources in Canada (https://animalhealth.ca/biosecurity-index/). This searchable database provides links to biosecurity resources for commodity groups that can be sorted by species, region, or lead organization.

To illustrate the breadth and variety of resources that are available, the following list highlights examples of national and provincial resources for biosecurity information, using swine as an example:

- Canadian Food Inspection Agency: National Farm-Level Biosecurity Planning Guide Proactive Management of Animal Resources (all commodity groups)
- Canadian Association of Swine Veterinarians
- Canadian Pork Council
- National Farmed Animal Care Council
- Small Farm Canada
- Provincial Pork Organizations (Alberta, BC., Manitoba, New Brunswick, Nova Scotia, Québec, Saskatchewan)
- Provincial Agriculture (Manitoba, Newfoundland, Ontario, Québec, Yukon)
- Biosecurity Nova Scotia, Farm Safety Nova Scotia
- Ontario Livestock and Poultry Council, Swine Health Ontario
- Farm Food Care PEI,, PEI Swine Emergency Response Team
- Ontario Veterinary Medical Association
- Prairie Swine Centre

Despite the availability of these resources, participants in the CAHS cross-Canadian virtual engagement sessions have commented that the diversity within livestock industries and the need for strategies that meet the varying needs of different producers presents a challenge. For instance, the beef industry includes multiple production stages (e.g., cow-calf, stockers, feedlot cattle) that involve different biosecurity approaches. Even within a sector, there may need to be different biosecurity practices and levels of support and education for commercial versus small holder operations or based on geographic location. In addition, management changes have to be economically and environmentally sustainable to be implemented (CAHS Virtual Engagement Finding, Round 1).

5.1.3 Biosecurity in Other Countries and Jurisdictions

Biosecurity has been reported to have played a fundamental role in the international jurisdictions that have been successful with AMS. In particular, biosecurity was described as having been critical to reducing the need for AMU by reducing disease pressure.

The European Union. Biosecurity has been promoted as central to the EU as the EU harmonized regulations and coordinated actions to address AMU across member states. In 2022, new EU legislation prohibited the routine use of antimicrobials in farming; this restriction included preventative group treatments (Alliance to Save our Antibiotics, 2020). Routine use of antimicrobials in food-producing animals refers to the regular or systemic administration of antimicrobial substances (such as antibiotics) for purposes other than treating specific infections. Regulation (EU) 2019/6 on Veterinary Medicines and Regulation (EU) 2019/4 on Medicated Feed includes a ban on the prophylactic use of medicated feed containing antimicrobials, requiring that “antimicrobial medicinal products shall not be applied routinely nor used to compensate for poor hygiene, inadequate animal husbandry, or lack of care or to compensate for poor farm management” (Article 107.1 of Regulation (EU) 2019/6).

In practice, this set of measures across the EU directs producers to improve animal husbandry and welfare, making biosecurity the front-line defense against the introduction and spread of pathogens between and within farms (European Environment Agency, 2024). To support producers in this task, the EU provides guidelines for feed and ingredient manufacturers to develop biosecurity plans, which cover various stages of the manufacturing process to prevent contamination and ensure compliance with biosecurity standards (American Feed Industry Association, 2019). In 2016, the European Union adopted the ‘Animal Health Law’ which required producers to ensure that their production operations received regular animal health visits from a veterinarian. This was to be implemented in all EU countries by April 2021 to improve disease prevention through enhanced biosecurity and early disease detection; however, this was only implemented in 23 EU countries (Federation of Veterinarians of Europe, 2024).

As a key informant from the EU noted, governments may not be the best entity to lead biosecurity initiatives. Farmer and veterinarian associations play a significant role in educating and implementing better management practices. However, government funds could support these efforts, as incentives are crucial to motivate farmers to adopt new practices. Without incentives, farmers may resist additional regulations due to the already extensive rules they must follow regarding animal welfare, environmental impact, and other concerns (Key Informant Interview, representing the Italy/European lens).

Biosecure, an ongoing EU-funded project, was established to support livestock farming decision-makers in implementing evidence-based, cost-effective, and sustainable biosecurity management (Biosecure, 2023). Biosecure’s implementation will involve university-led evidence checks on biosecurity practices to prevent infection and the spread of disease in livestock, and also evaluate their socioeconomic impact.

The European Green Deal also supports farmers in improving biosecurity as part of its broader commitment to sustainable agriculture and environmental health (European Commission, n.d.). Horizon 2020 European Green Deal committed €1 billion under 8 thematic areas that aligned with other strategies, including Farm to Fork and the Biodiversity and Ecosystems (European Commission Directorate-General for Research and Innovation, 2020). For example, the Green Deal prioritizes research into sustainable farming practices, including biosecurity measures, through funding programs like Horizon 2020 European Green Call (European Commission, n.d.). The Green Deal also prioritizes training and Advisory Services, so that producers are provided with training and education on biosecurity best practices through national and EU-level programs (Tridge, 2025).

The Netherlands. In the Netherlands, animal husbandry became the subject of public debate around 2008 when regulations were put in place to reduce the use of antimicrobials (Scherpenzeel et al., 2018). Implementing effective biosecurity measures was necessary for producers to adapt to the regulations and meet the national targets to reduce AMU. A ban on the preventive use of antimicrobials, such as applying blanket dry cow treatment, meant that alternative measures such as SDCT (selective dry cow therapy) were implemented (Scherpenzeel et al., 2018). As one key informant from the Netherlands said: "The one-to-one relationship (in the Netherlands) is continuous, with monthly farm inspections and yearly updates to farm health and treatment plans" (Key Informant, Netherlands).

One of the recommended priorities for action adopted in the Netherlands as part of their national strategy was to: "Improve biosecurity practices by implementing a nationwide plan to ensure good animal husbandry and biosecurity best practices and application are regularly assessed." (Government of the Netherlands, 2022). A number of actions were implemented specifically as part of this strategy, including applying a biosecurity plan for livestock farming sectors, beginning with a pilot project for farm-specific biosecurity plans for the poultry sector, and reducing zoonotic risks by reducing the transport of animals. Other basic biosecurity measures taken by Dutch producers which support the national strategy are incorporated into the rules under the private Integrated Chain Management (ICM) systems in the various sectors. Compliance with these rules is guaranteed by an independent certification body (e.g. presence of a hygiene barrier, showers and dedicated boots and overalls for visitors). Other biosecurity measures are set out in regulations (e.g. rules regarding the cleaning and disinfection of cattle trucks).

Denmark. In Denmark, integrating biosecurity measures with comprehensive farm management strategies was endorsed as part of "greater efforts to prevent infections" to reduce AMU in food-producing animals (Denmark Ministry of Health, 2017). The Danish Veterinary and Food Administration's National Action Plan for Antibiotic Resistance in Production Animals and Food (2021-2023) promotes greater biosecurity and hygiene measures within animal production. This includes specific guidelines and training for handling livestock to prevent the spread of resistant bacteria such as MRSA (Ministry of Food Agriculture and Fisheries of Denmark & Danish Veterinary and Food Administration, 2021). Producers have also received government support to help with herd-specific management programs (Denmark Key Informant Interviews). This government support is an example of a concrete action taken by the government that has aided in implementing enhanced management and biosecurity. Denmark emphasizes biosecurity and equal regulations for all producers; the collaboration between producers, veterinarians, and the government is key to managing and reducing AMU while maintaining animal health and welfare (Denmark Key Informant Interviews).

As an aside, although not extensively investigated, the prevalence of livestock-associated LA-MRSA seems to be low for the general population in Canada (Golding et al, 2010). A 2008 study on 20 pig farms in Ontario identified a high LA-MRSA colonization prevalence on 9 farms and LA-MRSA colonization prevalence in 5 pig farmers. Indistinguishable strains were found in pigs and pig personnel on all five farms with a colonized human (Khanna et al., 2008).

Australia. Australia relies heavily on supporting biosecurity to minimize the need for AMU (Commonwealth of Australia, 2023). This is done in part through Farm Biosecurity, an online hub that is part of Australia's Farm Biosecurity Program, and a joint initiative of Animal Health Australia (AHA) and Plant Health Australia (PHA) managed on behalf of members. This initiative provides information and resources on livestock and crops, including videos, tools, manuals, and a biosecurity planner and app to help producers manage biosecurity on their farms. This is similar to resources available to Canadian producers, although in Canada, initiatives in this area are shared by industry groups or provinces, as opposed to being uniformly applied at the national level. The program aims for promotion of biosecurity at the regional level through "broad engagement of the community, understanding the region's vulnerability, the source and nature of threats, knowledge of the skills base and resources available to the region, and a commitment from stakeholders to implement biosecurity measures, surveillance and reporting" (Farm Biosecurity, n.d.).

Key finding 6

An essential element to improving AMS is having evidence-informed, effective and sustainable management and biosecurity (infection prevention and control).

- Countries that have implemented strong regulations to restrict AMU have reported enhanced biosecurity and animal management; these were described as essential to successful AMU reduction without impacting animal health and welfare.
- In Denmark, Italy, Australia, EU and other jurisdictions, the government has taken steps to financially support biosecurity and animal management programs.
- International experience might be valuable, especially where there are similarities between Canadian production practices and those in other countries.
- There is evidence for efficacy - but it is scarce in the literature and studies often evaluate outcomes other than AMU.
- Biosecurity has many objectives (e.g., reducing AMU, preventing disease entry including exotic diseases, farm security, etc) and biosecurity practices tend to be based on plausibility rather than evidence.
- Commodity groups in Canada are interested in improved management practices for infection prevention and control. However, Canadian producers report that changes have to be economically and environmentally sustainable (CAHS Virtual Engagement Finding).

5.1.4 Gaps: Biosecurity

Biosecurity is a major pillar to support AMS efforts; however, there is very little high quality literature (specifically randomized controlled trials and meta-analyses of randomized controlled trials) in this area, particularly research that also examines the economics and sustainability dimensions. Publicly available evidence based on strong study designs is needed to identify best practices for biosecurity, both internal and external, across and within different sectors of all commodity groups.

The results of published literature on biosecurity are not always relevant to a Canadian context due, for example, to differences in geography, production systems, regulatory context, and industry structure. Beef industries are often very different across regions with respect to herd size, access to veterinary care, intensive vs extensive production practices, disease risks, and feasibility of potential interventions. In some European countries for example, there are a larger number of small farms with different density and disease pressures. In Canadian swine, there are also differences in disease pressures and regulatory environment between the provinces; thus, one size may not fit all, even domestically.

Application barriers to biosecurity. Application barriers exist for biosecurity and management. These include variable recognition of the importance of biosecurity and management in animal health (Power et al., 2024; Delabbio et al., 2005). In Canadian dairy operations, producers are motivated or deterred from biosecurity application for many reasons, including perceived value, disease risk, and financial incentives or deterrents (Power et al., 2024). Owners and managers of finfish operations in Canada and the USA were supportive of biosecurity programs in general, but had different beliefs about which diseases were of greatest concern, had different perceptions as to which activities were associated with the greatest risk of disease transmission, and which biosecurity practices were the most practical and effective (Delabbio et al., 2005).

Adoption of best practices for biosecurity varies across farms within and among commodity groups. A recent Canadian study demonstrated that many important biosecurity practices were not implemented on Canadian dairy farms (Denis-Robichaud et al., 2019). For example, biosecurity measures intended to minimize the spread of infection were not widely adopted; the majority of survey respondents at least occasionally housed sick animals in their calving pens and one-quarter of the open herds had no strategy for introducing new herd additions. In addition, less than 15% of the respondents reported having measures in place to limit or control farm visitors. A study on poultry farms in Québec also found many biosecurity protocol deviations, including non-compliance with practices intended to separate clean and dirty areas of the barns, failures to change boots or coveralls and to use foot baths, inadequate handwashing, and failures in recording in visitor logs (Racicot et al., 2011). Issues related to adoption and compliance with best practices for biosecurity were also raised in the CAHS Cross-Canadian virtual engagement sessions as being relevant across the commodity groups.

Reasons for non-compliance with biosecurity practices are not definitively known, but may include lack of training, lack of accountability for non-compliance, lack of understanding of the potential consequences of non-compliance, lack of communication or use of non-optimal communication methods on the importance of biosecurity, lack of social environment/social cues that promote biosecurity practices, lack of time, lack of incentives, and apathy towards risks associated with non-compliance, and increased situational uncertainty (Amalraj et al., 2024; Merrill et al., 2019; Trinity et al., 2020).

An additional consideration is the cost of biosecurity measures, both real costs and opportunity costs. Economic evaluations of biosecurity are rare in the literature. However, in a 2-year cohort study of 95 specific pathogen-free dairy herds in the Netherlands, herds that maintained a closed system were less likely to experience introductions of infectious diseases (van Schaik et al., 2002). Closed systems were defined as farms with no direct contacts with cattle from other farms and provision of protective clothing to professional visitors. An economic evaluation by the same authors found that closed farms had lower costs for veterinary services, lower average age at first calving, and a higher birth rate per 100 dairy cows, resulting in an increased net profit (van Schaik et al., 1998). While this example may not be directly relevant to the Canadian dairy context, it does illustrate that biosecurity practices can have multiple benefits and may be cost effective to implement and maintain.

Improving biosecurity application requires a combination of approaches, including on-farm education and awareness for producers, identification of the behavioral drivers of change, development of strategies for effective communication between veterinarians and producers, and potential government incentives. As an example of the latter, the governments of Canada and Ontario invested up to $7.5 million through the Sustainable Canadian Agricultural Partnership (SCAP) to create a cost-sharing program to help producers adopt biosecurity measures, entitled: the Biosecurity Enhancement Initiative (BEI) (Farmtario Staff, 2023). Such an example is similar to approaches taken by other countries in our international case studies to support adoption of biosecurity measures.

Biosecurity is essential to disease prevention and control and is an important component of AMS. Commodity groups, government organizations, and veterinary regulatory agencies in Canada have developed educational materials for producers and veterinarians. Many of the international key informants stressed that biosecurity and management were key to reducing AMU without negatively impacting animal health and welfare, and that changes to AMU needed to go hand in hand with enhanced biosecurity and management. However, in many cases, biosecurity practices are recommended based on plausibility, rather than evidence of effectiveness. Additional high quality research is needed to target specific biosecurity and management practices relevant to the Canadian commodity groups, to assess economic viability of specific biosecurity practices, and to identify the behavioral drivers of compliance with biosecurity. Countries that have successfully implemented enhanced biosecurity programs with program audits have specific organizations dedicated to this task, as well as government cost-sharing models to support the application of biosecurity and management across the relevant sectors.

Key gap 6

The application of management and biosecurity practices varies among farms and the limited available research does not address the needs of specific commodities, production scale and regional evidence for cost-effectiveness

- High quality literature on management alternatives is scant, in particular randomized controlled trials and literature that examines economic feasibility and are of relevance to the Canadian context.
- More research is needed to identify best practices for biosecurity across and within different sectors of commodity groups; highly variable farms across commodity groups and regions of Canada mean that one size will not fit all and the research needs to reflect this variability.
- Biosecurity approaches used in other countries may not always be relevant in the Canadian context due to differences in industry structure and disease pressures. In Canada, there are also differences in disease pressures and regulatory environment between the provinces.
- Barriers to application of improved biosecurity and management include variable recognition of its importance, costs of changing management practices, and real or perceived impacts on sustainability and productivity.

Related Action in the Pan-Canadian Action Plan

- Under the IPC pillar: "Support the increased implementation of enhanced IPC, biosecurity, and food safety protocols across the agriculture and agri-food sectors, prioritizing sound animal husbandry, access to veterinary care, and access to additional health and nutritional aids to promote animal health."

5.2 Vaccines

Vaccination is used to prevent infection, reduce the severity of disease, and eradicate infectious diseases globally. Vaccination was ranked highly for perceived feasibility and effectiveness in an expert ranking exercise involving 111 pig health experts from Belgium, Denmark, France, Germany, Sweden and Switzerland (Postma et al., 2015). Although vaccination can reduce susceptibility to infections, thus reducing AMU, as highlighted below, vaccination alone is not a sufficient strategy for control of disease.

Many different types of animal vaccines are available for use in food-producing animals, including: 1. live and modified (attenuated, or recombinant) live vaccines; 2. inactivated vaccines; 3. differentiating infected from vaccinated animals (DIVA) vaccines; and 4. autogenous vaccines. Vaccines support passive transfer of specific immunity, such as vaccination of pregnant animals as a means to protect newborn animals from specific diseases that occur early in life, or induction of a specific adaptive immune response to the vaccine target. Appendix 3 includes more information on types of vaccines and immunizations.

5.2.1 Literature on Vaccines for Different Commodities

Vaccines are available for some bacterial diseases, and for viruses which may predispose animals to bacterial diseases that require antimicrobials to treat. While there are trials to evaluate the effectiveness of many vaccines, systematic reviews that synthesize the literature across all available trials have only been conducted for a few vaccines. In some cases, there is strong evidence of effectiveness. However, for many vaccines, the evidence for effectiveness is not compelling. This may reflect the appropriateness of the vaccine as a match for field strains of the agent, infection pathways and pathogenesis, or the timing and application of these vaccines in the field. For example, it has been challenging to develop an effective vaccine for Porcine Reproductive and Respiratory Syndrome because of strategies for evading the immune system employed by the virus, along with the antigenic diversity found among field strains (Kimman et al., 2009). For some vaccines, evidence is ambiguous because of limitations with the trials reported in the peer-reviewed literature, including lack of replication of specific interventions and outcomes, and issues with risk of bias in the design or conduct of the studies. This will be discussed in the sections that follow.

Beef cattle**.** Bovine respiratory disease (BRD) is one of the most common reasons for AMU in feedlot cattle (Otto et al., 2024). Based on a systematic review and network meta-analysis, there is currently insufficient evidence to demonstrate that vaccines administered at or near arrival at the feedlot reduce the incidence of BRD (O'Connor et al., 2019, 14 studies in the meta-analysis). These results are consistent with the findings of a systematic review of vaccine efficacy specifically against *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus* *somni* in North American beef, dairy, or veal cattle (Capik et al., 2021). The outcomes evaluated in that study included BRD-related morbidity, mortality, or postmortem lung lesions; however, the populations in the 5 trials identified were too heterogeneous to allow summarizing the individuals study results. Challenges to effectiveness at feedlot arrival could include the stress of transport and commingling (Chen et al., 2022).

In contrast, in a systematic review and meta-analysis of vaccines administered in the lower-stress environment of cow-calf herds, vaccination appeared to reduce BRD. However, as most of the studies included in this review were challenge studies (animals were artificially exposed to virus, which can overestimate efficacy estimates) it is difficult to draw conclusions about vaccine efficacy (Theurer et al., 2015, based on 30 studies). More studies need to be conducted under field conditions with naturally infected cattle. One study of naturally infected calves indicated that calves preconditioned prior to arrival at feedlot were 2.8 times less likely ($P<0.0001$) than non-preconditioned calves to develop BRD within 40 days of arrival at the feedlot (Mijar et al., 2023). The preconditioning protocol spanned 5-7 months and consisted of: 1. vaccinating for common BRD pathogens and clostridial disease within 60 days of birth, growth implants, and castration; 2. At 3.5 - 5.5 months of age, calves were fence-line weaned for 5 days, with auditory and visual contact but no physical contact between calves and dams, and given booster shots during the 5 day weaning period; 3. being transported to a pasture pen located 5 km away and remaining in the pasture-pen on feed and water for 45 days. After 5–7 months, calves were transported to the feedlot.

Finally, a systematic review of vaccines against bovine infectious keratoconjunctivitis, commonly known as pinkeye (another disease associated with AMU in cattle), did not find evidence of effectiveness (Burns & O'Connor, 2008, based on 38 trials that used randomization and blinding).

Dairy cattle. Mastitis is the most common reason for AMU in dairy cattle and is caused by a variety of different bacteria (de Jong, Creytens et al., 2023). Available vaccines target different bacterial species (Rainard et al., 2021). The complex physiology of the mammary gland makes generating a protective immune response a challenge, and it is not as easy to prevent mastitis as it is to prevent some other diseases due to the localized nature of the infection. Milk production dilutes antibodies in the mammary glands. A recent narrative review concluded that mastitis vaccines have, to date, shown mixed results in lowering the incidence and severity of infection, and no vaccines are currently available that would prevent all types of mastitis (Rainard et al., 2021). Thus, vaccines are not comprehensive enough to consistently prevent cows from developing mastitis.

Neonatal diarrhea in calves is also associated with AMU and commercial vaccines have been developed for administration to either dams or calves to help prevent neonatal diarrhea. In a scoping review on vaccination for neonatal diarrhea, 12 controlled trials (in dairy or beef calves) evaluating the effectiveness of commercial vaccines were reviewed. Although 3 of the trials showed benefit of vaccination for reducing incidence or treating calf diarrhea, the opposite effect was found in 3 trials, no differences was found in 4 trials, and no statistical analysis was reported in 2 trials. Thus, the efficacy of vaccination for neonatal diarrhea is unclear (Maier et al., 2022).

Swine. A systematic review and network meta-analysis of bacterial vaccines against swine respiratory disease, reported an insufficient body of evidence to determine relative efficacy of these vaccines, attributed to a lack of replication of interventions and of outcomes, small sample sizes, and inadequate reporting in many individual studies. Most studies did not account for housing of pigs in pens, thereby potentially overestimating the statistical significance of the results. Thus, better quality data, rather than just more data, are needed to determine efficacy (Sargeant, Deb et al., 2019, based on 146 studies).

Despite methodological concerns with the studies done, there is some evidence that certain swine vaccines work. A network meta-analysis comparing 4 commercially available PCV-2 vaccines found that vaccination was associated with higher average daily gain compared to no vaccination (da Silva et al., 2014), although AMU was not evaluated as an outcome. A meta-analysis of 58 trials in 44 publications showed positive benefits of both live attenuated and inactivated vaccines for reducing colonization and shedding of *Salmonella* spp. in vaccinated animals, although neither clinical disease nor AMU were evaluated as outcomes in this review (de la Cruz et al., 2017).

Poultry. There is a dearth of published trials on efficacy of commercial poultry vaccines (Hoelzer et al., 2018). In a systematic review and meta-analysis, Paudel et al., (2024) based on 39 controlled trials, challenge studies and observational studies) found that vaccination against avian pathogenic *E. coli* reduced mortality in broilers, but the authors highlight that most of the evidence came from studies where birds were experimentally (as opposed to naturally) infected.

A recent systematic review and meta-analysis of *Campylobacter* and *Salmonella* vaccines indicated that both of these reduced infection, but inadequate reporting of study methods and publication bias limited conclusions (Castelo Taboada & Pavic, 2022, based on 13 *Campylobacter* and 19 *Salmonella* primary research studies). Consideration of reports such as this where study methodologies were limited highlights important limitations in the existing literature, which need to be addressed to build an evidence-based body of literature for decision-making.

Effective vaccines against enteric pathogens, such as *Clostridium perfringens* (the cause of necrotic enteritis in broilers) are a challenge (Hoelzer et al., 2018). Clostridial vaccines tend to require multiple doses, which isn't feasible in commercial production conditions, and effective vaccines require a mix of antigens. A recent narrative review highlights the progress and challenges for necrotic enteritis vaccination (Shamshirgaran & Golchin, 2024).

Aquaculture. In a systematic review of 23 articles on *Aeromonas hydrophila* vaccination in fish, the authors reported that oral delivery of recombinant vaccines could be of value, but currently are only useful for investigating pathogenicity (Mzula et al., 2019). The bacteria *Tenacibaculum maritimum* causes a condition called mouthrot, which is responsible for most of the AMU in farmed British Columbia (BC) salmon. However, there are currently no commercially available vaccines for mouthrot in Atlantic salmon (Wade & Weber, 2020). A recent narrative review (Miccoli et al., 2019) highlighted a lack of scientific data supporting efficacy of experimental vaccines against viral and bacterial pathogens infecting farmed marine finfish. Another recent narrative review discussed development and application of vaccines in aquaculture, but did not discuss the impacts on AMU (Mondal & Thomas, 2022). Thus, although there is a body of literature on vaccines in aquaculture, there appears to be a need for research (controlled trials followed by systematic review of trials) for fish vaccines which include AMU as an outcome.

Overall, vaccines work best when used according to manufacturer's recommendations and in the context of optimal management and biosecurity practices. Vaccines alone are not sufficient to compensate for inadequate herd management and biosecurity.

5.2.2 New Technological Developments in Vaccines

Some new progress in vaccine development and production could be promising to the food-animal sector in the long term. While traditional vaccine design identifies protective antigens for microbial agents, recent technological developments allow vaccines to be designed through a reverse vaccinology approach. New technology for rational antigen discovery and advances in knowledge of activation of innate and adaptive immune responses now allow for vaccine formulations with more focused, stronger immune activation. However, the development of these vaccines is expensive and their approval process time-consuming, which means that it might be too soon to rely on these as a disease prevention strategy (European Medicines Agency & European Food Safety Authority, 2017). In the future, vaccines that protect against more than one pathogen may be introduced, i.e., either as multivalent or as pan-vaccine-type to prepare for future emerging disease. Much of this will be based on platform technologies - RNA, subunit, or viral vectors - that allow rapid plug-and-play and can be produced domestically in Canada. The creation of such platforms requires computational antigen design and will have to be based on surveillance and large data sets. Therefore, these technologies will likely involve artificial intelligence in the future (Personal Communication, Key Informant).

Key finding 7

Vaccines can be an important tool for disease prevention and control to be considered in addition to livestock and poultry management and biosecurity practices.

- Disease prevention through vaccine use is important to reduce susceptibility to infections or disease severity, and to potentially reduce AMU.
- Vaccines are available for some bacterial diseases and for viruses which predispose animals to bacterial diseases that can require AMU.
- There are published trials evaluating the effectiveness of many vaccines, although systematic reviews have only been conducted for a few vaccines. Systematic reviews provide stronger evidence, because they combine results across multiple studies.
- In some cases, there is evidence of effectiveness for the disease in question; however, in many cases, the evidence for effectiveness is not compelling. This could reflect limitations in the vaccines or how these vaccines are used in the field. Evidence is sometimes also ambiguous because of methodological issues with the trials that have been publicly reported. Most studies do not evaluate the ability of vaccination to reduce the use of antimicrobials.
- Vaccines work best when used according to manufacturer's recommendations and in the context of optimal management and biosecurity practices.
- Additional work is needed to develop more effective vaccines and to identify best practices for vaccine use.
- Vaccines are not a replacement for inadequate management and biosecurity.

5.2.3 Gaps

Vaccines are an important tool to support stewardship efforts; however, there is a need for better understanding of vaccines. There is currently a lack of evidence for efficacy for some vaccines under current commercial use. There is also a need to optimize the use of vaccines, for example, BRD vaccines need to be used prior to arrival at the feedlot instead of or in addition to at the time of feedlot entry, and feedlots need a method of reliably determining whether calves have been vaccinated, with which products and when. This being said, there is no strong evidence on best practices for BRD vaccine use in nursing calves (Lazurko et al., 2023).

There are some important diseases for which vaccines have not been developed (e.g. bovine leukosis, various bacterial diseases) or diseases where available vaccines are not routinely recommended as they are not considered to be effective or cost-effective (e.g. the vaccine for *Histophilosis* in beef is not considered to be adequately effective for preventing disease in the feedlot). Furthermore, some diseases continue to evolve so that vaccine efficacy becomes reduced over time or where efficacy is farm-specific (e.g. Porcine reproductive and respiratory syndrome).

Finally, there is a need to understand the social determinants and motivators for vaccine uptake and use. There is limited research describing motivators and barriers to vaccine use in food-producing animals in the Canadian context. Ultimately, the decision to vaccinate or which products to use rests with the producer. In a qualitative study involving 24 dairy producers from the UK, producers considered veterinarians to be the most important influence on decision-making regarding vaccination (Richens et al., 2015). Producers may be motivated to vaccinate if they perceive that vaccination will prevent production loss or if vaccination is recommended by their veterinarian; however, producers may be reticent to vaccinate based on vaccination costs and perceived cost-benefit, current absence of the target disease in their herd or presumed low infection risk, or because of a negative experience with previous vaccines (Elbers et al., 2010). In a recent study of 131 Canadian cow-calf producers, the top three factors that producers considered when deciding what vaccines to use on their operations were the importance of disease in the herd, economic benefits of using the vaccine, and potential to minimize treatment rate and AMU (Lazurko et al., 2023). Producers also independently identified advice from their veterinarian as a top influencing factor in vaccine choice. Their top three reasons for choosing whether to vaccinate suckling calves were convenience, need for adequate labor to handle calves, and history of calf health problems.

5.2.3.1 Access to Vaccines

There are perceived barriers to accessibility of effective vaccines which have been deemed by the CAHS Virtual Engagement participants as an important issue impacting the commodity groups. The concerns include delays in the approval of vaccines and the high cost of licensing and labeling, and that vaccines conditionally approved in the USA cannot be used in Canada. These concerns were reported during the CAHS cross-Canadian virtual engagement process. It was stated in the virtual engagement (round 1) that preventative medicine should include vaccination programs and that more research on, and consideration of, vaccines in animal health programs is needed. Another participant reiterated this in round 2 of the virtual engagement:

"It's hard to change behaviour if we don't have practical, cost-effective alternatives to antimicrobials to prevent, control, and treat diseases." (CAHS Virtual Engagement Participant, Round 2)

However, these concerns may not be substantiated from the perspective of the Canadian regulators. The Canadian Centre for Veterinary Biologics at CFIA conducts an internal review of performance standards and has indicated that they are meeting their standards. In a presentation to the Canadian Animal Feed and Health Products Engagement Committee, CFIA indicates that they are meeting their service standards in terms of average number of days to perform initial reviews (Canadian Food Inspection Agency, personal communication, January 20 2024). CFIA also upholds that the fee for a veterinary biologic submission is low in Canada as compared to other jurisdictions and only recovers a small fraction of the cost of regulatory approval (CAHS Key Informant). Furthermore, while conditional licenses do not exist under Health of Animal Regulations, the Canadian Centre for Veterinary Biologics accepts new product dossiers for 'conditional approval'. The process and requirements are similar to conditional licensing in the US, where conditional licenses are authorised under "Title 9-Animals and Animal Health" in the US Code of Federal Regulations ("9 CFR") and are used to meet an emergency condition, limited market, local situation, or other special circumstance. The primary access concern from a regulatory perspective is not having sufficient incentives and effective vaccines for producers to use (CAHS Key Informant).

The fact remains that perceptions of a lack of access to veterinary biologics, including vaccines, can be a limiting factor to producers' ability to reduce AMU. Proposed approaches raised by virtual engagement participants included creating a process where inactivated vaccines that are conditionally approved in the USA can be made available for use in Canada, and re-evaluating restrictions on the use of autogenous vaccines. Some vaccines that are conditionally approved in the USA are unlikely to be fully approved due to technical issues involving recreation of the target disease.

Autogenous vaccines can be created to specifically target the strains on pathogens located on a farm. Therefore, this approach could be useful as a targeted intervention to prevent diseases, given appropriate consideration of expected quality control and safety standards (CFIA, 2023a). There also have been efforts to create autogenous regional vaccines for diseases like influenza in swine in Canada, where there is a lot of strain diversity and regional spread (The Pig Site, 2023; Farmtario, 2020).

Vaccines are potentially important elements to support stewardship and to ensure that producers have viable alternatives to the preventative use of antimicrobials to keep animals healthy, although they are not sufficient to compensate for inadequate herd management and biosecurity. Although commodity groups support the use of vaccines, the evidence of effectiveness varies among disease targets and commodities. In some cases, this may be related to the way that vaccines are used under current production systems or because the strains used in the vaccines are not protective for the stains circulating among farms. In other cases, the research has not been conducted or the research approach is not sufficient to build a body of evidence because of issues such as lack of replication of interventions and outcomes, and risk of bias in the study designs used.

Key gap 7

Major gaps exist in the development and application of vaccines and understanding of their efficacy.

- There is need for evidence on how to optimize the timing of the administration of vaccines to maximize effectiveness.
- There are some important diseases for which vaccines have not been developed or diseases for which available vaccines are not routinely recommended as they are not considered to be effective or cost-effective.
- There also are diseases that are evolving where vaccine efficacy is reduced over time.
- Commodity groups are concerned that barriers to accessibility of effective vaccines limit producers' ability to reduce AMU.
- Regulatory concerns include delays in the approval of vaccines and other alternative biologicals, and the high cost of licensing and labeling.
- Vaccines conditionally approved in the USA cannot be used in Canada.
- There are regulatory restrictions on the development and use of autogenous vaccines.
- There is a need to understand the social determinants and motivators for vaccine use.

Related action in the Pan-Canadian Action Plan

- Under the Research and Innovation pillar: "Develop and implement economic and/or regulatory incentives to support innovation and facilitate sustainable access to new and existing antimicrobials, diagnostics, and alternatives to antimicrobials.*"
- Under the IPC pillar: "Support the increased implementation of enhanced IPC, biosecurity, and food safety protocols across the agriculture and agri-food sectors, prioritizing sound animal husbandry, access to veterinary care, and access to additional health and nutritional aids to promote animal health."

* Note that vaccines are considered as "alternatives to antimicrobials" in the PCAP, whereas in this assessment they are considered separately from other alternative products.

5.3 Alternative Products & Strategies

Using products other than antimicrobials to prevent, control, or treat disease is an attractive alternative to AMU. However, there is no 'magic pill' to replace antimicrobials, and no known alternative products can entirely replace the need for AMU to treat bacterial disease. Some alternative products may be used to support animal health and thus reduce the need to use antimicrobials. Thus the term "alternative product" in this section, and consistent with definitions in the literature, is any substance that can prevent the need for, or be substituted for, antimicrobial drugs (Kurt et al., 2019). These products may be used alone for prevention or treatment of disease or in combination with other products, including antimicrobials. Alternative products, in this sense, can be supplements to food animal management when used in tandem with the other strategies considered in this assessment, such as biosecurity and vaccination.

Overall, the approach to the use of alternative products is highly variable among different commodities, and the literature on replacements in the forms of alternative drugs, supplements, or other approaches is fragmented and variable with no "one size fits all" solutions. Research into the development of effective alternative products need to be prioritized to ensure that scarce research resources are directed to the most promising products or approaches. A framework developed by expert consensus to describe the likely success of a new alternative product included economic viability (development costs versus expected revenue), product risks (such as safety, efficacy, acceptability by producers, veterinarians, and consumers), and product practicality and ease of use (Kurt et al., 2019).

Another framework for prioritizing interventions includes feasibility and cost considerations, but also includes the need to consider biological efficacy (the likelihood that the intervention suppresses AMR emergence, persistence, or transmission) and unintended consequences (both positive and negative) (Noyes et al., 2021). An example of unintended negative consequences was seen with oral use of zinc oxide. Zinc oxide has health benefits when administered to swine; a systematic review and meta-analysis found that diets containing zinc oxide were associated with higher performance and less diarrhea compared to control diets and other forms of zinc (Luise et al., 2024). The dose of zinc was important in influencing pig health, with high supplementation levels (> 1601 ppm) leading to higher performance, lower diarrhea, and better intestinal morphology compared to lower doses. However, in a scoping review of 73 studies, all of the included studies reported a link between heavy metals and AMR (Anedda et al., 2023). Furthermore, most studies (46.5%) established that heavy metals, including zinc, promote the spread of mobile genetic elements and AMR genes and are associated with tetracycline, sulphonamide, beta-lactam, aminoglycoside, and macrolide resistance genes. There are also environmental concerns due to the accumulation of these heavy metals in the environment. As a result of these concerns, the European Union banned the use of high doses of zinc oxide in feed in 2022 (Anedda et al., 2023). Canada is now also limiting the use of zinc oxide in pig feed to 350 ppm, which is similar to the regulations in the EU (Pig Progress, 2021).

The number of practical examples where there is an alternative product available to reduce the need for antimicrobials that are supported by evidence of efficacy is limited for food-producing animals, although this is an active area of research. However, selected examples are presented below to highlight alternative products with evidence for effectiveness and to illustrate the state of knowledge for active areas of research.

5.3.1 Types of Alternative Products

5.3.1.1 Internal Teat Sealants (Dairy Cows)

There is a substantial body of evidence from systematic reviews and meta-analyses that internal teat sealants (usually composed of bismuth subnitrate) are an effective tool in mastitis control (Dufour et al., 2019; Winder, Sargeant, Hu et al., 2019; Pearce et al., 2023, Kabera et al., 2021; Afifi et al., 2023). When different mastitis-related outcomes were evaluated, teat sealants helped prevent new intramammary infections during dry-off and at calving better than antimicrobial treatment (Dufour et al., 2019, based on 18 trials) or no treatment at all. Teat sealants also helped to prevent clinical mastitis in early lactation compared to no treatment (Pearce et al., 2023, based on 13 trials; Winder, Sargeant, Hu et al., 2019, based on 32 trials; Afifi et al., 2023, based on 17 trials). Systematic reviews have also evaluated teat sealants in conjunction with SDCT and concluded these helped prevent mastitis (Pearce et al., 2023; Kabera et al. 2021; Winder, Sargeant, Kelton et al., 2019).

5.3.1.2 Immunomodulation Approaches

Probiotics

Aquaculture. Probiotics are used in aquaculture for growth promotion, immune modulation, and to improve health, as well as to improve water quality, reduce harmful algae, and inhibit pathogens (Todorov et al., 2024, narrative review with no quantification of benefits). As with other commodity groups, the impact of probiotics can be affected by the environment. In particular, in aquaculture, water temperature, salinity, pH, and oxygen levels, as well as other substances present in the water influence outcomes.

Beef cattle. Data in a systematic review of 67 controlled trials (Alawneh et al., 2020) did not conclusively support probiotics as an alternative to antimicrobials to improve health of calves from birth to 1 year of age.

Dairy cattle. Francoz et al. (2017, 2 controlled trials), in a systematic review of lactating dairy cows with clinical mastitis, found no difference between intramammary probiotics and antimicrobials for the clinical or bacterial cure rate of mastitis. A single clinical trial reported that probiotics used intravaginally could lower the incidence of metritis in dairy cows (Deng et al., 2015).

Poultry. In broiler chickens, a meta-analysis of 42 controlled trials found that feeding probiotics caused a significant decrease in concentrations of *Clostridium perfringens*, *Escherichia coli* and other coliforms, *Enterococcus*, and *Salmonella* in the gut; however, there was high heterogeneity among studies and evidence of publication bias (Heak et al., 2018). In a meta-analysis of 17 studies, Hooge et al. (2013) found that a yeast cell wall product significantly improved weight gain, feed conversion, and mortality in broiler chickens compared to a non-active control; there was no difference between controls and birds fed dietary antimicrobials. A systematic review of probiotics given to laying hens (Jha et al., 2020) found positive effects of some probiotics; however, effects varied with bird health, dose of probiotics, food and water quality.

Limitations of evidence for probiotics. A potential issue with using probiotics is that some strains carry AMR genes which could potentially transfer to other bacteria (Tóth et al., 2021; Todorov et al., 2024). While there is evidence that, in some cases, probiotics confer a benefit, reviews highlight the heterogeneity in the reported outcomes. This heterogeneity may be attributed to differences between studies in probiotic strains and combinations of probiotics used, dosages, environmental conditions, and disease pressures. Thus, it is difficult to reach consistent conclusions.

Dietary Acids

Dietary acids (organic or inorganic acids or salts of acids) have been used as additives to feed and/or water for protection against infection, as an alternative to antimicrobials and for growth promotion.

Poultry. A meta-analysis of studies on broiler chickens reported that organic acids (particularly blends of acids) improved feed conversion ratios; however, the acids did not perform as well as antimicrobial feed additives in studies in which birds were experimentally infected with pathogenic bacteria (Polycarpo et al., 2017; 121 studies). In the same meta-analysis, some of the individual challenge studies demonstrated that organic acids reduced viability of were effective against *Campylobacter* (4 studies), *Clostridium* (2 studies), *Eimeria* (2 studies), *Escherichia (4 studies)*, and *Salmonella* (3 studies).

Pigs. A systematic review and meta-analysis of 52 experiments found that compared to a control diet, dietary acids performed better with respect to growth performance, average daily gain, and feed efficiency. However, when compared to a diet containing antibiotics, while feed efficiency was similar, diets with acidifiers performed less well with respect to average daily gain and feed intake (Wang et al., 2022). As with poultry, blends of acids performed better than individual acids.

Dietary Enzymes

Dietary enzymes are biologically active proteins that facilitate chemical breakdown of nutrients to smaller compounds for further digestion and absorption. Dietary enzymes have been used as an alternative to antimicrobials in feed for growth promotion in broiler chickens and pigs. Several meta-analyses have been published for a variety of in-feed enzymes in broilers. Jackson & Handford (2014), in a meta-analysis of 7 trials, found that broilers supplemented with ß-mannanase had improved weight gain and feed conversion compared to controls. A meta-analysis conducted by Swann & Romero (2014) found beneficial effects of a combination of xylanase, amylase, and protease in improving digestibility of crude protein for broilers. A systematic review of studies in broilers found that, in combination with probiotics, dietary enzymes helped reduce *Campylobacter* and *Bacteroides* in the ceca; however, the authors' noted that the studies included in the review involved a limited number of animals in experimental settings (Mekonnen et al., 2024). A systematic review and meta-analysis of 41 studies found that phytase in the diet improved body weight gain and feed conversion ratios in broilers, although health outcomes and AMU were not evaluated (Nuamah et al., 2024).

In pigs, a systematic review of 43 studies found that dietary enzymes improved growth during the weaning, growing, and finishing stages (Aranda-Aguirre et al., 2021). Also in pigs, Torres-Pitarch et al. (2017) completed a meta-analysis of ninety studies reporting the effects of feed enzyme inclusion. They reported that phytase supplementation demonstrated improvements in growth and feed efficiency, whereas enzyme complexes, including protease and mannanase, improved nutrient digestibility. Furthermore, enzyme complexes were found to have an impact on modulating the gut microbiota by increasing *Lactobacillus* spp. and *Bacillus* spp. while reducing *Salmonella* and *E.coli*; however, these effects were described qualitatively within the study. The mechanism of action is unknown and was speculated to be due to enzyme supplementation increasing the availability of specific substrates with prebiotic effect. Although often highlighted as an antimicrobial alternative, limited data exist surrounding the effect of dietary enzymes for the prevention of disease.

Hyperimmune egg yolk antibodies

Chicken egg yolk immunoglobulins are produced from hens which have been immunized with specific pathogens and are intended to provide passive immunity in livestock, poultry, and aquaculture. A systematic review and meta-analysis found that egg yolk antibodies for piglets (22 studies), poultry (7 studies), and calves (6 studies) reduced the risk of bacterial and viral diarrhea; however, there was considerable methodological variation among studies, specifically with respect to dose and formulation of the egg yolk antibodies (Diraviyam et al., 2014). A narrative review of use in aquaculture concluded chicken egg yolk antibodies may have value in controlling various bacterial and viral pathogens in fish and other aquatic animals (Bondad-

Reantaso et al., 2023). Specifically, IgY has been used for the treatment of White Spot Disease (WSD), *Vibrio harveyi* in shrimp, *V. anguillarum* and *Yersinia ruckeri* in rainbow trout, and *Aeromonas hydrophila* and *A. salmonicida* in carp.

Phytogenics

Phytogenic feed additives are natural bioactive compounds that are derived from plants and incorporated into animal feed. A recent systematic review of 77 poultry studies evaluated 83 different plant species, and reported that plant species shown to be effective for prevention and treatment of poultry disease are *Origanum vulgare* (oregano), *Coriandum sativum* (cilantro), *Artemisia annua* (sweet wormwood), and *Bidens pilosa* (part of the daisy family) (Farinacci et al., 2022). Since dosages and composition of the products used can affect outcomes, future primary research needs to employ comprehensive reporting of the specific characteristics of the additive used. Additionally, blinding of the products is difficult or impossible due to the sensory properties of the plants (Farinacci et al., 2022). A systematic review of 78 studies of medicinal plants for piglets and calves found that the most promising candidates were *Allium sativum* (garlic), mentha x piperita (peppermint), and *Salvia officinalis* (sage) to prevent or treat gastrointestinal diseases, and *Echinacea purpurea* (eastern purple coneflower), *Thymus vulgaris* (common thyme), and *Althea officinalis* (marsh mallow) to prevent or treat diseases of the respiratory tract (Ayrle et al., 2016).

5.3.1.3 Trace Vitamins and Minerals

Trace vitamins and minerals are known to be associated with production and reproductive performance. Dietary deficiencies of minerals may also be associated with characteristic metabolic disorders, such as milk fever in periparturient dairy cattle deficient in calcium. Vitamin and mineral deficiencies are also associated with immune system health. Thus, they are important for vaccine effectiveness and deficiencies can predispose to diseases that are treated with antimicrobials. Despite this importance, systematic reviews which evaluate their effectiveness in reducing clinical disease or AMU are uncommon in the literature.

Several narrative reviews have been published that provide an overview of associations between dietary mineral supplementation and animal health. A review of the association of specific minerals and mastitis in dairy cattle highlighted an increased risk of mastitis associated with hypocalcemia, a possible role of magnesium in promoting inflammation, and associations between both selenium and copper and the immune response to bacteria associated with mastitis (Libera et al., 2021). The authors proposed that mineral supplementation could, therefore, be considered a potential auxiliary tool for the treatment of mastitis in dairy cattle.

The use of injectable and dietary trace minerals in newly received feedlot cattle is an area of extensive research, as discussed in a narrative review by Galyean et al. (2022). These authors concluded that mineral supplementation did not appear to reduce BRD morbidity, although they noted methodological concerns with the literature and called for additional research in this area.

Zinc oxide has been widely used as a measure to prevent diarrhea and *E. coli* post-weaning colibacillosis in pigs; a systematic review and meta-analysis of 85 articles found that zinc oxide was associated with less diarrhea compared to control diets and other forms of zinc (Luise et al., 2024). High doses of copper have also been used as a mechanism to prevent gastrointestinal illness in food-producing animals (López-Gálvez et al., 2021). However, there can be substantial concerns with supplementing heavy metals. In a scoping review of 73 studies, all of the included studies identified a link between heavy metals and AMR (Anedda et al., 2023). Furthermore, almost half (46.5%) of studies established that heavy metals promote the spread of mobile genetic elements and AMR genes. Copper and zinc, the main heavy metals evaluated, have been associated with tetracycline, sulphonamide, beta-lactam, aminoglycoside, and macrolide resistance genes. Furthermore, there are environmental concerns due to the accumulation of these heavy metals in the environment. Because of these concerns, the European Union banned the use of high doses of zinc oxide in feed in 2022, and the use of copper compounds in animal feeds has been restricted (Anedda et al., 2023).

5.3.1.4 Bacteriophages

Bacteriophages are viruses that kill bacteria, are naturally derived, and therefore have been considered environmentally friendly (Wong et al., 2024). Bacteriophages can be selected for effectiveness against a single species of pathogenic bacteria, leaving commensal (i.e., beneficial) bacteria in the host untouched (Dec et al., 2020).

Poultry. A systematic review and meta-analysis of 12 studies in which chickens were experimentally infected with *Salmonella* or *Campylobacter* reported that bacteriophages lowered the concentrations of bacteria in tissues or fluids in the first two weeks after treatment, but not subsequently (Mosimann et al., 2021). The effect was greater for bacteriophages given in the feed, as opposed to drinking water or via aerosol spray.

Swine. A systematic review and meta-analysis of 19 experiments in which pigs were artificially infected (challenged), indicated that bacteriophages significantly decreased the concentration of *Salmonella* (but not *E. coli*) in tissues/fluids/feces, with the greatest effect 2 to 4 days (vs < 1 day) after administration of bacteriophages and in piglets, compared to market-weight pigs (Desiree et al., 2021).

Cattle. A recent narrative review concluded there is insufficient evidence to support the use of bacteriophages for feedlot cattle (Cusack, 2024). In another narrative review, there was evidence that bacteriophages may be effective for mastitis in dairy cattle, but few *in vivo* studies have been conducted (Nale & McEwan, 2023). Another narrative review found inconsistent results in using bacteriophages to combat metritis, but some evidence that bacteriophages can reduce clinical signs and mortality from pathogenic *E. coli* in 1-14-day old dairy calves (Dec et al., 2020).

Aquaculture. Bacteriophages have been used in aquaculture to eliminate *Vibrio*, *Pseudomonas*, *Aeromonas*, and *Flavobacterium* (Liu et al., 2022). A narrative review reported that bacteriophages have been successfully employed to lower mortality associated with *Aeromonas* and *Vibrio* infection in fish and crab larvae (Wong et al., 2024). There are no systematic reviews on the efficacy of bacteriophages in aquaculture.

There is substantial research addressing the efficacy of bacteriophages in different commodity groups and for different applications. Much of this research involves the use of experimental challenge models, wherein animals are administered bacteriophage and then deliberately exposed to the target bacteria. An experimental challenge approach is useful for evaluating proof-of-concept, but may not reflect efficacy in field conditions - results from this study design tend to show exaggerated benefit compared to field trials. Additional *in vivo* studies are needed to demonstrate efficacy of bacteriophages against specific pathogenic bacteria under commercial conditions with natural disease exposure. The possible role of bacteriophage in the mobilization and transmission of ARGs in bacteria from animals also needs to be further elucidated (Yang et al., 2020; Pilati et al., 2023).

5.3.2 Genetic Strategies

Genetic improvement to breed for improved resistance to disease is a potentially attractive approach to reduce the need for antimicrobials, but is not yet achievable for many commodity groups. However, in dairy, the High Immune Response (HIR) dairy cow has been implemented by Semex Canada in their Immunity Plus sire program, based on research such as Mallard et al. (2015); and Larmer & Mallard (2017). HIR cows have 19-30% lower disease incidence compared to herd averages, respond better to commercial vaccines, and produce higher quality colostrum, and thus this breed is marketed for higher profitability and lowered costs (Semex, 2014). More recently, breeding for traits such as disease resistance to mastitis has been added into the Semex genetic evaluation program (Semex 2013) and work is ongoing for Johne's Disease, bovine leukosis and calf health (resistance to diarrhea and respiratory disease in young calves). Some of these initiatives may ultimately translate into decreased disease pressure and less need for antimicrobials; however, this is a long term strategy and the potential impact has yet to be evaluated.

While this research is promising, the potential for gains with using breeds of cows that are disease resistant varies based on breeding management practices, current genetic variability in the herd, and variation in environmental conditions, nutrition and management practices used across the industry.

Similarly, the Pig Improvement Company (PIC) is working on developing a pig that is more resistant to Porcine Reproductive and Respiratory Syndrome (PRRS). Considering that most pig farms in Canada do not use pure-bred animals, the availability of this type of animal would likely have a significant uptake by producers (Pig Improvement Company, 2024).

Key finding 8

Alternative products could potentially reduce the need for AMU but are not replacements for antimicrobials, vaccines, good livestock and poultry management and biosecurity.

- There is evidence for the efficacy of some alternative products, such as internal teat sealants in dairy cows, but many alternative products have little evidence for efficacy to date.
- Some trace minerals and vitamins have been studied for their importance to immune system health and vaccine effectiveness, but few systematic reviews summarize evidence of efficacy and there are potential negative consequences associated with some heavy metal supplements.
- There are some data on the role of genetics in reducing disease susceptibility for some commodities (e.g. dairy), but the potential varies based on breeding management practices, current genetic variability, and the variation in environmental conditions and management practices used in the industry.
- There is no "magic bullet"; alternative products are not a replacement for antimicrobials for disease treatment or for good practices in farm management and biosecurity.
- Unintended consequences, including the potential for selection for AMR (as seen with zinc supplementations) or introduction of AMR with probiotics need to be evaluated for all alternative products.

5.3.3 Gaps in Alternative Products

Although considerable research has been conducted to evaluate the efficacy of alternative products, most alternative products do not have a sufficient body of research to support conclusions from formal systematic reviews. Alternative products may have limited research because the results of early studies did not warrant further research, may not have a body of evidence available for synthesis (e.g., single trials or lack of consistency in the interventions or outcomes evaluated), may have sufficient evidence that has not been synthesized, or may have been evaluated but the data may be proprietary and therefore not publicly available.

Additional evidence is needed to support the effectiveness of alternative products to reduce disease risk or to enhance animal health and thus prevent infections. As an example, while there is evidence that, in some cases, probiotics confer a benefit, many reviews highlight the heterogeneity of primary research due to different strains and combinations of probiotics used, different dosages, different environmental conditions, or different health of the animals, all of which make it difficult to reach definitive conclusions. Furthermore, some probiotic strains carry AMR genes, which could potentially transfer to other bacteria (Tóth et al. 2021).

There is some information on the role of nutrition including trace minerals and vitamins in supporting the immune system, although information specific to Canadian feeding practices and management conditions is limited for many commodities.

5.3.3.1 Access to Alternative Products

While our review shows that there is a lack of scientific evidence to support the effectiveness of many alternatives, participants attribute the lack of availability of effective alternatives to lack of flexibility in the regulations. Concern was expressed in Canadian key informant interviews and in virtual engagement sessions that access to alternative products to keep animals healthy is limited and decreasing significantly. Some participants articulated the need for flexibility in the regulation of low-risk veterinary health products, for example by allowing efficacy and prevention for control of diseases claims on labels and reciprocity of approvals with trusted jurisdictions.

In response to the question "What are the levers, at a policy level, for enabling alternative practices that support AMU reduction?" one Canadian key informant says: "Approvals are challenging on the regulatory side - these gaps need to be filled. Companies producing these don't have incentives to come to Canada. United States companies are 10x larger. We need a 'Made in Canada' solution" (Canadian Key Informant Interviews).

A written survey respondent offers their thoughts as well: "As science develops around alternatives to continuous feeding of in-feed AMs, labels will need to change. That science doesn't necessarily need to be Canadian - I get the sense that sometimes Canada's regulators are slow or hesitant to accept international (particularly US) research. But not all international science needs to receive equal weighting - strongest emphasis must be placed on research done under commercial conditions (or situations reasonably approximating that) that most closely reflect Canada's environment and production practices. The importance of this likely varies with commodity, but is highly important for species raised outside (ruminants)" (Written Survey, Round 2).

These accessibility concerns are echoed in the literature. A qualitative study published in Québec last year reported that a "lack of availability of alternative treatments, the long delays related to diagnostic tests and the fear of economic consequences" were among the factor that created challenges for Québec producers and veterinarians in implementing the 2018 changes to the Canadian regulations around AMU (Millar et al., 2023).

Key gap 8

Alternative interventions to antimicrobials require evidence-based evaluation of effectiveness.

- While considerable research has been conducted to evaluate the efficacy of alternative products to AMU, there are many gaps in availability of synthesized evidence.
- There is a need for additional work to develop and evaluate the effectiveness of alternative products to reduce disease risk.
- While there is some information on the role of nutrition including trace minerals, vitamins, and probiotics in supporting the immune system, information specific to Canadian feeding practices and management conditions is limited for many commodities.
- Perceived barriers to accessibility, as well as the few products and practices with evidence to support effectiveness, limit currently available options to reduce AMU.

Related action in the Pan-Canadian Action Plan

- Under the Research and Innovation pillar: "Develop and implement economic and/or regulatory incentives to support innovation and facilitate sustainable access to new and existing antimicrobials, diagnostics, and alternatives to antimicrobials."
- Under the IPC pillar: "Support the increased implementation of enhanced IPC, biosecurity, and food safety protocols across the agriculture and agri-food sectors, prioritizing sound animal husbandry, access to veterinary care, and access to additional health and nutritional aids to promote animal health."

The use of alternative products is a potentially important element to support stewardship and to ensure that producers have viable alternatives to the preventative use of antimicrobials to keep animals healthy, although they are not sufficient to replace antimicrobials in disease control or to compensate for inadequate herd management and biosecurity. There is a large volume of literature on alternative products and this is an active area of research. To date, there is only strong evidence of effectiveness for a few products, such as internal treat sealants at dry-off for the prevention of mastitis. For many products, the available literature is restricted to proof-of-concept approaches (such as challenge studies) or a small number of trials. It is important to build a body of evidence for alternative products that appear promising and to synthesize the research when possible to provide veterinarians with the best evidence possible to advise on alternatives to antimicrobials.

5.4 Validated Decision-Making Tools

Validated decision-making tools could be used to inform prescribing decisions to effectively refine antimicrobial usage. Laboratory diagnosis of disease is a valuable component of on-farm health management as it provides identification of causative disease agents. However, it is of less value for immediate treatment decisions because there is a time delay for results due to shipping time and time for laboratory tests to be conducted and reported. Rapid diagnostic tools that could be applied on-farm and provide immediate results could be of value. For example, there are some on-farm tools, such as rapid diagnostic tests, currently available that could improve assessment of the need for antimicrobials. This might include tests that allow differentiation of viral versus bacterial infections or illness related to bacterial infection versus toxin production. Individual animal-side tests may be useful for animals and diseases managed at the individual level (e.g., mastitis in dairy cattle). There is also research into genomic strategies using population-level sampling to support AMS at the group level in food-producing animals such as feedlot cattle. Access to validated decision-making tools was identified as a priority area by virtual engagement participants.

5.4.1 Literature on Validated Decision-Making Tools in Commodity Groups

Most research in this area has focused on refining the preventative use of antimicrobials either by limiting the extent of the application (e.g., only administering antimicrobials to subsets of animals that exhibit risk factors for illness) or by altering the timing and duration of application. The section below reviews the use of validated decision-making tools to inform prescribing decisions in each of the major commodity groups.

Dairy. The use of rapid on-farm diagnostic tests to identify animals with mastitis that will not benefit from antimicrobial treatment is promising in the dairy cattle industry. In a systematic review and meta-analysis of 15 within-herd comparisons, selective treatment protocols for clinical mastitis were not inferior to blanket treatment protocols in terms of bacteriological cure (de Jong, Creytens et al., 2023). The selective treatment protocols involved the identification of the causative pathogen. At the individual cow level, there is a range of available, validated rapid diagnostic tests for detecting mastitis (Chakraborty et al. 2019), many of which are available in Canada. Such tests could be a useful tool to inform selective treatment protocols of non-severe mastitis to avoid unnecessary use of antimicrobials. No systematic reviews were identified that evaluated diagnostic test accuracy for identifying specific mastitis pathogens or effectiveness in reducing AMU for these diagnostic tests. This information, in addition to cost effectiveness, is needed for producers and veterinarians to use these tests for diagnostic decision-making.

Another example in dairy cattle is the use of selective dry cow therapy instead of treating every quarter of every cow with antimicrobials at dry-off. Selective dry-cow treatment has led to substantial reductions in AMU on dairy farms that applied this practice (McCubbin et al., 2022). Winder, Sargeant & Kelton et al. (2019) conducted a systematic review and pairwise meta-analysis comparing blanket dry cow therapy to only selectively treating high risk cows with antimicrobials at dry-off. They found that the risk of intramammary infections was higher in selectively treated cows compared to those that received blanket therapy, although in the sub-set of trials where an internal teat sealant was used, no differences were found between the risk of intramammary infections at calving between selective and blanket therapies. Santman-Berends et al. (2021) reported, after a ban on blanket dry cow therapy in the Netherlands in 2013, only minor increases in the percentage of cows with a high somatic cell count (as an indicator of udder health) and new cases of cows with high somatic cell count (i.e. it did result in a considerable reduction in AMU without a major worsening of udder health).

To maximize the effectiveness of SDCT, however, it is important to select the cows who receive treatment correctly. Tools have been developed to inform this decision-making. There are a number of methods that can be used to select cows for selective treatment, including somatic cell count at cow or quarter levels, pathogen identification-based methods, or other diagnostic procedures such as the California Mastitis Test (McCubbin et al., 2022). Algorithms for decision-making based on disease severity and pathogen identification have been proposed (de Jong, McCubbin et al., 2023).

In dairy calves, Gomez et al. (2017) illustrated the use of an algorithm for the antimicrobial treatment of diarrhoeic calves on dairy farms that resulted in a reduction of 80% in antimicrobial treatment rates, with no negative impact on the health of the calves. The algorithm included a consideration of fecal consistency, the presence of blood in the feces, rectal temperature, changes in behaviour and milk intake. The algorithm was only tested on 2 farms; however, the results are promising and further validation of this algorithm is warranted.

Veal. Research has been conducted to validate several parameters and tools to identify veal calves that are at high-risk of developing disease, particularly during the first 21 days following arrival, which present the highest risk of mortality (Renaud & Pardon, 2022). Calves with low levels of Immunoglobulin G (IgG), certain white blood cells, and low levels of cholesterol at arrival, all markers associated with [poor] nutrition prior to transportation and age at transport, influence the risk of disease on arrival at veal farms. As technology becomes available to test for these parameters on farms, it may be possible to generate a risk profile to allow producers to separate high- and low-risk calves and manage them differently.

Beef. Interventions in beef cattle may be given at the group (pen) or individual level, and most injectable AMU in Canadian feedlot cattle is due to BRD (Otto et al., 2024). Treatment decisions are usually made based on risk factors on arrival at feedlot (i.e., calves from auction are at higher risk) and clinical signs (rectal temperature, off-feed, depressed), rather than based on the results of laboratory tests (Otto et al., 2024). However, the diagnostic accuracy of using clinical signs varies widely among studies (Timsit et al., 2016). Kamel et al., (2024) reviewed approaches to BRD diagnosis, such as evaluation of clinical signs and animal behavior, biomarker analysis, molecular diagnostics, ultrasound imaging, and prognostic modeling. Although the prognostic value of these approaches was discussed, an explicit discussion of the usefulness of the various approaches to antimicrobial decision-making was not provided. Puig et al., (2022), in a narrative review of 104 articles, concluded that use of new advanced technologies using real-time data analysis was the most promising approach to the early detection of BRD. The authors argued that early diagnosis of BRD would lead to reduced AMU.

Otto et al. (2024) investigated the potential application of integrating results of laboratory data from pen-mates into information quality value stream maps to evaluate the appropriateness of BRD treatment protocols. This work builds on a longitudinal study in feedlot calves that involved sequential deep nasopharyngeal sampling and laboratory diagnosis of BRD bacterial pathogens at several time points during the early feeding period (Abi Younes, Campbell, Gow et al., 2024). The findings of the study indicated that culture and sensitivity results from samples taken early in the feeding period might be of value for informing treatment decisions both for individual calves and to inform pen-level treatment protocols.

A recent scoping review on diagnostic tests for the rapid detection of bacterial respiratory pathogens and ARGs (AMR genes) in animals using respiratory samples revealed there is an opportunity to detect multiple pathogens and ARGs using a single diagnostic test, using long-read metagenomic sequencing (Adewusi et al., 2024). However, the authors identified the need for studies that evaluate tools that directly detect bacterial respiratory pathogens and ARGs.

Antimicrobial metaphylaxis at arrival accounts for most injectable AMU in feedlots. In an approach that is conceptually similar to SDCT in dairy cattle, Nickell et al. (2021) evaluated an approach to selected (rather than blanket) metaphylaxis based on individual risk predictions generated by a novel technology called Whisper On Arrival. AMU was lower using the Whisper On Arrival program without evidence of negative impacts on health, performance, and carcass metrics.

Using rapid on-farm diagnostic tests to identify animals that do not benefit from antimicrobial treatment is one of the research priorities for the Beef Cattle Research Council. In future, international policy and trade regulations may require diagnostic testing to justify the choice of antimicrobial used for prophylaxis or treatment of disease in beef cattle (Otto et al., 2024).

Swine. In swine, interventions tend to be at group level. No specific diagnostic tests for managing antimicrobial treatment decisions were identified for this sector. However, in a UK survey of veterinarians, swine veterinarians stressed the need for rapid tests to identify bacterial causes of disease and their resistance profile, although these tests were not regarded as the universal solution for AMU reduction across all production (Buller et al., 2020).

Poultry. Interventions in poultry also tend to be at flock level. Many rapid tests exist for the diagnosis of viral diseases in poultry. While on-farm rapid diagnostic tests for bacterial infections are not currently available, veterinarians see potential for these to direct targeted AMU as part of a broader approach to reducing unnecessary AMU, according to one UK study (Buller et al., 2020).

Aquaculture. There is very little literature available on rapid diagnostic tests for bacterial infections in aquaculture, and none were identified for the purpose of this assessment. As with poultry and swine, interventions also are mostly implemented at the group (i.e., pen) level.

Key finding 9

Validated decision tools to inform AMS protocols can be useful to refine antimicrobial usage.

- Some on-farm tools are currently available that could improve assessment of the need for antimicrobials.
- Individual animal-side tests may be useful for animals and diseases managed at the individual level (e.g., mastitis in dairy cattle).
- Using rapid on-farm diagnostic tests to identify animals that do not benefit from antimicrobial treatment is promising in the dairy industry, and is also one of the research priorities for the Beef Cattle Research Council.
- There is research into rapid genomic strategies using population-level sampling to support antimicrobial stewardship in food-producing animals such as feedlot cattle. However, they are not yet feasible for on-farm or veterinary clinical application.

5.4.2 Gaps in the Use of Validated Decision-Making Tools

There are significant gaps affecting the use of decision-making tools in food-producing animals. Laboratory testing to support immediate treatment decisions is not currently feasible for most food-producing animal commodities, given the time between shipping samples to the laboratory and getting results, cost, and other factors. Factors encouraging producers to send samples to diagnostic laboratories include outbreaks, unusual levels of mortality, or problems with potential herd implications (Sawford et al., 2013).

A number of rapid diagnostic tests have been developed. There is a need for validation of the tools and algorithms used, including outcome assessment (both clinical and AMR outcomes and economic analysis) for identifying animals that do not require treatment with antimicrobials or for shifting to lower importance antimicrobials based on diagnostic test results.

There has been work to develop group level disease antimicrobial management protocols using various diagnostic strategies to target AMU rather than applying it to the whole group. However, additional studies are needed to evaluate the cost-effectiveness of these approaches. An example that would have the potential to substantially reduce AMU in feedlots would be validated evidence-based protocols for targeted metaphylaxis.

Group level (management group) decision tools/algorithms are emerging and may be used prior to implementing treatment to meaningfully change the use of antimicrobials; however, there is limited evidence to date to support these applications.

5.4.2.1 Access to Validated Decision-Making Tools

Access to validated decision-making tools was identified as a priority area by virtual session participants. However, results of surveys of professionals from the UK point to a slightly different perspective. A survey of veterinarians across the dairy, pig, and poultry sectors indicated that they did not regard diagnostic tests as a panacea solution to reducing AMU. While they perceived a gap in the market for rapid and point-of-case diagnostic tests, they regarded these devices as part of an extended diagnostic pathway to simply confirm or rule-out disease and lead to more investigative testing, rather than to reduce unnecessary AMU. What was regarded as most useful to this group was a simple test that could distinguish bacterial from viral infections to provide a starting point for diagnosis (Buller et al., 2020).

Key gap 9

There currently are few options for validated decision tools and on-farm diagnostics that could meaningfully inform the choice of antimicrobials for disease in real-time.

- The application of testing strategies to inform targeted metaphylaxis in BRD management for high risk feedlot cattle has shown mixed results to date.
- Group level (management group) decision tools / algorithms are emerging and could potentially be used prior to implementing treatment to evaluate the appropriateness of AMU protocols; however, there is little evidence to date.
- Laboratory testing to support immediate AMU treatment decisions is not feasible in most food-producing animal commodities given the time to ship samples to the laboratory, turnaround time, cost, and other factors.
- There is a need for validation of the tools and algorithms that have been developed to support AMU decision-making.
- There is a need for outcome assessment for shifting to lower importance antimicrobials based on diagnostic test results. Outcomes must include both clinical and AMR outcomes.

Related Action in the Pan-Canadian Action Plan

- Under the Research and Innovation pillar: "Develop and implement economic and/or regulatory incentives to support innovation and facilitate sustainable access to new and existing antimicrobials, diagnostics, and alternatives to antimicrobials."

The area of rapid diagnostic tests and group level algorithms for aiding in AMU decisions is an evolving area of research, with potential to contribute to AMS. A number of animal-side diagnostic tests have been developed, although there is a need to evaluate their accuracy and cost-effectiveness. Group-level approaches, such as selective antimicrobial treatment rather than blanket treatment, are used in dairy cattle at dry-off and are being investigated for beef cattle. These types of tests and algorithms, once developed and validated, could be an increasingly important component of AMS programs.

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 6:

Surveillance of Antimicrobial Resistance and Antimicrobial Use in Food-Producing Animals

Introduction

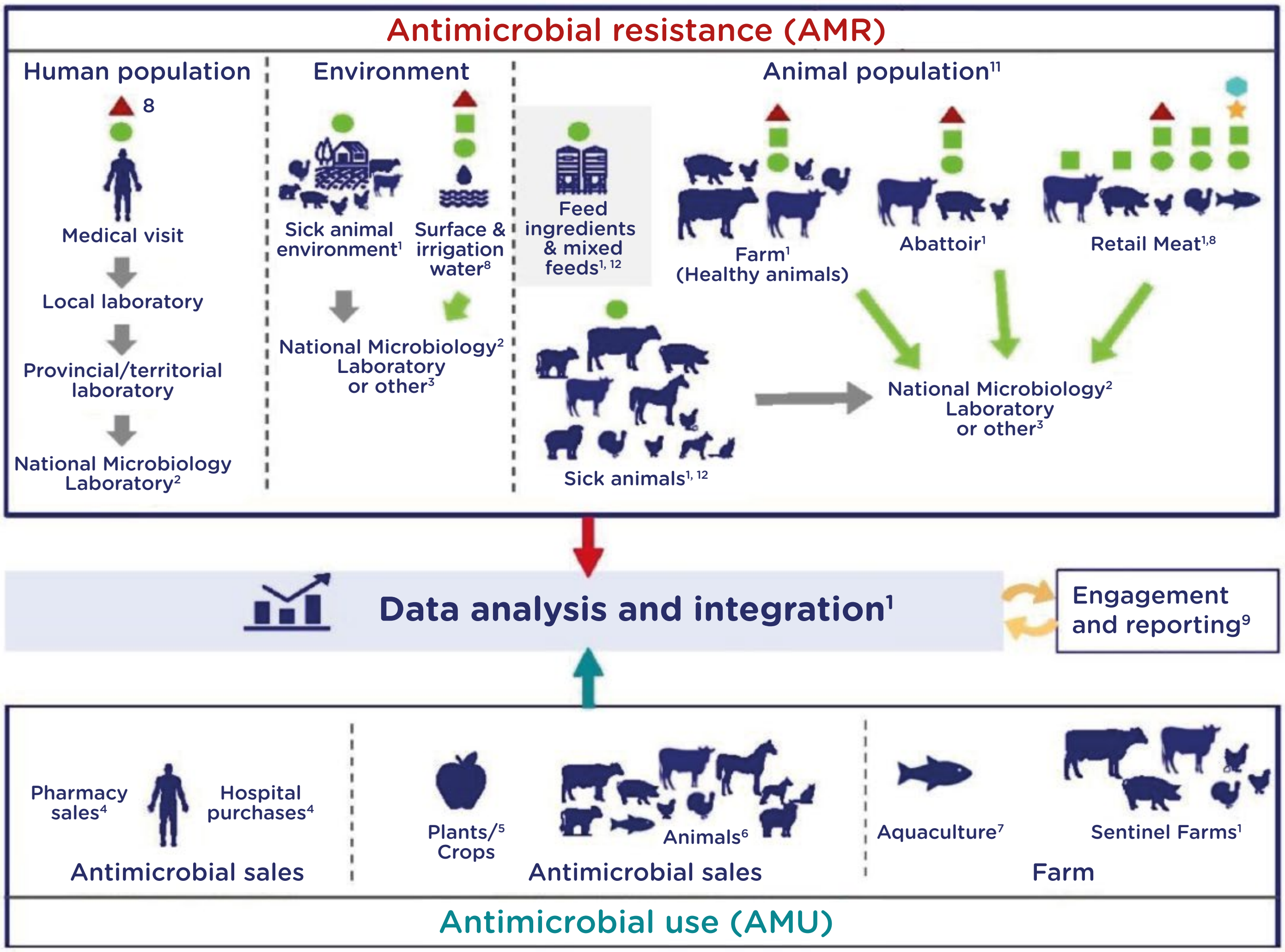
It is essential for a One Health framework to be the integrating factor at the core of surveillance efforts to address AMR and AMU, with the ultimate goal of providing information to support and assess AMS interventions and minimize the impact of AMR on the health of humans, animals, plants/crops, and the environment. The key informants and participants in the CAHS virtual engagement sessions unanimously agree that a One Health surveillance system that captures and shares timely and accurate information about AMR and AMU is necessary. Canada has a number of organizations supporting AMS efforts in food-producing animals. However, the key Canadian surveillance programs for AMR and AMU are managed by CIPARS.

6.1 AMR/AMU Surveillance in Canada for Food-Producing Animals

6.1.1 Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)

CIPARS has been in place in Canada for assessing AMR/AMU in food-producing animals, plants/crops and humans for the past 22 years (PHAC, 2024e). CIPARS is very well recognized and respected internationally, particularly as an example of a One Health approach to surveillance, although largely lacking an environmental component.

CIPARS primary mandate includes integrated monitoring of trends in AMR, AMU, and antimicrobial sales. CIPARS monitors AMR trends in animals, retail meat, and people across Canada. Data are included from healthy animals (on sentinel farms), sick animals, healthy animals at slaughter plants, retail meat and humans to evaluate AMR in *Campylobacter spp*, generic “indicator” *Escherichia coli*, and *Salmonella spp*. (Figure 6-1). CIPARS also reports trends in antimicrobial sales and farm-level AMU data from multiple sources. Antimicrobial sales data from mandatory reporting by importers and manufacturers through the Veterinary Antimicrobial Sales Reporting (VASR) system are reported, along with sales for antimicrobials for use in humans, and on-farm AMU from crops, aquaculture, and sentinel farms (PHAC, 2024a; Figure 6-1). Figure 6-1 presents an overview of CIPARS inputs from various sources and surveillance and notification programs.



1 Centre for Foodborne and Environmental and Zoonotic Infectious Diseases (CFEZID), Infectious Diseases and Vaccination Programs Branch (IDVPB), Public Health Agency of Canada (PHAC)
2 Bacterial Pathogens, AMR and Wastewater Division and Division of Enteric Diseases, National Microbiology Laboratory Branch, PHAC
3 Provincial animal health laboratory, university laboratory or private laboratory
4 Canadian Antimicrobial Resistance Surveillance System (CARSS), PHAC. Data source !QVIA
5 Pest Management Regulatory Agency, Health Canada
6 Veterinary Antimicrobial Sales Reporting (VASR), Veterinary Drugs Directorate, Health Canada and CFEZID, PHAC
7 Fisheries and Oceans Canada
8 Foodnet Canada, CFEZID, IDVPB, PHAC
9 CIPARS engagement and reporting including: Annual Stakeholder Webinars, Integrated Findings Reports, Data Visualizations, Farm Surveillance Technical Reports (including health and biosecurity data), Fact sheets, Infographics, Journal publications, VASR Highlights Reports, and CARSS Reports
10 Canadian Food Inspection Agency (CFIA)
11 Laboratory analysis reporting of *Clostridium perfigens*, *Enterococcus* spp., and bovine respiratory pathogens occurs for select years and species
12 AMRNet-Vet shares data for bovine respiratory disease bacterial pathogens

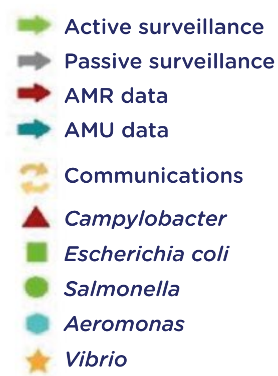
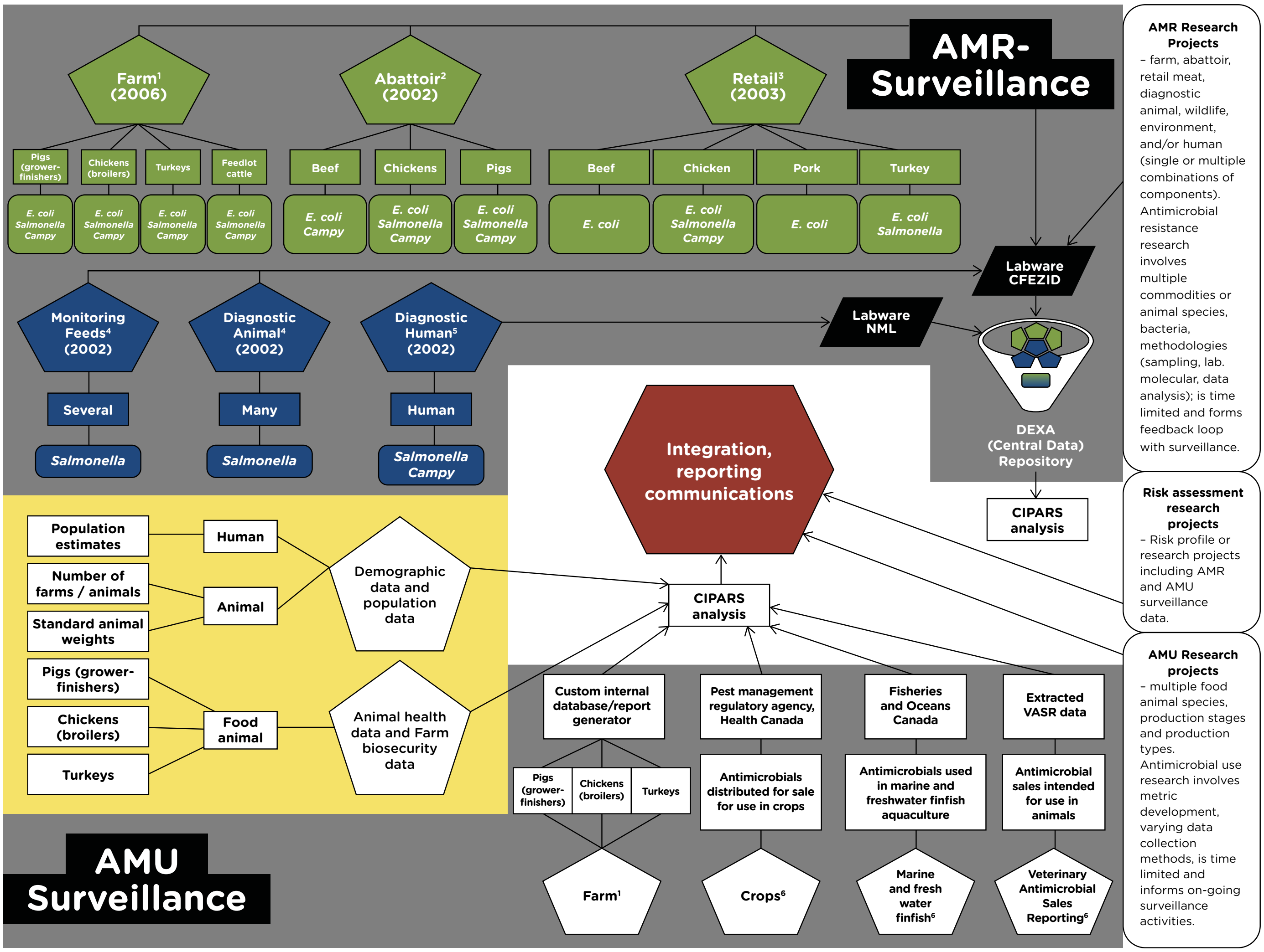


Figure 6-1. An overview of CIPARS surveillance of AMR and AMU (PHAC, 2024a)

CIPARS sampling strategy. The CIPARS food-producing animal component involves farms, abattoirs, and retail outlets, and involves a combination of **active surveillance** (primary data, intended for AMU, AMR and bacterial prevalence estimation) and **passive surveillance** (secondary data, for AMR detection). The CIPARS sampling strategy and data flow are outlined in Figure 6-2.



■ = Active surveillance; primary data, primarily for prevalence estimation. ■ = Passive surveillance; secondary data, primarily for AMR detection.
CFEZID = Centre for Food-borne, Environmental and Zoonotic Infectious Diseases. NML = National Microbiology Laboratory.

1-6 CIPARS project leads: 1 David Léger (david.leger@canada.ca), Sheryl Gow (sheryl.gow.@canada.ca) and Agnes Agunos (agnes.agunos@canada.ca); 2 Anne Deckert (anne.deckert@canada.ca); 3 Brent Avery (brent.avery@canada.ca); 4 Brent Avery (brent.avery@canada.ca), Colleen Murphy (colleen.murphy2@canada.ca); 5 Brent Avery (brent.avery@canada.ca), Michael Mulvey (michael.mulvey@canada.ca), Colleen Murphy (colleen.murphy2@canada.ca); 6 Carolee Carson (carolee.carson@canada.ca).
CIPARS Program Coordinators: Rebecca Irwin (rebecca.irwin@canada.ca); Richard Reid-Smith (richard.reid-smith@canada.ca); Michael Mulvey (michael.mulvey@canada.ca).

Figure 6-2. CIPARS AMR and AMU samples and data flow summary (PHAC, 2024f). An updated version of this figure may be published by 2025.

CIPARS's on-farm programs employ a standardized system that includes annual collection of on-farm AMU and AMR data from volunteer sentinel farms for broiler chickens, grower-finisher pigs, dairy cattle, feedlot cattle, layers, and turkeys. The on-farm program is led by the Centre for Foodborne, Environmental and Zoonotic Infectious Diseases at the Public Health Agency of Canada. Specifically, for sentinel farms, in 2006 on-farm AMR and AMU monitoring was implemented in grower-finisher pigs, followed by broiler chickens and turkeys in 2013, and feedlot cattle and dairy cattle in 2019 (Fonseca et al., 2022). The dairy program collects AMU data from veterinary prescribing records and the beef feedlot data are collected electronically directly from the farm's recording system. AMU data for the other commodities are gathered via questionnaire. Some commodity groups or production stages within sectors are not represented in CIPARS farm data, such as cow-calf, veal, suckling/nursery pigs, broiler-breeder chickens, and other smaller commodities such as sheep and goats and other alternative livestock.

6.1.1.1 Other Data that Integrate into CIPARS

As shown in Figure 6-1, CIPARS has input from other Canadian surveillance and stewardship initiatives providing AMR, AMU and sales data. These initiatives are discussed in section 6.1.2. While many different surveillance systems exist, they are fragmented, and not fully integrated, leaving Canada far from having a One Health system for AMR/AMU that is geographically representative of Canada.

The Veterinary Antimicrobial Sales Reporting (VASR). VASR data are collected as part of mandatory reporting requirements through the Veterinary Drugs Directorate (VDD) (Health Canada, 2024b). This system is jointly operated by VDD and CIPARS and results are reported through CIPARS (Health Infobase, 2024a). The VASR reporting requirements apply to manufacturers, importers, and compounders of medically important antimicrobials (MIAs) for veterinary use. Sales reports of veterinary drugs containing antimicrobials of importance to human medicine as active pharmaceutical ingredients on List A must include the total quantity sold or compounded, and the approximate quantity sold or compounded for each intended animal species (Health Canada, 2024d).

FoodNet Canada. FoodNet Canada is a multi-partner initiative facilitated by PHAC and integrated with CIPARS, with a goal to monitor and engage in activities that reduce the burden of enteric disease in Canada. Towards this end, FoodNet Canada monitors trends in food-borne pathogens from animals, food, water, and humans, including investigation of food-borne and waterborne diseases and exposures. The program operates through sentinel sites in British Columbia, Alberta, Ontario, and Québec. Its approach is consistent with international recommendations from US, EU, Australia, and New Zealand (Health Infobase, 2024b). Isolates generated by FoodNet Canada surveillance are shared with CIPARS for AMR testing and reporting (see Figure 6-1).

Fisheries and Oceans Canada. The Department of Fisheries and Oceans Canada monitors trends in quantities of antimicrobials and pesticides in marine and freshwater fish aquaculture (Department of Fisheries and Oceans, 2022). Aquaculture is currently the only example of mandatory reporting requirements for on-farm AMU in Canada. This is discussed more below.

A Closer Look: AMR and AMU Surveillance in Aquaculture

Aquaculture is currently one of the fastest growing food production sectors worldwide, and AMR within aquaculture is potentially a significant issue impacting this sector. An international review spanning 39 countries across six continents shows that AMR, as gauged by the detection of ARGs, is found in at least 44 families of fish and crustaceans and 75 genera of marine bacteria (Kemp et al., 2020).

Aquaculture: The only example of mandatory farm-level AMU data collection in Canada

In Canada, there is a mandatory requirement for reporting of farm-level AMU in finfish. This is unique as compared to approaches taken with other food-producing animals in Canada. The Department of Fisheries & Oceans Canada (DFO) monitors trends in quantities of antimicrobials and pesticides in marine and freshwater fish aquaculture. These data are then incorporated into CIPARS reporting. The reporting includes antimicrobials used in medicated feeds, represented as grams of active antibacterial per tonne of marine fish produced. Additionally, some data on AMR in aquatic animals are gathered through the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) (Ceric et al., 2019).

AMR surveillance in aquaculture: A gap to be addressed

Contamination of aquatic food products by bacterial AMR and ARGs can occur in two ways: 1. through handling or processing, and 2. directly in the marine environment, where ARGs associated with different aquaculture species can accumulate through surface contact with seawater or sediments, respiration or the food chain (Bourdonnais et al., 2024). While global data indicate that AMR is a concern in aquaculture, Canada has no standardized monitoring for AMR or identification of potential pathways of impact on aquaculture workers and communities in Canada (Ochs et al., 2021).

6.1.1.2 CIPARS reporting

CIPARS communicates AMR and AMU findings in annual reports, stakeholder meetings/ webinars, infographics, peer-reviewed scientific journals, and other means (Bosman et al., 2024). CIPARS reporting particularly emphasizes the use of and resistance to antimicrobials of critical importance to human medicine. Findings reported include "trends in AMU and AMR, trends in AMR within animal populations, across bacterial species, and in human AMR, detection of new resistance or developing resistance patterns, and potential links between AMU and AMR." (Bosman et al., 2024).

CIPARS has also recently developed a web-based interactive data visualization dashboard. AMR data for broiler chickens, pigs, turkeys, cattle, and humans are included in these visualizations. In addition, antimicrobial sales data are presented for all animal species but farm-level AMU data are only currently available for broiler chickens, pigs, and turkeys (PHAC, 2024g).

6.1.1.3 CIPARS: Impact on Policy

CIPARS reporting and engagement has impacted policy in both the private and public sectors. In the chicken sector, the identification by CIPARS surveillance of increased rates of ceftiofur resistance in both chicken meat and human cases of salmonellosis in Québec in 2004 led to industry engagement and a voluntary temporary withdrawal of the in-ovo use of ceftiofur in broiler chicken hatcheries (Dutil, 2010). Subsequently, CIPARS surveillance reporting contributed to the development of the Chicken Farmers of Canada Responsible AMU Strategy as well as the monitoring of the impact of this strategy on AMU (Chicken Farmers of Canada, n.d). The National Beef Antimicrobial Research Strategy also utilized CIPARS Surveillance data in determining research objectives and priorities for beef research that is funded by the primary research funding agencies in Canada (Beef Cattle Research Council, 2016b).

The voluntary provision of veterinary sales data to CIPARS by the Canadian Animal Health Institute, highlighted the need for a transition to mandatory reporting of this surveillance data. CIPARS worked closely with Health Canada in the development of a regulatory change implemented in 2018 which included mandatory reporting of drug distribution and sales data. At the international level, CIPARS surveillance data is shared with the World Organization for Animal Health (WOAH) global database on ANImal antiMicrobial USE (ANIMUSE), the World Health Organization (WHO) Global Antimicrobial Resistance and Use Surveillance System (GLASS), the Food and Agriculture Organization (FAO) Antimicrobial resistance monitoring (InFARM), and the Transatlantic Task Force on Antimicrobial Resistance (TATFAR), in recognition of the global nature of antimicrobial resistance and the need for international policy approaches. In addition to surveillance data, the expertise developed within the CIPARS program, has led to the involvement of CIPARS personnel in international guideline development, and participation in committees, advisory groups, and working groups with Codex, WOAH, TATFAR, and the United States' National Antimicrobial Resistance Monitoring System (NARMS) (Bosman, 2024). This ensures that the Canadian context is considered in the international arena.

6.1.1.4 CIPARS: Areas Under Development

CIPARS is evolving, and a number of new developments are taking place. For example, CIPARS is moving towards tracking resistance using ARGs via whole-genome sequencing (WGS) methods and has implemented this for human *Salmonella* (PHAC, 2024f). The ability to expand into these areas in the future, while maintaining existing surveillance activities, will be dependent on the availability of long-term sustained funding.

Animal pathogens. A One Health AMR/AMU surveillance system needs to include data on animal pathogens (pathogens that are of primary importance to animal health). CIPARS active and passive surveillance has focused primarily on indicator bacteria and foodborne pathogens of concern to human health. CIPARS animal pathogen surveillance has been limited to *Salmonella* from diagnostic laboratory submissions that are tracked in multiple species. Over the last two years, bovine respiratory disease pathogens that cause clinical disease in feedlot cattle have been included in surveillance activities (PHAC, 2024h). Feedlot surveillance has been incorporated into CIPARS as a core surveillance activity, although animal health pathogen surveillance is funded by external sources (Beef Cattle Research Council, 2019b). Dairy surveillance is included on a regional basis and includes herd-level detection of AMR in three sentinel enteric pathogens (generic *Escherichia coli*, *Campylobacter* spp., and *Salmonella* spp. (Fonseca et al., 2022). The dairy and feedlot initiatives have been funded primarily by the respective industries through research grants.

Environment. Likewise, a One Health AMR surveillance system needs to provide an understanding of the contribution of animal and human related activities to the environment. CIPARS has recently started surface water testing for AMR. However, future work is required to identify and understand other areas where environmental surveillance is needed.

6.1.2 The Canadian Antimicrobial Resistance Surveillance System (CARSS)

CARSS was launched in 2015. It is not a surveillance system but a reporting venue. CARSS integrates information from the Canadian Nosocomial Infection Surveillance Program (CNISP), Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), Antimicrobial Resistance Network (AMRNet), and other human-specific pathogen-targeted programs, and reports annually on these data (PHAC, 2022b). CIPARS is a major component of CARSS. CNISP includes data from a sentinel hospital network (106 hospitals) across Canada (PHAC, 2024i). Human antimicrobial consumption in Canada is estimated based on the Canadian Drugstore

& Hospital Purchases (CDH) and the Canadian Compuscript (CS) (PHAC, 2023b). The CARSS Report is published every two years and presents a "summary of available national-level data on AMR and AMU in human and animal populations" generated by the PHAC and its partners. The CARSS Report supports PHAC's targeted AMR and AMU surveillance outcomes ("Detect, Understand, and Act") by providing data on AMR/AMU to inform work across many sectors. In addition, CARSS has human and animal dashboards on AMR and AMU that provide information on trends on antimicrobial resistant organisms and on AMU in Canada. Interactive CARSS dashboards are available to provide seasonal updates on AMR and AMU (Health Infobase, 2024c; 2024d).

Antimicrobial Resistance Network (AMRNet). AMRNet is a recent and promising initiative for a One Health approach to AMR surveillance under development at PHAC's National Microbiology Laboratory (PHAC, 2022b). As one of the initiatives that feeds into the CARSS report, AMRNet surveillance system captures information on antimicrobial susceptibility testing from human clinical and veterinary laboratories, including both public and private facilities (Rudnick et al., 2022).

AMRNet-Vet is the component of AMRNet focussing specifically on veterinary data. The program, currently in its pilot phase, will gather information from other existing surveillance systems, such as CIPARS and combine it with data from veterinary diagnostic laboratories (Canadian Animal Health Surveillance System, n.d.).

In the future, the AMRNet system will also capture and integrate relevant data from existing PHAC surveillance systems for AMR including CIPARS, the Canadian Nosocomial Infection Surveillance Program and the Enhanced Surveillance of Antimicrobial-Resistant Gonorrhea program, and contribute to the CARSS. The program is a collaboration between PHAC, provincial and territorial public health organizations as well as clinical (human health) and veterinary laboratories across the country. AMRNet and AMRNet-VET will provide a new source of data (Rudnick et al., 2022); however, limitations exist in that there is no defined denominator. The data are also based on isolates from animals that may have been ill, may have been treated, and may not have entered the food chain. This type of data is useful as an "early warning" of developing AMR, but not in monitoring trends over time; this is an important distinction.

6.1.3 Other Initiatives Relevant to Food-Producing Animals

Veterinary Laboratory Investigation and Response Network (Vet-LIRN). As part of the US Food and Drug Administration's (FDA) Laboratory Investigation and Response Network, five laboratories in Canada engage in whole genome sequencing of selected animal pathogens in Canada, supported by Vet-LIRN. Vet-LIRN is a collaborative project with veterinary diagnostic laboratories in the United States and Canada that is working to enhance the One Health initiative by using whole genome sequencing to monitor AMR of animal pathogens. This program focuses on *Salmonella* and aquatic isolates in fish (Ceric et al., 2019).

Other important Canadian initiatives include, but are not limited to:

- **The Canadian Cow-Calf Surveillance Network:** This industry-sponsored program reported AMU at the farm-level in cow-calf herds in different regions of Canada in 2019-2020 and provided a framework for research on AMR in enteric and respiratory organisms from cow-calf herds in 2021;
- **Stewardship of Antimicrobials by Veterinarians (SAVI):** This initiative involves reporting of antimicrobial prescription data for cattle, swine, and poultry from a voluntary sample of veterinary clinics;
- **Québec Multispecies AMU Surveillance System:** This AMU monitoring system is based on multispecies sales data on production animals at the farm or veterinary clinic level.

There are also regional surveillance networks, such as the Western Canadian Animal Health Network (WeCAHN), which summarizes AMR from regional laboratories and surveyed vaccine use data in western Canadian beef.

Key finding 10

The CIPARS surveillance system is and has been an asset for understanding AMR and AMU in Canada for the sectors included in the surveillance system; however, it requires sustained funding and additional resources for representativeness and additional functionalities and coverage

- CIPARS represents a unique platform to develop a fully integrated One Health surveillance system for AMR and risk factors associated with it (including AM exposure).
  - CIPARS would benefit from including more animal pathogens.
  - CIPARS is expanding into environmental surveillance. Wastewater sampling is one alternative to provide environmental inputs; currently, CIPARS/FNC latest reported data on AMR in water is from raw water (surface water and irrigation water).
  - Water and wastewater surveillance are starting points, but not the only aspects to consider in broader environmental AMR surveillance. For example, wastewater sampling does not provide any information about risk of transmission of AMR from water to animals or humans, which is an important gap.
- Long-term sustainable resources are required (people, money, infrastructure) to maintain and to broaden representativeness, data acquisition, implementation, communication, and improve reporting timeliness with respect to data and key findings.

6.1.4 Foundational and Structural Gaps in Surveillance

A number of key gaps exist that present a challenge to the food-producing animal component of an animal health surveillance system, for which the goal is to provide data to support and assess AMS interventions. Some of these gaps pertain directly to CIPARS, and others impact the broader surveillance context. These will be discussed under two broad categories of foundational vs. structural gaps.

Foundational gaps. There are important foundational strategic and scientific gaps that must be addressed. An important consideration is to clearly outline the objectives of future AMR and AMU/sales surveillance in order to align future developments and coordinate with existing initiatives (Canadian Council of Chief Veterinary Officers, 2016). A recent evaluation of the status of integrated AMR/AMU/sales surveillance in Canada noted the need for action in three "crucial areas" (Otto et al., 2022). These include:

1. **One Health scope.** Currently, many different surveillance initiatives exist, but they are fragmented, not fully integrated, and we are far from having a One Health system for AMR/AMU that is geographically representative of Canada. The current lack of a complete, integrated AMR/AMU/sales One Health surveillance program with explicit One Health objectives, such as surveillance of AMR in animal pathogens and the environment, is a key gap.

   CIPARS would be a key component of such a program since its primary mandate includes integrated monitoring of trends in AMR, AMU, and antimicrobial sales in humans and animals, and CIPARS supports "measures to contain the emergence and spread of resistance between animals, food, and people" (PHAC, 2024e). Surveillance of AMR in animal pathogens is currently occurring on a limited basis, with some specific pathogen testing supported by industry, and wastewater is included as an aim in the action plan. Environmental sampling is currently being added by CIPARS on a limited basis within its current scope. However, expansion of CIPARS into these areas would require a change to the current mandate and increased sustained resources to develop and implement this expansion.

2. **Animal pathogen AMR testing and reporting.** There is no policy, regulatory, or data framework for reporting AMR in animal pathogens. AMRNet-Vet, currently in its pilot phase, is intended to provide data from diagnostic laboratories but the representativeness and utility of this passively acquired information is limited.

3. **Resources.** More resources are required for AMR/AMU/sales surveillance, including dedicated persons, funding, and enabling structures and policy. For example, on-farm data collection is currently limited by resources (money, people, infrastructure).

Structural gaps. Structural gaps refer to gaps in the technical elements of the surveillance system. Identified limits to the CIPARS farm-level data could be remedied, in principle, with increased resources. Table 6-1 summarizes the structural gaps and whether they pertain to AMR and AMU.

Table 6-1. Structural gaps in farm-level AMU surveillance

Structural gaps	Gap pertains to:	
	AMR	AMU
1. **Small sample size.** Due to the original CIPARS goals [and resources], data from CIPARS rely on a relatively small number of farms within selected commodities, each one with different sampling weights.[1,2]	Yes	Yes
2. **Lack of geographical representation.** The samples taken to measure AMR and to quantify on-farm AMU are collected with defined inclusion and exclusion criteria. Nevertheless, the results can not be extrapolated across the respective commodity groups because they are not all fully geographically representative of Canada's food-producing animal populations.	Yes	Yes
3. **Voluntary participation.** Although the intention is to achieve representativeness in sampling, in general, veterinarians are selected by convenience and willingness to participate and participating veterinarians identify volunteer farms for sampling.	Yes	Yes
4. **Missing commodity groups.** There are commodity groups missing from existing AMR/AMU/ surveillance systems in Canada, such as cow-calf herds, nursery and suckling pigs, horses (for meat production), broiler-breeder chickens, and other smaller commodities such as sheep and goats.	Yes	Yes
5. **Lack of AMR surveillance in aquaculture.** Aquaculture is not currently included in CIPARS AMR surveillance, although some AMR reporting on aquaculture is done through Vet-LIRN.	Yes	N/A
6. **Animal pathogens.** There currently is very limited surveillance of AMR in animal pathogens. For example, current BRD pathogen surveillance in feedlot cattle is funded through time-limited research grants.	Yes	N/A
7. **Challenges in measurement and reporting.** There are challenges in on-farm AMU data collection and reporting due to differences between commodities with respect to routes of administration and types of antimicrobials used. In-feed is the primary route of administration for AMU in pigs and poultry, and an important route in feedlot cattle. However, in-feed AMU is a minor route of administration for dairy cattle. These differences require different approaches to AMU data collection, with in-feed AMU relatively more complicated to measure and report.	N/A	Yes

1 At the time of the preparation of this report, an up-to-date detailed document about the design was not available and this assessment is based on the 2019 CIPARS Design and Methods document (PHAC, 2024f), April 18).

2 CIPARS samples from abattoirs represent between 75 and 90% of food-producing animal production in Canada (for pigs, chicken, beef cattle), thus, this component of CIPARS sampling is fairly representative of farm data.

Structural gaps	Gap pertains to:	
	AMR	AMU
8. Absence of health outcomes data. Since there is no standardized collection of animal health data in most commodities, there is currently limited or no ability to link AMU to AMR and animal health outcomes. Linkage to health data enables researchers and veterinarians to understand the association between AMR and treatment failure, or other health outcomes related to morbidity and mortality in animal herds. There may be an opportunity to link to industry initiatives to collect this data (e.g. proAction in dairy cattle).	Yes	Yes

Key gap 10

There is a critical gap in overall representativeness of herds and flocks in the current CIPARS AMR/AMU surveillance.

- Current surveillance data are limited due to the number of herds and sectors represented within the commodity groups assessed.
- Important production sectors are missing for AMR and AMU, such as cow-calf, suckling/nursery pigs, broiler-breeder chickens, and other smaller commodities such as sheep and goats and AMR data for finfish and shellfish.
- Environmental AMR is currently a very limited component of CIPARS.
- Ongoing program support for surveillance of AMR in animal pathogens is needed.
- On-farm AMU data collection and reporting is challenging due to differences between commodities with respect to routes of administration (feed vs injectable) and types of antimicrobials used.
- Due to a lack of representativeness and the absence of animal pathogen data, there are limitations to integration of available data on AMR and AMU in food-producing animals.

Related Action in the Pan-Canadian Action Plan

- Under the Surveillance pillar: “Expand sources, coverage and integration of AMR and AMU surveillance data, including the use of modern laboratory technologies and standardized reporting, to help monitor AMR/AMU across One Health sectors, with specific focus on improving data from the environment; transmission pathways between sectors; and population groups disproportionately impacted by AMR and inappropriate AMU.”

6.2 Antimicrobial Sales Data

As discussed earlier, as a component of CIPARS, VASR provides antimicrobial sales data for Canada. This section highlights the most recent trends in sales in the period between 2018-2022.

It is important to note that overall reduction of sales based on absolute weight does not take into account which categories of antimicrobials are sold, and can be misleading. For example, any shifts to the sales and use of higher category of importance antimicrobials will negatively impact stewardship goals, but decrease overall sales measured by weight, since the lower category of importance antimicrobials have higher product weight per dose. For example, the antimicrobials with the current greatest sales are from the tetracycline class which is a Category III drug of medium importance to human health, but also has a much higher weight per dose than many of the more important classes of antimicrobials that are less commonly used by the livestock industry.

6.2.1 Antimicrobial Sales

The most recent published data in Canada show that antimicrobial sales decreased by 14% in terms of quantity of antimicrobials sold for use in all animals in 2022 compared to 2018, after accounting for the number of animals and their weights using an average weight at treatment (mg/population correction unit or mg/PCUCA) (Figure 6-3). However, sales (adjusted for animal biomass) have remained fairly stable since 2019.

Two-thirds of MIAs sold were Category III or "medium importance" antimicrobials to human health, with Category II or "high importance" antimicrobials making up most of the remainder. In 2023, the percentage of total sales (in kg) by Category of Importance to Human Medicine was:

- Category I (very high importance): less than 1% (similar rank to 2018)
- Category II (high importance): 26% (decreased from 33% in 2018)
- Category III (medium importance): 59% (decreased from 67% in 2018)
- Uncategorized Medically Important: 2% (similar rank to 2018)

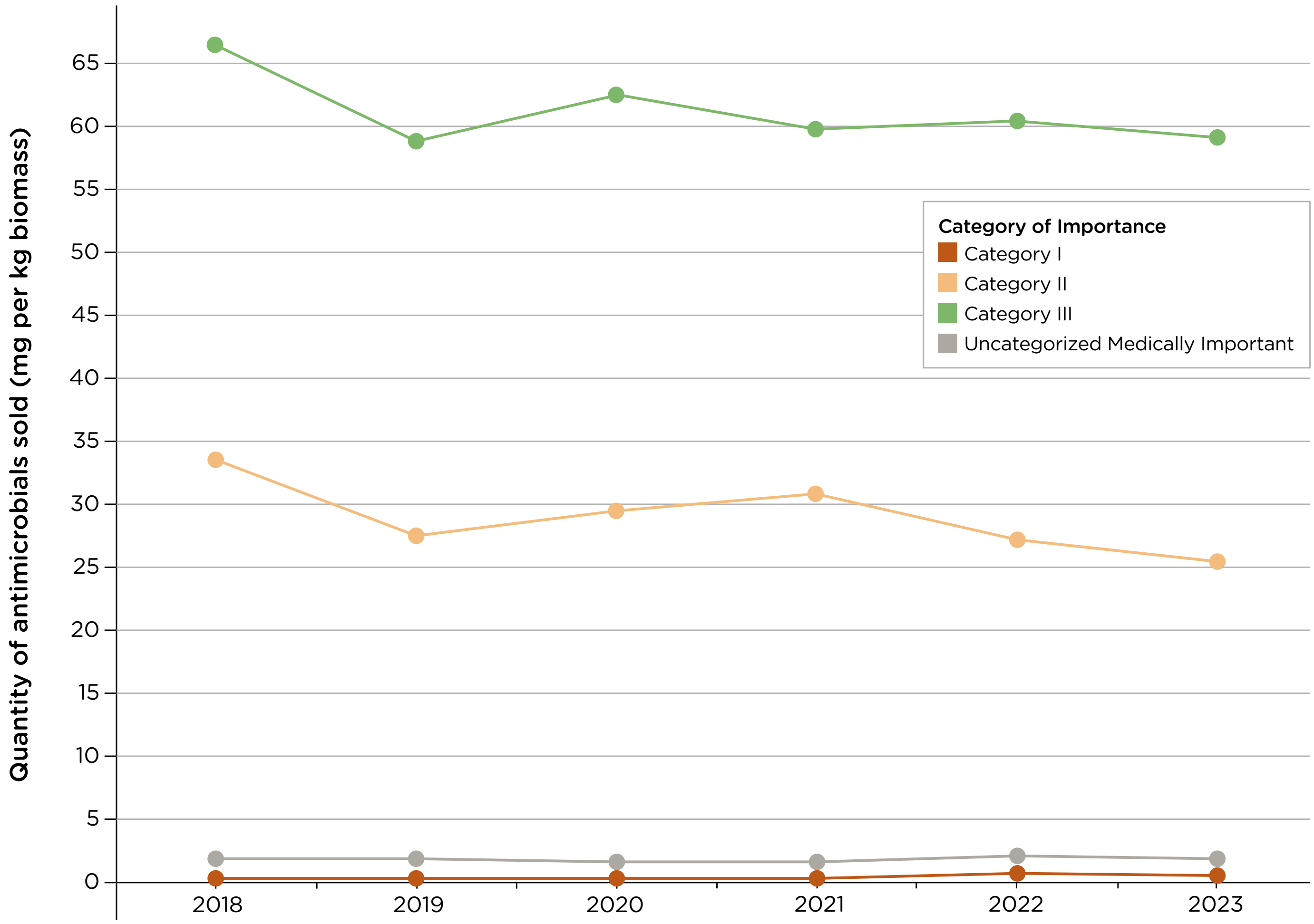


Figure 6-3. Annual quantity in mg per Canadian PCU of MIAs sold by manufacturers and importers (2018-2022) by Health Canada's Category of Importance in Human Medicine, for use in all animals, Canada (PHAC, 2024a)

As noted previously, tetracyclines (Category III antimicrobials) were the most common type of antibiotic used in food-producing animals. In 2023, tetracyclines had the highest quantity of sales, followed by macrolides, penicillins, and bacitracins. Over the past four years, between 40-60% of tetracycline sales each year have been for pigs, and 40-50% have been for beef cattle, primarily for use in feed. However, tetracyclines were one of the classes of antibiotics with the largest decreases in sales over the preceding year, along with penicillins (Category II).

Sales data have some limitations. For example, most of the antimicrobials are administered in feed (e.g. in poultry, swine, beef cattle), and often, producers purchase more feed than they need for a particular time period to ensure adequate inventory for consistent feeding schedules and account for wastage. Purchase does not always directly correlate with actual use. Although sales data can be a practical option to summarize the overall trends in the country regarding potential exposure to antimicrobials in food-producing animals, it has limitations in terms of providing guidance for stewardship interventions, due to differences between sales and use data. There are challenges in accurately quantifying the true biomass (both number and representative weights) of the animals within each commodity exposed to antimicrobials due to significant fluctuations in market conditions and external forces between and within years. For example, avian influenza has resulted in frequent and substantial impacts on poultry numbers in recent years. It is expected that sales data will also differ from AMU recorded at the farm level mainly due to the lack of representativeness of the on-farm system and for specific commodities, due to some stages of production not included in on-farm surveillance. The exception to this would be aquaculture since AMU recording is mandatory in this sector. Additional limitations arise from the fact that the attribution of sales to different commodity groups is an estimate provided by the pharmaceutical companies who provide the data. There is no ability to ascertain use by production stage within commodities or reasons for use (treatment vs prevention). However, it is important to note that the Fisheries and Oceans Canada's aquaculture AMU data and the VASR sales data are almost equivalent (PHAC, 2024a).

6.2.2 Antimicrobial Sales Within Commodity Groups

Comments in this section are specific to MIAs, as reported by CIPARS, as VASR reporting does not include Category IV antimicrobials. Ontario, Québec, Alberta, and Manitoba, the major livestock producing and dairy provinces in Canada, account for most antimicrobials sold. After adjusting for biomass, most antimicrobial sales in Canada are estimated to be for pigs, veal calves, and poultry, followed by beef cattle, aquaculture, dairy cattle, and small ruminants.

CIPARS-VASR data show that the quantity of antimicrobials adjusted for biomass (mg/ PCU_{CA}) decreased between 2019-2023, particularly in swine, the sector with the highest sales. According to PHAC (2024h), "it is important to note that the first two years of VASR (2018, and 2019) was a time of regulatory and policy changes implemented by Health Canada to promote the responsible use of antimicrobials in animals." Figure 6-4 compares antimicrobial sales by commodity groups between 2019 to 2023.

Category I antimicrobials continue to constitute a very small fraction of the overall reported AMU (less than 1%) (PHAC, 2024a).

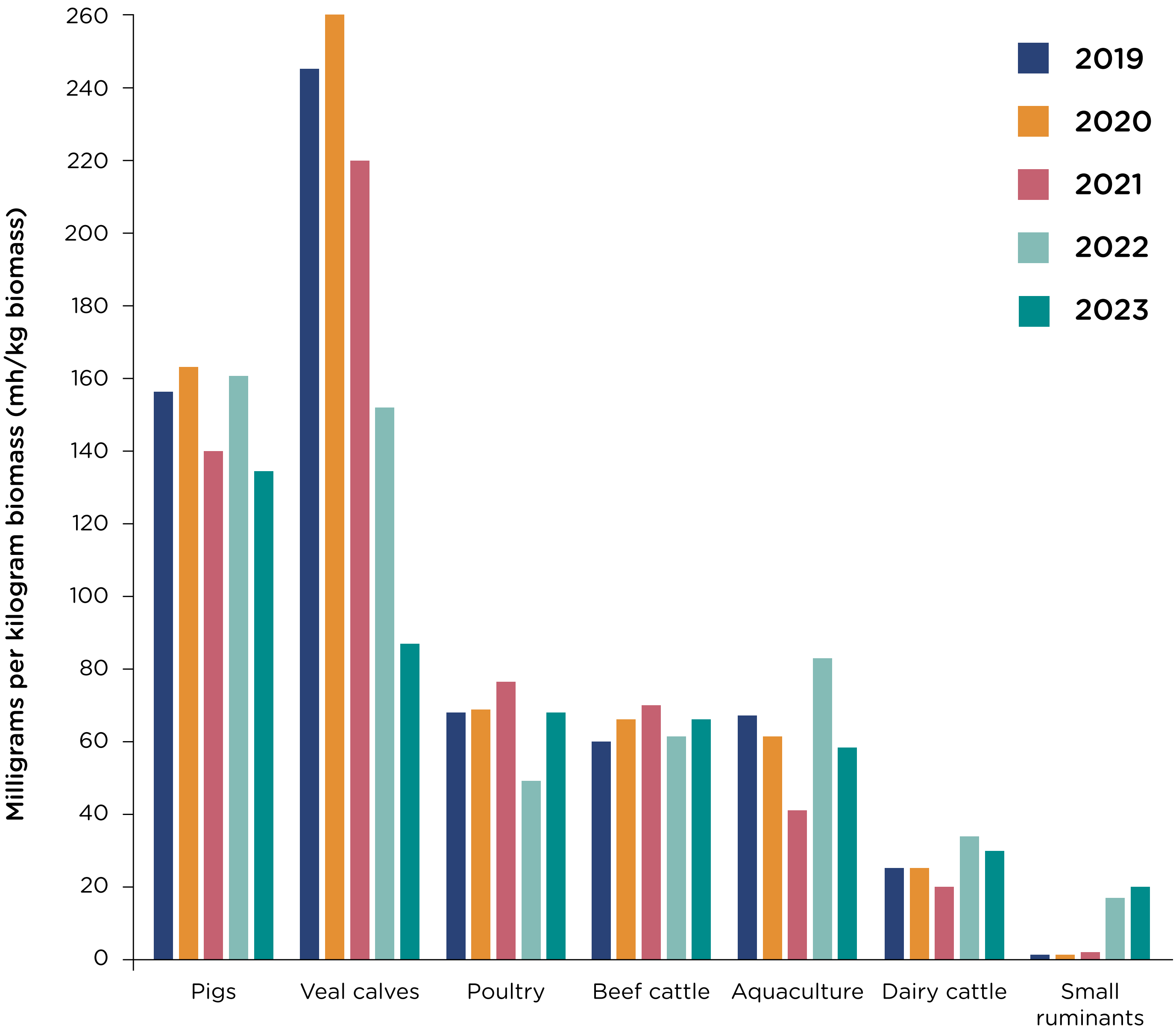


Figure 6-4. Quantity of medically important antimicrobials (MIAs) sold for use in animals, by animal species group, 2019-2023. Data exclude antifungals, antiparasitics, antivirals, Category IV antimicrobials, and uncategorized not medically important antimicrobials (Health Infobase, 2024c; modified to include only species within scope of assessment).

6.3 Farm-Level Antimicrobial Use

Farm-level AMU is an essential component of antimicrobial stewardship efforts. This section briefly describes farm-level AMU in Canada, and more extensively discusses farm-level AMU in other countries.

6.3.1 Farm-Level Antimicrobial Use in Canada

Data for on-farm AMU trends in Canada is based on sampling at sentinel sites (broiler chicken, turkey, layers, grower-finisher pigs,feedlot cattle, and aquaculture), as discussed in section 6.1.1.

Appendix 4 shows the available CIPARS data in each of the major commodity groups that are within scope of this assessment (PHAC, 2024a). While we do not know the actual AMU in each sector, we may estimate it based on sentinel farm data. Although this approach has the potential for volunteer bias and lack of representativeness, this is the approach that was developed by the CIPARS farm advisory group during the initial implementation of the CIPARS Farm program and is currently used by CIPARS (Léger et al., 2011). Since most AMU is estimated to be for pigs and broilers, the trends identified by CIPARS in those sectors will be highlighted briefly.

Poultry. The period of CIPARS reporting (2019-2023) marks the 5 year period following the Chicken Farmers of Canada's implementation of Step 2, of their AMU reduction strategy, removal of the preventive use of Category II antimicrobials. According to CIPARS, the data in broiler chickens show that AMU was stable overall but decreased slightly as compared to 2019 levels. AMU in turkeys decreased by over 35% during the five year period. According to the CIPARS, the decrease was driven by the reduced use of category II and III antimicrobials, although substantial increases in AMU in both these categories were seen between 2022-2023 (PHAC, 2024a).

Swine. AMU in swine decreased by 40% over the most recent reporting period (2019-2023), and by 4% between 2022 and 2023. Most of the decrease was due to a decrease in use of Category III antimicrobials.

Figure 6-5 is from the CIPARS 2024 webinar and summarizes antimicrobial sales and farm-level AMU from sentinel sites over the 2019-2023 reporting period (PHAC, 2024a).

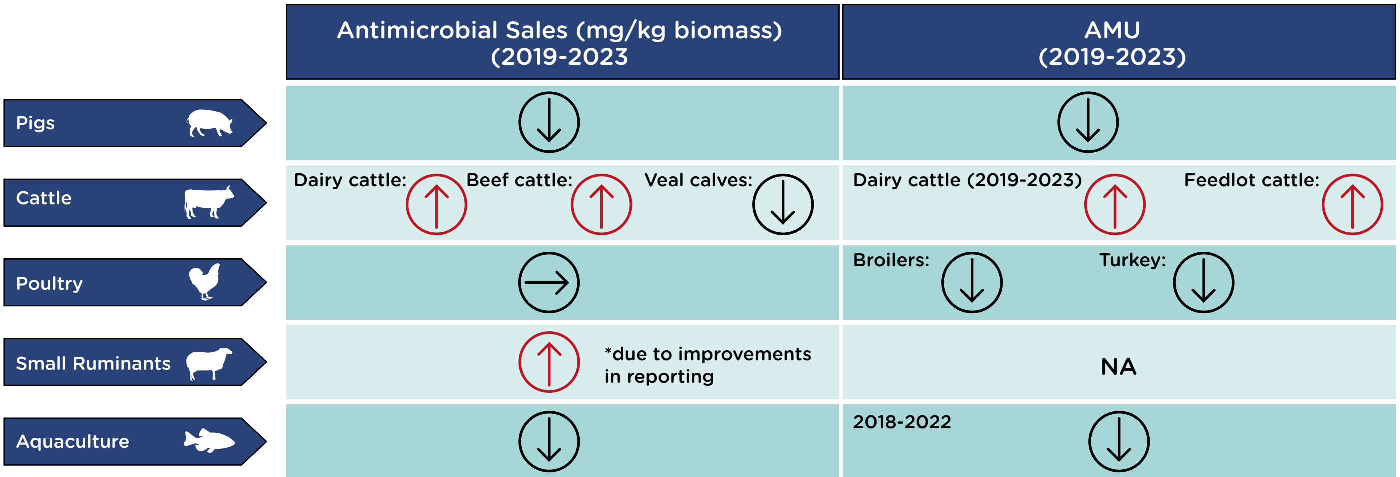


Figure 6-5. Summary of antimicrobial sales and AMU in major commodity groups during the 2019-2023 reporting period (PHAC, 2024a; modified to represent species within the scope of this assessment)

Sales vs. AMU data: What may account for differences in trends?

VASR sales data can provide important insights that inform the need for on-farm AMU data collection. This is because comparison of AMU on-farm data from sentinel sites to mandatorily-reported sales data can illustrate where CIPARS AMU data may not be fully representative of AMU in the broader food-producing sectors in Canada.

VASR reporting includes sales of all antimicrobials sold for use in animals in Canada. Thus, if CIPARS AMU data (collected from sentinel farms) were representative of AMU in each sector in Canada, we would expect to see similar four-year trends in terms of increase or decrease of AMU, as we do for antimicrobial sales. However, that is not always the case.

Inconsistency between sales and AMU data may be due to many reasons, such as (but not limited to) lack of inclusion of production stages and/or other species (e.g. cow-calves, suckling and nursery pigs, and minor species groups) in the CIPARS on-farm data sampling strategy. Alternatively, it may be that the AMU on the sentinel sites is different than on non-sentinel sites due to limits to geographic representation and volunteer biases. Finally, the difference may also be due to producers purchasing more medicated feed than needed to maintain their feed supply. Only mandatory farm-level AMU data can provide the answer.

Without farm-level data collection that is inclusive of all sub-sectors, such as nursery pigs, it is impossible to accurately assess changes in AMU trends over time and reasons for those changes, and to target stewardship initiatives accordingly.

6.3.2 Farm-level Antimicrobial Use in Other Jurisdictions

In our review of other jurisdictions, it was clear that countries with strong national AMS frameworks have utilized farm-level AMU surveillance as a key component of their overall approach. Below, Denmark's DANMAP is presented as a case study highlighting a comprehensive and streamlined system for monitoring farm-level AMU.

Case Study Highlight
VetStat: Denmark's farm-level AMU database

DANMAP is the Danish Integrated Antimicrobial Resistance Monitoring and Research Program, monitoring AMR and AMU in animals and humans. Since 2001, data on all medicines prescribed for use in animals, including vaccines and coccidiostatic agents (non-prescription) have been recorded in the national database VetStat (Sanders et al. 2020).

Since 2010, the VetStat database has been hosted and maintained by the Danish Veterinary and Food Administration. Veterinarians are required by law to report all use of antibiotics and prescriptions for production animals to VetStat monthly. VetStat contains detailed information about the source (veterinarian, pharmacy, or feed mill) and consumption for each prescription item.

- Date of sale
- Identity of prescribing veterinarian
- Source
- ID (identity of the pharmacy, feed mill, or veterinary practice reporting)
- Package identity code and amount
- Animal species
- Age group
- Disease category
- Code for farm-identity (CHR Danish Central Husbandry Register)

Three important aspects of farm-level AMU systems include: 1. their coverage (proportion of the animal population included from the target animal sectors), 2. the main funder (either private or governmental), and 3. participation in the system (voluntary or compulsory) (Sanders et al., 2020). Table 6-2 compares Canada alongside five of the eight jurisdictions included in the international case studies; these countries have existing systems for farm-level AMU data collection and have been featured in an international review of farm-level AMU by Sanders et al. (2020).

Table 6-2. Core characteristics of currently existing systems for farm-level AMU data collection in some reviewed jurisdictions (reproduced using subset of data from Sanders et al., 2020)

Country	Name of system	Animal types included	Input of AMU data	Compulsory by	Weight, dose or count based	Benchmarking (Y/N)	Parties involved in benchmarking
Denmark	VetStat	Pigs, dairy, beef, calves, broilers, turkeys, laying hens, goats, sheep, fish, mink	Veterinarians Feed mills Pharmacies	Legislation	Dose	Y	Producers
The Netherlands	SQS|SDa	Pigs, dairy, beef, calves, broilers, turkeys, rabbits	Veterinarians	QAS	Dose	Y	Producers Veterinarians
	SDa	Goats, sheep, horses, pets, mink	Veterinarians	N/A- Survey	Veterinary benchmark indicator	N	–
Germany	HIT	Pigs, beef, calves, broilers, turkey	Producers Veterinarians	Legislation	Count	Y	Producers
	QS	Pigs, calves, broilers, turkey, ducks	Veterinarians	QAS	Count	Y	Producers
	VetCAb-ID	Pigs, dairy, beef, calves, broilers, laying hens, turkeys, goats, sheep, horses, fish, pets	Not specified	Not specified	Count	N	–
	VetCAb(-S)	Pigs, dairy, beef, calves, broilers	Producers Veterinarians	N/A- Survey	Count	N	–
France	CLIPP	Rabbits	Producers Veterinarians Technicians	N/A- Voluntary	Days	Y	Producers
	GVET	Pigs	Producers	N/A- Voluntary	Weight, dose, and count	Y	Producers
	INAPORC	Pigs	Producers Veterinarians Technicians Feed mills	N/A- Voluntary	Weight and dose	N	–
	REfA2vi	Broiler chickens Turkey	Producers Veterinarians	N/A- Voluntary	Dose	N	–
	VEAL	Veal, cattle	Producers Veterinarians	N/A- Voluntary	Weight, dose, and count	N	–

Country	Name of system	Animal types included	Input of AMU data	Compulsory by	Weight, dose or count based	Benchmarking (Y/N)	Parties involved in benchmarking
UK	BEIC	Laying hens	Producers	QAS	Dose	N	–
	BPC-AS	Broilers, turkey, ducks	Veterinarians	PB	Weight	N	–
	eMB-Pigs	Pigs	Producers Veterinarians Feed mills	QAS	Weight	Y	Producers
	GFA	Game birds	Veterinarians Feed mills	N/A-Voluntary	Weight	N	–
	SSPO	Fish	Veterinarians	N/A-Voluntary	Weight	N	–
Canada	CIPARS	Broiler chickens, grower-finisher pigs, dairy cattle, feedlot cattle, layers, and turkeys	Producers Veterinarians	N/A-Voluntary	Weight, dose, and count	N	–
	FAOC	Fish	Producers	Legislation	Weight	N	–

QAS= Quality assurance scheme
PB = Professional body

Table 6-2 shows that Denmark, the Netherlands, and Germany had the most extensive species representation in their AMU data; all had some form of mandatory farm-level AMU reporting in place, resulting in the highest proportion of their animal populations being represented in the farm-level data. France did not have mandatory farm-level reporting requirements. It is not clear what percentage of producers participate in the five farm-level data collection systems in France or how the data from these five systems are integrated/compared.

The UK has mandatory reporting in place for poultry, laying hens, and pigs, as per the requirements of quality assurance schemes and professional bodies. Multiple systems were in place for these species, without any representation of dairy or beef cattle sectors. Finally, of interest but outside of the scope of this assessment, is that the Netherlands and Germany were the only jurisdictions in the subset that collected AMU data on pets.

In Sanders et al., (2020) funding source for the surveillance systems appeared to be associated with the extent of coverage of the animal sector(s) included. Those farm-level AMU systems that were implemented by government regulations used data collected based on sampling of a subset of farms, or self-reported surveys (e.g. Germany's VetCAb-S, Netherland's MARAN, or Canada's CIPARS), and in only a few cases, had full sector representativeness (e.g. Germany's HIT, Denmark's VetStat, Canada's DFO). On the other hand, most farm-level AMU systems driven primarily by industry funding had at least partial sector coverage (e.g. France's CLIPP, RefA2vi; Germany's QS), and in many cases, had full coverage (e.g. Netherland's SQS/DA, UK's SSPO) (Sanders et al., 2020).

Canada has room for improvement as compared to most of the other jurisdictions examined, in terms of the breadth and comprehensiveness of its farm-level AMU. Crucial to any effort to improve farm-level AMU collection is sufficient and sustained resources (people, funding, and infrastructure). Commodity groups, veterinary organizations, and veterinarians must be engaged in any efforts to expand surveillance of farm-level AMU, including data related to indication for use; they also act as key partners in involving producers.

Data input. Data collection can be automated or manual. In the jurisdictions examined, input of data typically occurs by veterinarians, feed mills, or producers. Several countries, such as France also utilize veterinary technicians for inputting data. In Canada, the CVMA has discussed utilizing registered veterinary technicians (RVTs) within their scope of practice to assist with tasks that may support veterinarians (Tremblay, 2024); this may include farm-level AMU data input. This strategy is particularly important to accommodate manual data collection in light of the issue of shortage of veterinarians being faced in Canada (Canadian Animal Health Institute, 2024).

Automated data capture on AMU may also be used to estimate farm-level AMU digitally through software-linked data sources, e.g. prescription records from veterinary practices, or data on AMU from farm management software. Automated farm-level AMU data capture with user-friendly functions has the benefit of increasing producer compliance with data collection, reducing the administrative burden of data input, and also reducing the risk of data entry errors (Sanders et al., 2020). Our key informants in Europe consistently mentioned automated data capture as essential to increasing buy-in from producers. A key informant for the European Union case study, speaking specifically of Belgium's mandatory farm-level AMU data utilizing prescribing records, stated: *"Data collection was streamlined, using invoice information already available, making it easier for producers and reducing reluctance" (Key Informant, Belgium, European Union Case Study).*

Some research groups are working on developing automated systems to capture prescription records from veterinary clinics; despite the limitations of prescription data, this could be a practical tool for benchmarking in some commodities. Electronic records of feed deliveries are already utilized by many swine and poultry producers and could be a potential source of automated AMU data in these species, since most AMU in pigs and poultry is through feed.

As a final comment, animal health services are almost exclusively used and provided for private sector needs, unlike in public health. Costs and the impacts of AMU, and potentially also the costs of assessing farm-level use, are therefore borne by producers, including possibly affecting the strength of their brand. This key contextual factor is often unrecognized by people outside the animal health or production sectors but may influence any new program development, delivery or data quality.

Key finding 11

Farm-level AMU surveillance is an essential component of antimicrobial stewardship efforts.

- Mandatory sales data are not sufficient for stewardship purposes, although they are complementary to farm-level AMU data.
- Countries that have engaged in farm-level AMU surveillance and other measures have reported reduced AMU.
- Commodity groups, veterinary organizations, and veterinarians need to be engaged in efforts to expand surveillance of AMU, including data related to indication for use / dose / duration, and act as key partners in involving producers.
- The only farm-level mandatory reporting of AMU in Canada is for finfish aquaculture.
- Software using automated data capture of prescription records from veterinary clinics or feed delivery records could be a helpful tool for benchmarking in some commodities and may increase producer compliance with data collection, however there may be practical challenges associated with getting such infrastructure in place.

6.3.3 Gaps and Limitations in Farm-level AMU Surveillance

Canada has a mosaic of AMR and AMU surveillance initiatives. However, key aspects of the systems presented in this report are fragmented, and each offers, at best, an incomplete picture of AMR/AMU in Canada, leaving Canada without a fully integrated system for AMR/AMU. There is a need for Canada to move towards a fully integrated AMU and AMR surveillance system that includes all key sectors of major commodity groups as well as pathogens that impact animal health.

A fundamental issue that limits expansion of AMU surveillance at the level of the veterinarian or producer is the lack of defined and agreed upon objectives for such surveillance (Canadian Council of Chief Veterinary Officers, 2016). Policy-makers and key actors must determine the objectives for collecting AMU data, such as using producer or veterinary-level data for benchmarking and AMS interventions, and at what level those interventions will be implemented. Only then can the surveillance programs be expanded with appropriate design and resources to support these objectives.

The key gap that currently limits Canada's ability to measure AMU in food-producing animals is a lack of wide-scale representative farm-level AMU data by indication and reason for use, as well as dose and duration. This creates major limitations for the conclusions that can be drawn from existing data to inform more granular (e.g., farm-level) AMS interventions. CIPARS is not currently equipped with the appropriate infrastructure to conduct farm-level AMU beyond its sentinel farm program, due to reliance on volunteers, limited resources, sampling of only a small subset of farms, and lack of validation of self-reported data.

Furthermore, there are currently no systematically collected data on antimicrobial prescribing patterns that capture reasons for AMU. These are needed to support evaluation of interventions and implementation of AMS.

Canada does not currently engage in systematic collection of veterinary prescription records, aside from DFO data. If it were to do so in the future, it is important to acknowledge that surveillance through prescription records to support AMS has some important limitations and prerequisites, discussed below.

Limitations of veterinary prescribing data. Similar to data from CIPARS-VASR, differences between prescription volumes and the volume of antimicrobials actually used will always be present. In addition, farms can obtain prescriptions from more than one veterinarian or clinic based on differing accessibility, cost and convenience. For these reasons, prescription records do not represent true use on each farm. Further, in dairy cattle, feedlot cattle, cow-calf and small ruminants, AMU is often via injection or bolus, where potentially only a portion of the product is administered (i.e. partial bottles of injectable medication). This issue is particularly likely in small holder operations which are still very numerous across the country for beef and small ruminants, as well as dairy in some parts of Canada. In pigs, poultry, and for some uses in feedlot cattle, AMU often is administered in feed and water, and prescriptions may be written to order more than what is needed to ensure that there is no gap in feed supply. There might, however, be some situations where prescription data are more meaningful with one Québec study suggesting a correlation between prescription data and the results of a garbage can audit (where drug containers placed in a central repository are inventoried) in dairy cattle (Lardé et al., 2021). An additional limitation may be the issue of non-standardized veterinary medical record keeping systems that can complicate automated extraction or increase clinic costs to enter data for surveillance purposes.

Need for standard definitions for reasons for use. To make effective use of prescribing data to support AMS, there is a need for standardized definitions for reasons for AMU on veterinary prescriptions. These are currently lacking in Canada; the information provided on veterinary prescriptions regarding the reason for use is left to the discretion of prescribing veterinarians. The case study on Denmark VetStat is an example that shows capture of "disease category" information as part of prescribing data.

Key gap 11

Lack of wide-scale representative farm-level AMU surveillance limits AMS recommendations and assessments of AMS programs.

- There is no national level objective for collecting representative AMU data in Canada; this would be required to design AMU surveillance systems, particularly if farm-level benchmarking is to be considered in the future.
- There is no systematically collected data in Canada on antimicrobial prescribing patterns or farm use that capture reasons for AMU. These data are needed to support evaluation of interventions and implementation of stewardship.
- Standardized definitions for reasons for AMU in veterinary prescriptions are lacking, and this is left to the discretion of prescribing veterinarians.
- Surveillance through prescription records can be problematic due to differences between prescription volumes and the volume of antimicrobials actually used as well as logistical challenges.
- Prescription records might overestimate farm-level AMU; for AMU administered via injection, or bolus, potentially only a portion of the product is administered (i.e. partial bottles of injectable medication). This overestimation is more likely to occur for AM administered in feed since larger amounts of AM are ordered to ensure the required feed supply.
- CIPARS is not currently equipped with the appropriate infrastructure to capture a valid estimate of farm-level AMU, due to reliance on volunteers, limited resources, sampling of only a small subset of farms, and lack of validation of self-reported data.

Related Action in the Pan-Canadian Action Plan

- Under the Surveillance pillar: "Expand sources, coverage and integration of AMR and AMU surveillance data, including the use of modern laboratory technologies and standardized reporting, to help monitor AMR/AMU across One Health sectors, with specific focus on improving data from the environment; transmission pathways between sectors; and population groups disproportionately impacted by AMR and inappropriate AMU."

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 7:

Impacts of Interventions to Reduce Antimicrobial Use on Antimicrobial Resistance

Introduction

This chapter outlines the impact of interventions to reduce AMU on AMR, explores the impacts, both positive and negative, perceived and actual of interventions to reduce AMU in food-producing animals, and looks at the importance of measurement to management of AMR/AMU.

7.1 Impact of Reduced AMU on AMR Reduction

The most notable well-established impact of reductions in AMU in food-producing animals is a reduction in AMR in animal pathogens or surveillance indicator bacteria. There are numerous examples of this from countries that have reduced AMU in food-producing animals. Some are described below.

Canada has an excellent example of the impact of reduced AMU in reducing AMR in a human pathogen, widely recognized around the world. In Canada, the presence of ceftiofur-resistant S. Heidelberg in retail chicken was first associated with third-generation cephalosporin resistant S. Heidelberg in human infections in 2005. After the voluntary withdrawal of ceftiofur in ovo use in 2005 in Quebec, there was a reduction in prevalence of ceftiofur resistance. However, there was subsequent partial resumption of extra-label use of ceftiofur in and after 2007 with an associated increase in ceftiofur/ceftriaxone resistant Salmonella Heidelberg in retail poultry in Canada followed after an almost imperceptible lag by an increase in human isolations (Figure 7-1, Carson et al., 2019). The drug was also being used in broiler chickens in other provinces. The problem ceased after the formal elimination in 2014 of extra-label use of ceftiofur in poultry by the Chicken Farmers of Canada.

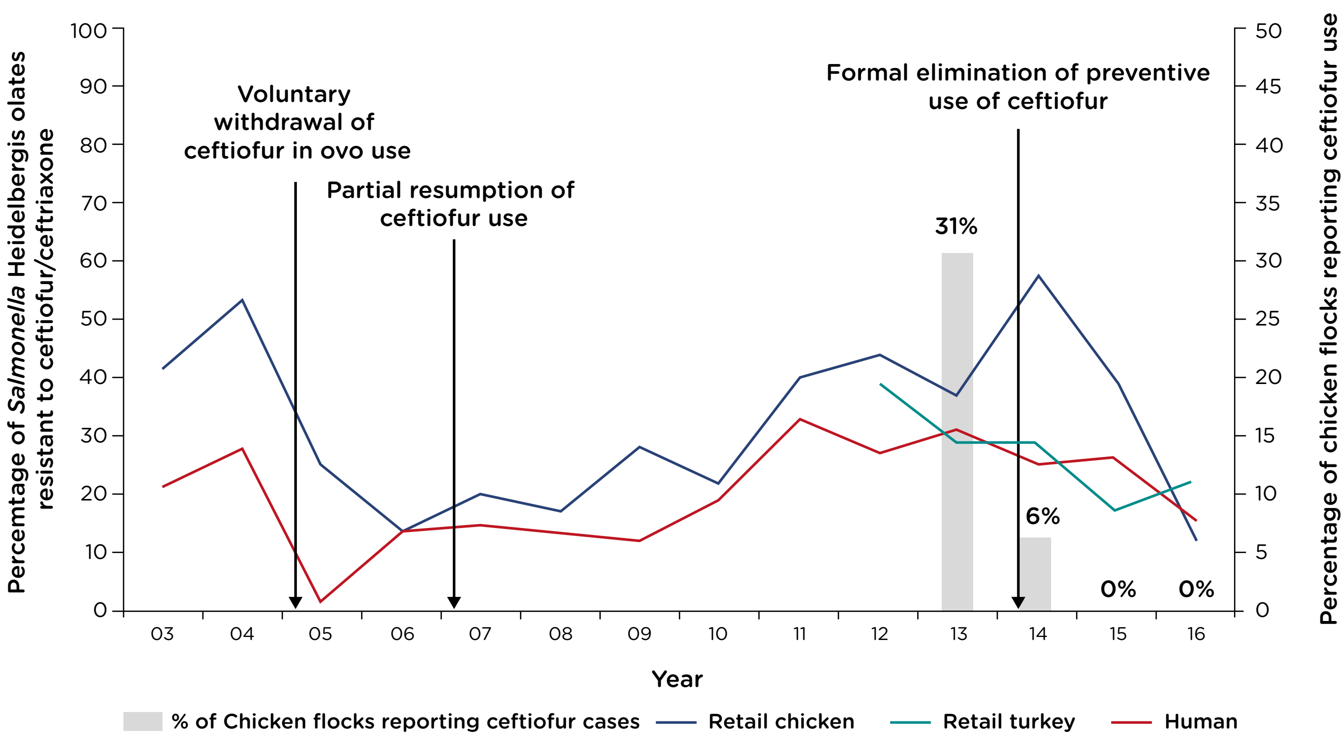


Figure 7-1. Percentage of ceftiofur/ceftriaxone-resistant *Salmonella Heidelberg* from retail poultry and from humans, and ceftiofur use in chicken flocks (Carson et al., 2019)

As discussed in Chapter 4, there has been an increase in pan-susceptible *E. coli* in broiler chickens at slaughter and in retail products following the formal removal by the Chicken Farmers of Canada of prophylactic use of Category I and Category II antimicrobial drugs (Figures 4-1, 4-2).

The isolation of similar *Salmonella* Heidelberg from humans supports a contribution to human disease. The evidence led the Chicken Farmers of Canada to impose a ban on the extra-label prophylactic use of Category I antimicrobials such as ceftiofur and later of Category II antimicrobials, with a clear temporal impact in decreasing resistance (Figures 2.3, 4.1, 4.2, 7.1).

This important Canadian experience illustrates the impact of AMU in animals as a driver of AMR in bacteria that may infect people, and the importance of reducing AMU to reduce AMR. As a side benefit, AMU is also easier to measure than AMR. These studies also show the importance of measurement at the national level. Other reasons that we emphasize this Canadian experience is that several other "made in Canada" issues flow from this CIPARS work. These include the importance of federal and provincial jurisdictional role differences in drug approval versus actual drug use, in this case the impact of extra-label use of a product under veterinary prescription not approved specifically for use in poultry, and of how AMU was regulated by the voluntary actions of an animal industry rather than of a government.

Another well-established example of the relation between reduced AMU and subsequent reduced AMR is the reduction in vancomycin-resistant enterococci following the withdrawal of avoparcin as a growth promoter for swine and poultry in Europe (Boerlin et al., 2001).

Compelling reductions in AMR can also be seen over time in jurisdictions that have dramatically reduced AMU. In the Netherlands, well-integrated data show the decline in food-producing animal AMU and parallel decline in AMR in indicator bacteria (De Greeff et al., 2022, Figure 7-2). These trends have also been observed in countries including Denmark that have adopted national policies to limit AMU.

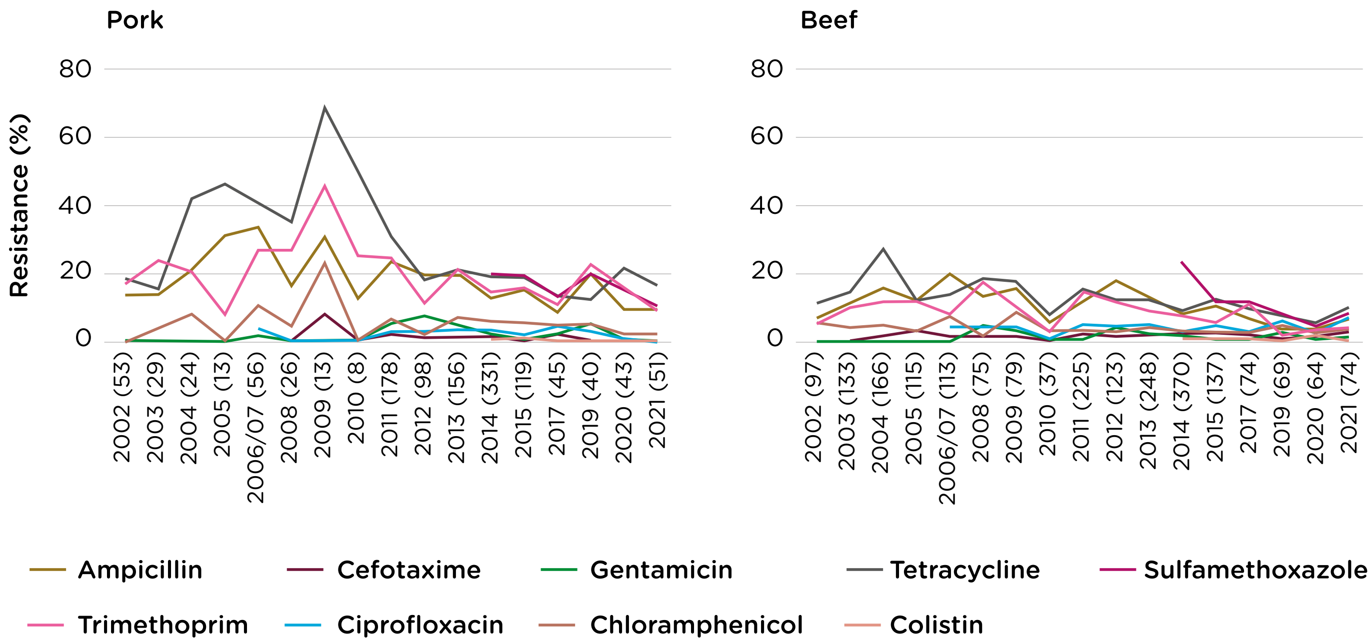


Figure 7-2. Trends in resistance (%) of *E. coli* isolated from pork and beef in the Netherlands from 2002-2021 (De Greef et al., 2022)

Scientific reviews for pigs, cattle, chicken, and small ruminants have demonstrated that limiting non-therapeutic applications of antimicrobials was followed by a reduction in AMR in these animals, and some literature has also suggested reduction of AMR in humans with direct exposure to food-producing animals. Conversely, exposing animals to antimicrobials resulted in higher resistance to those antimicrobials than exposing animals to no or lower doses of antimicrobials. (Tang et al., 2017; Scott et al., 2018) In broiler chickens and swine, complete restriction of antimicrobials has been associated with a decrease in the odds of AMR development in fecal *E. coli* to fluoroquinolones and aminoglycosides when compared to conventional farming (Costa et al., 2023).

Key finding 12

Interventions to reduce AMU in food-producing animals reduce AMR in animal pathogens and in surveillance indicator bacteria.

- Jurisdictions such as the Netherlands and Denmark that have dramatically reduced AMU have experienced a decline in AMR in indicator bacteria.
- In Canada, there was a reduction in ceftiofur-resistant *E. coli* and *Salmonella* Heidelberg in retail chicken as well as a marked reduction in MDR indicator *E. coli* from chicken meat at retail and an increase in pan-susceptible E. coli following the voluntary changes in AMU and restriction of Category I and later of Category II antimicrobials by the Chicken Farmers of Canada. Importantly, the reduction of ceftiofur use in chickens was followed by a concomitant reduction in resistance to third-generation cephalosporins in *Salmonella* Heidelberg in human infections in Canada.
- Scientific reviews in pigs, cattle, chicken, and small ruminants have shown that limiting non-therapeutic applications of antimicrobials was typically associated with a reduction in AMR in these animals, as well as in farm workers exposed to these animals.

Related Action in the Pan-Canadian Action Plan

- Under the Surveillance pillar: "Work with partners to establish baselines, goals and measures of progress for increasing appropriate AMU and reducing AMR in the agriculture and agri-food sectors."
- Under the Leadership pillar: "Increase Canada's contributions to global efforts to advance key bilateral and multilateral commitments by prioritizing generating improved data/ evidence on AMR/AMU and strengthening surveillance systems and data standards."

7.2 Other Impacts of Efforts to Reduce AMU: Unintended Consequences

A breadth of unintended consequences have been discussed in relation to efforts to reduce AMU, including impacts on animal welfare, production, and trade. These will be elaborated in the following section.

7.2.1 Impacts on Animal Welfare

It is important to ensure that any reductions in AMU do not compromise animal health and welfare.

Concerns regarding the impact of efforts to reduce AMR on animal welfare have been documented. For example, Canadian commodity groups have expressed the concern that antimicrobial-free practices, and any new regulations aimed at reducing AMU could be associated with increased animal morbidity and mortality, creating animal welfare concerns. (CAHS Virtual Engagement Finding, round 1).

Some evidence in the literature has started to emerge to support these concerns. Literature from the US surveying the perceptions and experience of producers and veterinarians across the major commodity groups, including both those with and without experience with antibiotic-free production, indicated that they perceived that antibiotic-free production has negative impacts on animal health and welfare, will increase production costs, and will have questionable effects on consumer demand for meat, egg or dairy, but that the Raised Without Antibiotics label takes priority over animal welfare (Singer et al., 2019). A strictly Raised Without Antibiotics approach will in some circumstances adversely impact animal welfare through increased disease in animals, although in Europe, animal welfare assessments have concluded that this might not necessarily be the case if appropriate management practices are in place (Iannetti et al. 2021).

Antimicrobial stewardship in animals however does not mean "Raised Without Antibiotics", which could adversely impact animal welfare and production costs (Salois et al., 2016; Karavolias et al., 2018). Rather, AMS needs to be focused on improved use of antimicrobial drugs so the benefits are clear and substantial.

Lack of producer buy-in to regulations reducing AMU can lead to negative impacts, particularly for implementation of new regulations. A qualitative study in Québec examined how the implementation of changes in the Québec regulations in 2019 relating to restriction of Category I antimicrobials on dairy farms resulted in challenges for producers and veterinarians (Millar et al., 2023). The study found that "fear of economic consequences" was one of the barriers to the implementation of the regulation. A small number of dairy producers also perceived that the regulation negatively impacted the health and welfare of their animals, despite the fact that regulations also resulted in the implementation of increased preventive practices on their farm.

7.2.2. Impacts on Selective Pressures for AMR

Ironically, some of the efforts to reduce AMR may produce selective pressures that might lead to more AMR. This includes efforts to reduce AMR by replacing antimicrobials with "alternative products", or implementation of certain disinfection protocols to prevent disease.

The selection of MRSA in swine by zinc oxide was an important consequence of the removal of growth promoters in Europe which drove the use of in-feed zinc oxide in pig farming (Slifierz et al., 2015). Similarly, enterococcal bacteria have been noted to develop resistance to copper, which is associated with resistance to antimicrobial drugs such as macrolides and glycopeptides such as vancomycin (Yazdankhah & Bernhoft, 2014). However, with proper measurement, such consequences can be identified and understood, as in MRSA in swine (Slifierz et al., 2015), and remedied.

In addition, frequent use of some biocides or disinfectants (for example the quaternary ammonium compound) as part of management practices can co-select for various AMRs (Wales & Davies, 2015). Another recent study demonstrated that sub-optimal disinfectant concentrations allowed *E. coli* O157:H7 to adapt and survive disinfection and develop antibiotic resistance (Kirchner et al., 2024).

7.2.3 Impacts on Productivity, Competitiveness, Production Quality, and Sustainability

A systematic review was conducted to evaluate European countries with AMU restrictions such as mandatory or voluntary prohibition of AMU, limitations on specific drug classes, and incentives for reduced AMU. Based on 14 European studies, it was concluded that unintended consequences of increased mortality, reduced productivity (assessed in various ways), and disease lesions found at slaughter from national-level restrictions on AMU in food-producing animals were "temporary and minor" (McEwen et al., 2018).

In addition, in Denmark, introduction of the Yellow Card system (where pig farms that used twice the average quantity of antimicrobials had a government order to reduce AMU below a threshold in 9 months), led to no adverse effects on mortality and production, although mixed effects (increases and/or decreases) were found in different lesions at slaughter (reviewed by McEwen et al., 2018). In the Netherlands, the discontinued use of fluoroquinolones and third generation cephalosporins was reported to have no adverse effects either on broiler chicken mortality or on selected disease (McEwen et al., 2018).

A study by Belay & Jensen (2022) of the economic costs to the 2% of pig farms affected by the Yellow Card scheme in Denmark concluded that the benefits of the Yellow Card regulation in terms of reducing future health risks of AMR are likely to substantially exceed the initial small increase in immediate costs for affected farms.

It is important to qualify study findings by considering differences among the commodity groups being examined, interventions being compared, and context for the European studies that are different from North America in a number of important aspects, including management practices, structure of the commodity groups, and average size of farming operations that account for most of the production. The extent of any differences, which we have not analyzed, varies considerably across sectors. Other differences include market pressures selecting for low- or no- AMU, and overall willingness of producers to engage in efforts to reduce AMU.

7.2.4 Impacts on Trade

AMU in food-producing animals is a potentially important trade issue. There is a threat based on EU regulations to restrict importation of meats from countries where this practice is allowed. International key informants have also actively discussed AMR/AMU as a potential trade barrier as part of the international case studies (CAHS international case studies).

The USA, Japan, UK, China, and Mexico comprise sizable export markets for Canada's food-producing animal products. Among these major trading partners, the UK and US were included among the CAHS international case studies, due to comparability and relevance to Canada from a policy perspective, with the other jurisdictions being out of scope of this assessment. The United States is Canada's current trading partner for more than half of all exports, and 94% of animal production (Agriculture and Agri-Food Canada, 2024). In 2023, Canada also exported $34.4 million in meat, fish, and seafood preparations to the UK. In interviews, key informants in the US and UK indicated they did not currently experience trade issues, but remained vigilant of them in the future (CAHS US Key Informant Interviews).

It is likely that improving antimicrobial stewardship in food-producing animals could avoid unintended trade consequences, and indeed has the potential to benefit trade, possibly opening doors for new trading partners.

Key finding 13

Effective antimicrobial stewardship is key to avoiding or mitigating unintended consequences of AMU reduction, replacement, and refinement policies.

- Rearing farm animals “antibiotic free” can have serious and unacceptable adverse welfare consequences.
- Studies from other jurisdictions, like Denmark, that have successfully reduced AMU by national-level restrictions in food-producing animals have shown the unintended consequences to be “temporary and minor”, or to have no adverse effects.
- The selection of MRSA in swine by zinc oxide was an important unintended consequence of the removal of growth promoters in Europe.
- It is critical that improvement in AMS including any reductions in AMU do not have unintended consequences of reduced animal welfare through increased disease.
- The ability to demonstrate effective antimicrobial stewardship in food-producing animals in Canada may have important trade consequences and is part of Canada’s international obligations relating to AMR.

7.3 Key Gaps in Impacts of Interventions to Reduce AMU

During the cross-Canada engagement component of this assessment, many virtual engagement and written survey participants, and key informants, repeatedly expressed concern that any changes to existing AMU practices in Canada might have unintended consequences of increasing disease or decreasing farm productivity. Although this fear is largely unsupported by the evidence from countries that have made marked advances in improving and reducing AMU in food-producing animals, it is a very important consideration. Any improvements to how Canada addresses AMU in food-producing animals, outlined in the promising Strategic Interventions in Chapter 9, need to include measures to identify and address any adverse consequences of any agreed additional interventions.

Key gap 13

There is a lack of a well-designed and managed food-producing animal national AMS system.

- The coordination and measurement at the national level is currently lacking, including measures that could identify and address any adverse consequences of any agreed major stewardship changes in a timely manner.

Related Action in the Pan-Canadian Action Plan

- Under the Stewardship pillar: "Develop, implement and promote guidelines/standards for appropriate AMU in humans and animals through policy and regulatory initiatives, monitoring and educational interventions/accreditation requirements for health professionals and prescribers."

7.4 Measurement of Impact

There was emerging consensus among key informants and virtual engagement participants that additional farm-level data collection and farm benchmarking would allow collection of the critically lacking data that are needed to improve AMS in food-producing animals and to document success. Refining and reducing AMU in food-producing animals such that the benefits are measurable, clear and substantial requires assessment on a case-by-case basis by a herd veterinarian, and cannot be achieved through a 'one size fits all' approach. It involves development of a sustained culture of AMS in veterinarians, producers and regulators.

Jurisdictions that have been most successful at reducing AMU and improving AMS have shown that farm-level benchmarking are powerful drivers of improved AMS.

As a clear example, the Netherlands, a global leader in AMS in food-producing animals, achieved a 56% reduction in AMU between 2007-2012, with a 92% and 59% reduction in use of 3rd generation cephalosporins and fluoroquinolones respectively between 2009-2012. It is important to note that the use of these classes in Canada is very low relative to category II and III drugs. The reduction was achieved by setting targets and tracking progress using mandatory farm-level benchmarking data. In 2013, the government target for AMU reduction was raised to 70% by 2015 compared to the 2009 baseline. This target was met in 2022 with a 77.4% reduction in sales of antimicrobials for use in livestock (Autoriteit Diergeneesmiddelen, 2024).

The decline in AMR in indicator *Escherichia coli* isolated from caecal samples of healthy food-producing animals at slaughter and the clear reduction in the proportion of animals positive for ESBL/AmpC producing *E. coli* was attributed to the AMU measures taken in Holland since 2010 (De Greeff et al., 2022).

This Netherlands case study shows what can be achieved when there is a commitment and concerted effort initiated by the government to improve AMU in food-producing animals and shows two ways in which success can be measured.

7.4.1 How to Measure Success

The ultimate measure of success of a reduction of AMU in food-producing animals is a reduction in AMR in animal pathogens and in resistant bacteria and/or their mobile resistance genes reaching people and the environment. Another, less direct, measure of success is evaluation of the broader AMS approaches, described in Chapter 3 (summarised in Figure 3-1). Successful implementation of AMS in food-producing animals can thus be measured in many different ways. Success can be both qualitative and quantitative, but the key is measurement. Governments and industries can measure success through:

- Documented engagement of producer organizations.
- Development and uptake of stewardship training programs across the producer groups and by veterinarians.
- Successful development of and compliance with regulations or voluntary standards relating to food-producing animal AMS.
- Setting reduction objectives in AMR and AMU and/or improved appropriate use. objectives through collaboration with industry groups and stakeholders such as reduced use of Category I medically important antimicrobials (MIAs).
- Developing farm-level benchmarking with the different sectors, including thresholds for changes needed.
- Progress in the implementation of the PCAP.
- Achieving international standards and commitments.

Canada could leverage CIPARS to measure success, building on its well-established track record in assessing AMR in indicator bacteria and in assessing AMU, especially if the Promising Strategic Intervention 2 identified in this Assessment is adopted. Clearly some of the actions identified above have taken place in Canada, and different farm and veterinary groups can take credit for progress made to date. The Promising and Strategic Interventions identified in this assessment would enable the "next step" needed to improve AMU in food-producing animals.

7.4.2 Data Drive Change: "If You Can't Measure It You Can't Manage It".

The international case studies of countries that have significantly reduced and improved AMU in food-producing animals show that the management of AMU in food-producing animals and the measurement of success must be data driven. The key informant interviews unanimously supported the importance of data collection in documenting AMU in food-producing animals and in comparing use on farms. For example, representatives from the Canadian producer groups emphasized the value of AMU and AMR data collection and sharing, and of peer-to-peer engagement and benchmarking as a cornerstone of AMU reduction efforts.

As discussed earlier, CIPARS is an excellent example of the value of collecting AMU and AMR data. CIPARS identified the important problem of ceftiofur-resistant *Salmonella* Heidelberg and indicator *E. coli* in chicken samples, and the occurrence of these same *Salmonella* in humans (Figure 7-1). This resulted in exceptional and ground-breaking leadership by the Chicken Farmers of Canada to implement an exemplary and effective voluntary policy change (Figures 4-1, 4-2, 7-1). This is an example of the importance of AMU and AMR surveillance data.

Numerous Canadian and international key informants acknowledged the critical importance of CIPARS to Canada's attempts in providing the data on which to base improvement of AMS in food-producing animals, but Canada currently does not have the detailed and comprehensive data it needs to demonstrate good AMS in food-producing animals.

CIPARS has developed a strong and impressive network of surveillance partners across industry, veterinarians, and provincial-territorial governments which collects information important for national information for decision makers and key actors. For example, a key finding resulting from this is that food-producing animal antimicrobial sales (adjusted by populations and weights) in Canada is over twice that of the median sales in many European countries, and this is largely attributable to use in swine (Figure 7-3). However, there is a need for far more information including how the use of different antimicrobial classes compares. For example, we do not know enough about why there are substantial differences among provinces in AMU in grower-finisher swine AMU, including marked differences in preventative and therapeutic use. This highlights a specific gap in current AMU surveillance data - lack of reasons for use (indication data), dose, and duration.

Many possible factors may explain these differences, such as:

- Differing AMU for disease prevention purposes
- Differences in duration of use of antimicrobials in feed for preventive or treatment purposes
- Legacy use of AMU based on outdated practices
- Addressing variations in management, biosecurity, housing or hygiene
- Differences in prescribing practices among veterinarians

We currently do not have these data. In the absence of detailed data, Canada cannot answer these and other important questions.

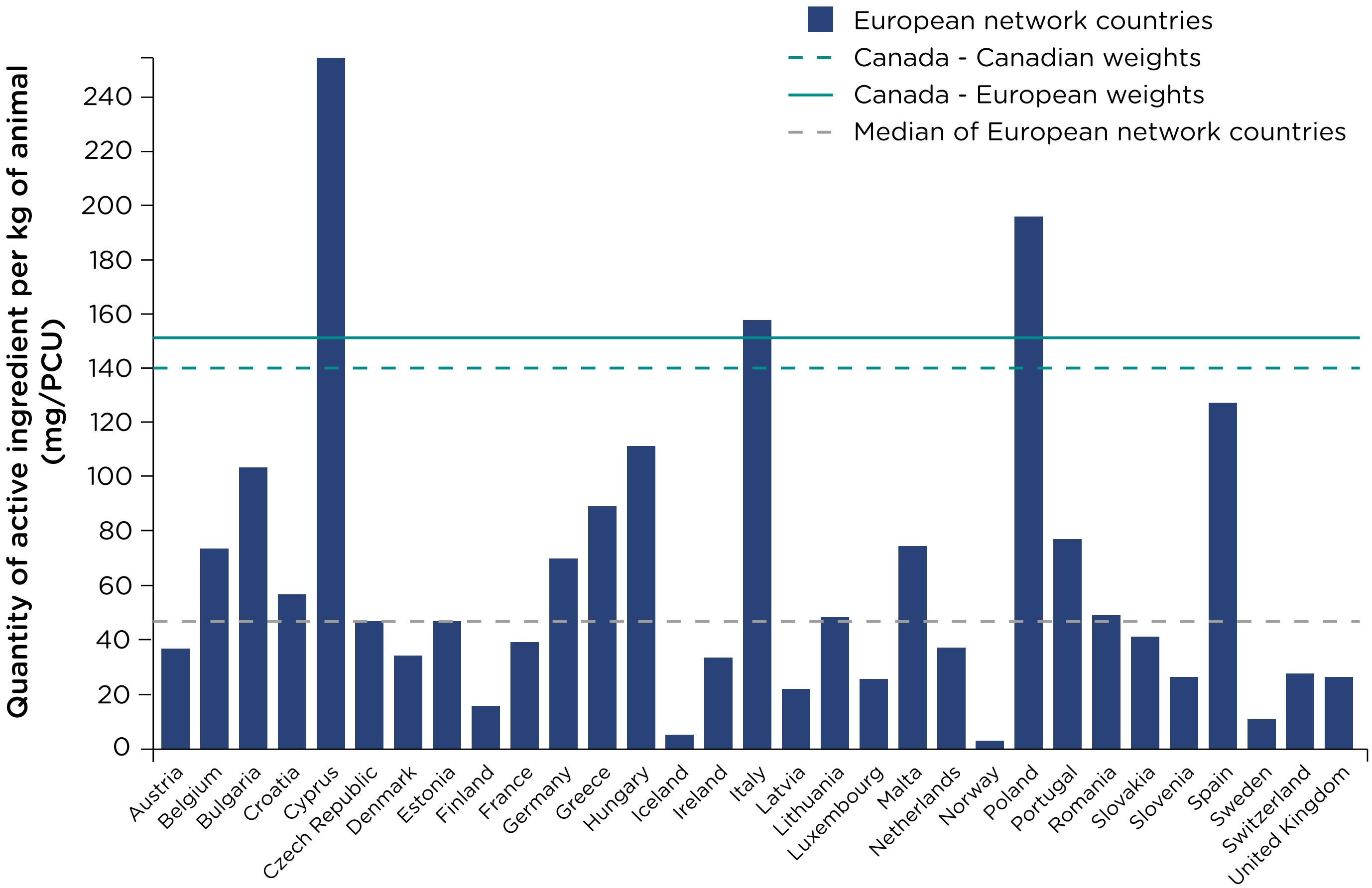


Figure 7-3. Quantities of antimicrobials sold for use in animals (adjusted by populations and weights) in Canada and countries participating in the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) network (Health Infobase 2024c)

A universal theme among the Canadian key informants, and as discussed extensively in Chapter 6, was that the lack of data on food-producing animal AMU and AMR makes it challenging to provide guidance on the best strategies to support AMS and reduce AMU in Canada. While the Canadian food-producing animal production system is now primed and poised to make further improvements in AMS, Canada just does not have the data with which to measure progress. If we cannot measure, we cannot make real progress, and the uncertainty, confusion and frustration expressed by key informants will continue.

7.4.3 Benchmarking as a Driver for AMS

Assuring the health and welfare of food-producing animals is a major objective of producers and veterinarians alike. AMS is directed at protecting antimicrobials, an irreplaceable resource, while balancing effective treatment of bacterial infections and minimization of AMR. The international case studies of countries that have most successfully reduced and improved AMU in food-producing animals consistently show the power of improved stewardship is benchmarking at the farm level.

As discussed by Speksnijder et al. (2025), benchmarking is an effective tool to induce change. When producers are given the opportunity to compare their AMU with peers (i.e. benchmarking is in place), they can become motivated to critically reflect on their own AMU. Benchmarking requires detailed data collection at the farm level in collaboration with the producer's veterinarian, and a robust and efficient system for data collection, analysis, and reporting. Benchmarking is aimed at intrinsic motivation ('carrot') to be as good as, or better than, peers, or for showing improvement over time.

The benchmarking system has also been used in The Netherlands and Denmark to identify farm or veterinarian outliers ("stick"), but in these cases it was set within a national framework of government mandated targets in AMU in food-producing animals. The data obtained from benchmarking can be used to document usage at a farm and sector level and to identify farms within different sectors where corrective actions are needed, without necessarily applying penalties. Excess AMU revealed by benchmarking could be a valuable indicator of the need of a farm within a sector to make changes in management, housing, other interventions or biosecurity, and could improve animal and farm health.

The German case study indicates the importance of starting with a user-friendly basic benchmarking system to ensure preliminary data are available. Uncertainty about which 'metric" to use was identified as an important issue during consultation with key informants. Creating sound, automated infrastructure behind-the-scenes to create an efficient process to get to the metrics is an important consideration.

7.4.4 The Use of Targets or Thresholds

A system that involves setting targets for AMU is an additional tool for making changes, and differs from benchmarking. Targets are often, but not always, based on farm data analysis linked to and/or sourced from veterinary records. This system can motivate producers and their veterinarians not to exceed the targets (being a good producer, improving animal health, saving money, or other incentives) or can be combined with an enforcement system when targets are exceeded (the "stick").

A classic example of the use of thresholds is the Yellow Card scheme developed in Denmark in 2010. Following the withdrawal of antimicrobial growth promoters in Denmark, there was a slow increase in therapeutic AMU in swine from 2000 onwards. Following public debate, in 2010 there was a two-year voluntary ban on third-generation cephalosporin use and introduction of the Yellow Card scheme (named after the warning system used for infractions under the rules of soccer). Producers whose AMU was over twice the national average were notified by the Danish Veterinary and Food Administration that they would receive a Yellow Card at the end of 2010 which would restrict oral medication usage and require external supervision. This led to an immediate 25% reduction in AMU. About 2% of swine producers received Yellow Cards.

Key informants and virtual engagement participants suggested that allowing the relevant commodity groups and veterinarians to determine how best to identify and achieve targets is more efficient than the government mandating the specifics, and is more likely to be accepted by producers.

7.4.5 Not Just Numbers: Improved Stewardship

Although AMU reduction targets were used in most of the international case study countries included in this assessment, the improved use of antimicrobials in food-producing animals that is needed is not just about total weight of antimicrobials used. Improved stewardship needs a far more nuanced and thoughtful approach (Chapter 3). Improved stewardship will almost certainly involve a reduction in use to where the benefits are clear and substantial, which is currently not always the case. As discussed by Canadian key informants, producers are wary of mandated targets for AMU. Mandated targets for AMU reduction could be regarded as arbitrary and unrealistic, or simply as involving burdensome and complex data collection mandated by bureaucrats but with uncertain impact on AMR in human (and animal) pathogens. Nevertheless, the national producer organizations recognize the benefits of industry led programs that allow self-monitoring and target setting, and of a multi-stakeholder (government, veterinarians, producers, others) approach to improving AMS.

Although veterinarians are now the ‘gatekeepers’ of food-producing animal AMU in Canada, federal regulation cannot mandate the AMU benchmarking of veterinarians that has been used in other countries, given the provincial-territorial rather than federal jurisdiction over veterinary medicine. This is discussed further in Chapter 4. Nevertheless, AMS could quickly be made a standard of practice by provincial veterinary regulators. The Canadian Council of Veterinary Registrars could be asked to require that a new auditable standard include annual audit and benchmarking of prescription/sales data for farm clients making antimicrobial purchases over a certain value, and reporting these to a central authority. This might be a requirement for establishing a Veterinary-Client-Patient-Relationship by food-producing animal veterinarians with producers. This type of system might require substantial resources to implement. A requirement that producers only source antimicrobials through one veterinarian might improve data quality. However,unless appropriately designed it could be a serious inconvenience for some producers and a potential negative impact on animal welfare for out of hours emergencies or remote locations underserviced by veterinarians. The considerations described here are the reason that we identified making AMS a standard of veterinary practice as a Promising and Strategic Intervention.

Use of digital record keeping, when available, could support efficiency for the collection of AMU data and of benchmarking within some farm animal sectors as well as of prescribing at the veterinarian level. It is a valuable peer assessment and management approach - as business management expert Peter Drucker said, “you can’t manage what you don’t measure”. An important lesson for Canada from German interviewees was that implementing electronic transfer methods to reduce producer and veterinarian’s workloads was important, together with the use of an indicator that is easy for producers and veterinarians to understand. Common sense, good judgment and transparency are always required since collecting data for comparison or meeting targets may have notorious unintended consequences, such as encouraging gaming the system (i.e., cheating), by moving the focus from intent to just meeting a number.

Key finding 14

Measurement is fundamental to assessing antimicrobial stewardship in food-producing animals: If you can’t measure it, you can’t manage it.

- Successful reduction of AMU and implementation of AMS can be achieved in different ways.
- Jurisdictions that have been most successful at reducing AMU have shown that farm-level benchmarking and the use of thresholds based on these are powerful drivers of improved AMS.
- Mandated targets from governments are also powerful incentives for change. Allowing the industries to determine how best to achieve an objective for reduction is more efficient than governments dictating the specifics, and is more likely to be accepted by producers.
- The entire food production system is now primed and poised to make further improvements in AMS.
- There is an emerging consensus that farm-level data collection in collaboration with veterinarians and farm benchmarking would allow collection of the necessary data needed to improve AMS and to document success.

7.5 Gaps and Challenges That Affect Farm-Level Benchmarking

Currently there is no actionable commitment to improve AMS and explore the reduction of AMU in food-producing animals at the farm and sector level. More commitment is needed to develop a sustained and integrated culture of AMS in food-producing animal veterinarians, producers and indeed regulators.

The integration of veterinarians and producers in farm-level benchmarking and joint commitment to improved AMS has not occurred in Canada, and there is no clear plan of integrated coordination to support the goal of measurable progress to improve AMS in food-producing animals. Furthermore, demonstration of AMS is not a current standard of practice required by provincial veterinary regulators. There is no standard of requirement that veterinarians perform an annual review and benchmarking of AMU for farm clients making AM purchases.

Canada does not have the AMU and AMR data to understand what is happening at the farm-level beyond the sentinel farm program from CIPARS. This information is necessary to support development of optimal strategies to reduce AMU, and to measure progress. It would also support improvements for farm animal health. There must be a clear objective to achieve these benefits together with secure resources and support of an effective surveillance program..

Challenges in addressing the gaps

Farm-level benchmarking and capturing of data at the producer and government level is challenging (Table 7-1), but there are some potential mitigations.

How to capture benchmarking data. The most obvious challenge is how to capture relevant data. One approach would be to rely on the CIPARS-VASR data (See Chapter 6). However, this does not reliably attribute the sale to a specific farm sector or describe reason for use, or doses and durations which are important to understand in a stewardship context (e.g., treatment vs prophylaxis). It would not provide the specific sector information needed. The other approach would be to have an annual farm-level report within each of the major sectors and users (feedlot beef, dairy cattle, swine, poultry, veal calf, small ruminants, aquaculture). A challenge to this is the absence of a national association of smaller commodities or veterinarians such as small ruminants, veal production, bison, cervids, etc.

Incentivization and cost-sharing. With the current distribution model for veterinary antimicrobials in Canada, veterinarians profit from the sale of antimicrobial drugs. However, producers profit from their use. It is therefore inherent that there is a potential vested interest for both parties to collaborate towards benchmarking as an objective. Support for educational initiatives is needed once data begins to emerge. Some commodity groups may need more incentives and/or support to achieve a benchmarking objective.

Benchmarking software is increasingly promoted in the production and clinical veterinary sectors to monitor relevant aspects of operations. Benchmarking measures for AMU could be built into new or existing systems that provide other knowledge advantages to producers/veterinarians. An example of an existing initiative in benchmarking within the Canadian commodity groups is the Dairy Farmers of Canada’s electronic automated farm-level AMU data system.

Table 7-1. Challenges that may impact benchmarking and potential ways address them

Challenges that impact benchmarking	Potential ways to address challenge
Deciding how to capture the farm-level benchmarking data to document AMU and the effects of benchmarking and AMS initiatives	Annual farm-level report within each of the major sectors to producer associations
Agreeing on the data to be collected at the national level	Focus on minimum measures required to conduct benchmarking, as per other successful jurisdictions
Adopting or developing robust and efficient automated systems with compatible software for veterinary record data collection and ways to summarize data	Farm-level benchmarking software that confers other operational benefits to producers/veterinarians. The data needs to include ways to assess and report the effectiveness of farm-level benchmarking and remedial AMS actions
Deciding who pays for benchmarking	Negotiate a cost-sharing partnership model between government, veterinarians, and producers
Determining appropriate incentives for producers and their veterinarians to collect farm-level data and to implement benchmarking and assess its value	Engage producers and commodity organizations to determine, for example, whether tax credits, incentives and other financial/non-financial incentives may be be used to offset costs, particularly for minor species (eg sheep, goats, other)
Developing a central coordinating system that integrates Canada's actions to promote and measure AMS stewardship actions and that promotes the multi-group (veterinarian, producer, regulators, other) collaboration critical to success	Part of this system would have to support the research required to evaluate the impact of different AMS initiatives. For example, research is needed to identify whether well-established practices in food-producing animal AMU are in fact necessary. A central coordinating group, which need not be large or permanent, would also take a role in continuing education of and feedback into the different sectors
Need for commitment and for local, provincial and national champions	Leverage national and provincial commodity groups and veterinary associations to identify local champions with close ties to producers
Shortage of food-producing animal veterinarians could be a further challenge	Engage Registered Veterinary Technicians in farm data collection (Tremblay, 2024)
Issues of confidentiality of farm benchmarking and of AMU data generally	Confidentiality agreements negotiated between government, commodity groups, veterinary groups, and other entities representing the interests of impacted parties
Linking producer/farm-based AMU data collection to AMR data	Decide the relative value of AMR indicator bacteria and selected animal pathogens

Key gap 14

Canada currently does not have the detailed farm-level data that is needed to be able to demonstrate good antimicrobial stewardship in food-producing animals.

- There is no actionable commitment to improve AMS and explore the reduction of AMU in food-producing animals at the farm and sector level.
- More commitment is needed to develop a sustained and integrated culture of AMS in food-producing animal veterinarians, producers and regulators.
- The integration of veterinarians and producers in farm-level benchmarking and joint commitment to improved AMS has not occurred.
- AMS is not included as a standard of practice by provincial veterinary regulators.
- There is no clear plan with integrated coordination for demonstrating progress in improving AMS in food-producing animals.
- Canada does not have the AMU and AMR data to be able to understand what is going on at the farm-level beyond the sentinel farm program from CIPARS to provide guidance on the best strategies to reduce AMU, and to measure progress.

Related action in the Pan-Canadian Action Plan (PCAP)

- Under the Surveillance pillar: "Work with partners to establish baselines and targets for national, provincial, and territorial levels of AMR and appropriate AMU in human health."
- Under the Leadership pillar: "Increase Canada's contributions to global efforts to advance key bilateral and multilateral commitments by prioritizing generating improved data/ evidence on AMR/AMU and strengthening surveillance systems and data standards."

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 8:

Antimicrobial Resistance Awareness and Education in Consumers

Introduction

Consumers are important actors in the conversation about AMU in food-producing animals, and could be a key driver for changes to AMU by creating market pressure for industry and producers to limit or eliminate AMU. However, "antibiotic free" initiatives may be less about stewardship than as an effort by companies to differentiate their products from the competition. Limited public awareness or misinformation about AMU in food-producing animals has the potential to create market incentives for antibiotic-free products. The section below discusses key findings on consumer awareness and concern about AMR/AMU in food-producing animals relevant to the North American context, and particularly Canada.

8.1 Awareness & Concern Regarding AMR/AMU

8.1.1 Cross-Canadian Focus Groups

Two rounds of cross-Canadian consumer focus groups were commissioned by CAHS for this assessment and were conducted by Léger, a Canadian market research firm, in April and July 2024. An overview of the demographics of focus group participants is provided in Appendix 1. A total of eight focus groups were conducted (six for round 1 and two for round 2). Each focus group included 8-10 participants, representing a diverse cross-section of ages, genders, socio-demographic backgrounds, and provinces.

Participation was limited mainly to those who consumed animal products (limiting vegetarian or vegan participants to a maximum of two per group) and possessed limited professional knowledge of food growth and production. Each focus group was also limited to a maximum of two members aged 55 and over to ensure accommodation of diverse age groups. Due to the nature of the methodology, demographic trends were not evaluated; the intention of the qualitative focus groups was to obtain detailed information on public perceptions from a wide range of participants, rather than to conduct comparative analyses.

Consumer awareness is low and misconceptions prevail. Findings from both rounds of focus groups indicate that there is a low level of awareness among Canadian consumers regarding AMR and AMU in general, and in food-producing animals specifically. Participants often did not know what these terms meant prior to the discussions. This lack of knowledge was accompanied by misconceptions about AMU, with some mistakenly associating the term "antimicrobial" with preservatives or disinfectants (cleaning products) and others associating it with positive attributes such as higher product quality and improved health benefits. There was considerable confusion about the implications of AMU in food production. For example, some consumers conflated "antimicrobial-free" with organic products, assuming that the absence of antimicrobials automatically indicates a product is organic, while others believed the use of antimicrobials in animal farming could enhance the nutritional value of the food produced.

Misconceptions were prevalent; some respondents mistakenly believed that AMU leads to near sterility in animals, residual antibiotics remain in dairy products, and AMR increases due to unnecessary applications. Additionally, concerns were voiced about the adverse health implications for humans consuming meat from animals treated with high doses of antibiotics, including potential developmental issues in adolescents (CAHS Consumer Focus Groups, Round 1).

In both rounds of focus groups, when moderators explained the concept of AMR, participants expressed more nuanced views on AMR. Many recognized that prolonged or excessive use of a single antibiotic could lead to resistance. Additionally, some noted that microbes might evolve, rendering medications ineffective. One participant explained, "maybe the animal has had the disease repeatedly and received the same treatment, which eventually stopped working" (Focus group participant, 18-34, Female).

There is concern for animal welfare. Round 2 of focus group discussions revealed a strong concern for animal welfare among participants, yet this concern is not automatically linked to the use of antimicrobials in farming without explicit discussion. While participants valued products labeled as "raised without antibiotics", they associated this with better animal treatment (CAHS Consumer Focus Groups, Round 2). This indicates a gap in understanding of the actual role of antimicrobials in animal health.

Consumers want to learn more, but are not willing to pay more. The findings indicate a high interest among participants in receiving more education about AMU and AMR in food-producing animals. The government was reported to be a trustworthy source of information about food derived from animal products. However, despite the interest in learning more about AMR/AMU, there is little evidence to suggest that the current level of awareness significantly impacts purchasing behavior.

Participants were asked whether they think about AMU in the food items when buying groceries, restaurant food, or other ready-to-eat food for your household, and whether that impacts their eating or shopping habits. Cost remained the decisive factor influencing purchasing decisions across various regions and age groups, though its significance varied based on regional economic conditions, average income, and local cost of living. For instance, some consumers saw cost as a direct indicator of quality and were willing to pay more for perceived better quality, others believed higher prices inherently guarantee superior quality. Participants from Québec and the Atlantic regions were notably less concerned with factors beyond cost, primarily due to their high level of trust in Canada's food safety standards or availability of local food options (CAHS Consumer Focus Groups, Round 1).

In general, participants admitted that while they are concerned about AMU and AMR when discussed, these concerns do not actively influence their routine shopping decisions. This disconnect suggests that while consumers recognize the importance of the issue when prompted, it does not yet weigh heavily in their everyday choices.

8.1.2 Consumer Awareness and Concern in the Literature

The research literature is useful to contextualize the Cross-Canadian focus group findings within the broader international landscape, and drawing from a larger body of evidence. A scoping review by Barrett et al. (2021) identified a high level of consumer concern surrounding AMU in food-producing animals, based on 124 studies of consumer perceptions of AMU in pork, beef, poultry, and dairy in the United States, Canada, and the European Union. Most studies (65%) demonstrated that consumers were concerned about AMU in animal agriculture. In the studies that investigated why consumers were concerned, reasons primarily included personal health and safety, with animal welfare concerns being the second most common reason. The emergence of AMR bacteria was not a common concern; however, this could be due to lack of awareness of the phenomenon and its consequences. The demographic characteristics most consistently associated with consumer concern about AMU in food production included being female, older, highly educated, and high-income.

The Barrett et al. (2021) review cited above included studies specific to the Canadian context. Barlow (2011) reported that consumers are concerned about AMU in food production, but have limited knowledge of how antimicrobials are used in food production, which is consistent with the findings of the consumer focus groups conducted for this assessment. However, antibiotic use in food-producing animals was cited as important to purchasing decisions in many studies. Parents participating in a focus group in British Columbia preferred to purchase organic dairy products, as they believed other products were "contaminated" with antibiotics (Bourne et al., 2018). A national survey revealed that consumers are highly concerned about antibiotics in meat and that they regard organic and traditional pork more favorably than conventional pork, with the absence of antibiotics cited as a reason for their preference (Muringai & Goddard, 2010). A Canada-wide survey revealed that women, older age, and people with higher education and with children under age 6 were more likely to be aware of organic (or raised without antibiotics) pork and that people with more knowledge about these types of pork products tended to purchase them (Tong, 2011). Among Canadian consumers, production type (use of antibiotics, hormones, vaccines) was the most important attribute for purchasing decisions related to beef, followed by price and environmental impact (Belcher et al., 2007). Most participants in an Alberta focus group were unaware that organic producers could use antibiotics. Most considered antibiotic use in food-animal production to be "somewhat or very important" when buying meat and were more likely to buy natural products (Goddard et al., 2017). A series of one-on-one interviews in Ottawa revealed that consumers identified health as a primary motivator for consumption of organic food and that the motivation for this was avoidance of antibiotics (Hamzaoui Essoussi & Zahaf, 2009). According to another consumer survey, the use of antibiotics in food production was considered one of the highest risk food safety issues (Veeman & Li, 2007). The results of these Canadian studies suggest that perceptions related to antibiotic use in food-producing animals might contribute to purchasing decisions.

In the UK, an online questionnaire evaluated consumer perceptions of AMU in livestock. A total of 5,693 online questionnaires were administered in supermarkets across the United Kingdom. Overall, only 40% of those surveyed agreed that the use of antibiotics to treat disease in food-producing animals delivers more benefit than harm. Consumers were asked about the level of risk of different interventions related to food-producing animals, such as vaccines, vitamins, and homeopathy as comparators to the perceived risks of antibiotics in food-producing animals. The least risky intervention was considered to be homeopathy, with around 35% rating this as high or very high risk, compared to vitamins at 40%, vaccines at 50% and antibiotics at 70%. Overall, many responses were neutral which the authors suggested was due to uncertainty or a lack of concern about AMU in food-producing animals (Adam & Bruce, 2023).

Case Study Highlight: The USA
Consumer Misconceptions Translating to Demand for Food That Is "Raised Without Antibiotics"

In the United States, studies show that low consumer awareness is influencing AMU behaviors in producers. McKernan et al. (2021) highlight many psychosocial factors that impact producers' AMU behavior; one of those factors is that producers perceive consumer misconceptions and marketing tactics as influencing regulations. This leads to a market-driven scheme for animals to be "raised without antibiotics" (RWA).

As discussed in Ch. 7, literature from the US surveying the perceptions and experience of producers and veterinarians across the major commodity groups indicated that although they believed antibiotic-free production to have negative impacts on animal health and welfare and have questionable effects on consumer demand for meat, egg or dairy, the Raised Without Antibiotics label takes priority over animal welfare (Singer et al., 2019).

The implications of consumer misconceptions driving marketing strategies and policies are apparent, as demonstrated by the widespread adoption of the RWA scheme. The authors conclude that "it is important that the message of AMU in agriculture is communicated carefully with consumers; namely that agricultural AMU needs to be reduced but not completely eliminated, as this will have negative ramifications for animal welfare" (McKernan et al., 2021).

8.2 Public Educational Approaches Regarding AMR/AMU

Consumer education can help to create an understanding of the importance of AMU in food-producing animals and industries' commitment to AMS. In CAHS consumer focus groups, the low level of consumer awareness might have been related to a lack of educational initiatives that increase awareness of AMR and clarify misconceptions about AMU and AMR in general, and particularly with respect to AMU in food-producing animals. Focus group participants had no recall of educational campaigns addressing AMR/AMU in general, or specifically in relation to the agriculture sector, despite having an interest in these topics.

A primary issue highlighted is the need for greater transparency in how antimicrobials are used, enabling consumers to make informed decisions. Many participants emphasized that clearer communication could enhance consumer trust and alleviate doubts. Some expressed a preference for a choice between foods treated with antimicrobials and more natural options, noting that while they might accept meat with antibiotics in fast food, they would prefer options without antibiotics for personal or home-cooked meals (Consumer Focus Groups, Round 2).

It is also unclear whether and to what extent consumers are aware of the primary modes of transmission of AMR from food-producing animals (e.g. foodborne, via animal fecal contamination) and non-animal sources and are educated on how to mitigate this risk.

8.2.1 What Kind of Education do Consumers Want?

In both rounds of focus groups, participants showed a preference towards passive, rather than active modes of education. Participants wanted transparent information about AMU in food production, accessible through channels such as social media, food labeling, and trusted websites and materials. Participants suggested that clear, regulated labeling on food products and inclusion of QR codes that link to detailed content about AMU would be helpful. Incorporating information about AMR and AMU into the formal education systems and using digital media was also mentioned.

8.2.2 What Sources of Information are Trusted by Canadians?

Cross-Canadian focus group participants felt that the government and public health agencies are a trusted source of information about AMR/AMU (CAHS Consumer Focus Groups, Round 1). Consistent with that, in a subsequent round of focus groups, participants showed a preference for transparent information about AMU in food-producing animals, accessible through channels such as social media and food labeling, from trusted public health sources such as government (CAHS Consumer Focus Group, Round 2).

The Canadian Food Inspection Agency was unanimously trusted, and most participants also trusted other government sources, though not universally. Farmer groups, university professors, and public health agencies were trusted by most, with the latter having nearly unanimous trust. Veterinarians received a mixed level of trust – trusted by about half of the participants, and provincial governments and doctors were trusted by only a few.

These findings are somewhat different from the overall trends of institutional trust in Canada (Steinburg, 2024). The latest Canadian barometer on trust places trust in government at 51%, around the same level as that of business (52%) and media (52%) (Edelman, 2023, p. 4). The government in particular saw an increase of trust at the beginning of the COVID-19 pandemic that has since decreased, from 50% in 2019 to 70% in May of 2020, then 59% in late 2020 (Edelman, 2021, p. 7). In terms of the credibility of spokespeople, government officials were also rated quite low amongst the public in terms of trust (38%), as compared to technical experts (65%), academic experts (64%), or even “a person like yourself” (58%) (Edelman, 2019, p. 15).

An earlier survey by Léger (2018) focusing specifically on opinions on science found that Canadians had both high trust and interest in science, and 83% agreed that they “would like to know more about science and how it affects our world” (p. 11). However, when asked where Canadians turn to check the accuracy of scientific findings, their first choice was most often scientists and professors (47%), rather than government.

A consistent finding has been that Canadians’ overall trust in most institutions and public figures has been low both before and after the COVID-19 pandemic, with total rates of trust between one third and one half of the public that was surveyed (e.g., Edelman, 2023; Proof Strategies, 2023; Environics, 2023 (p. 2). Trust in government grew from 50% in late 2019 to 70% in May of 2020, then declined to 59% in late 2020 (Edelman, 2021, p. 7). In particular, interview data collected during the COVID-19 pandemic suggest that perceptions of pandemic communication, decision-making, and implementation of countermeasures during the pandemic impacted trust in a negative way (Herati et al., 2023). In the later study, while participants did not trust the government, they were accepting of measures and messages as presented through government channels.

Key finding 15

There is a lack of consumer knowledge and awareness about AMR/AMU in food-producing animals.

- Evidence from consumer focus groups shows a lack of consumer awareness in Canada about AMR/AMU in food-producing animals, and many misconceptions prevail.
- Canadians are concerned for animal welfare and want to learn more about AMR/AMU and its role in animal health; however, this interest does not necessarily translate into an impact on purchasing behavior. In other jurisdictions (e.g., EU), consumer pressure has been a strong driver for change.
- Canadian consumers in focus groups suggested that they trust the government as a source of information about AMR/AMU in food-producing animals, although the literature indicates that scientists and academic experts are more trusted.
- It is unclear whether consumers are aware of the primary modes of transmission of AMR and are educated on how to mitigate this risk.

8.3 Gaps: Consumer Knowledge and Awareness

The CFIA has had a Science Fact Sheet on AMR for a number of years (CFIA, 2017) and provides information on its website regarding efforts to address AMR through the Pan-Canadian Action Plan (CFIA, 2023b). Other sector-specific educational materials on AMR in food-producing animals are found on the websites of commodity groups. Despite the availability of this information, our assessment suggests that awareness of information on AMR and AMU in food-producing animals is low.

Many retail outlets are also advertising "raised without antibiotics" product lines, which sends a negative message about the use of antibiotics in food-producing animals. The potential influence of retail advertising raises the question of whether the public understands antibiotic-free marketing strategies, and whether and to what extent these campaigns influence their purchasing decisions.

Human and animal experts in our panel believe that educational initiatives on AMR could ideally use a One Health approach and a broad transdisciplinary lens when discussing AMS/AMR/AMU at the interfaces of humans, animals and the environment, rather than focusing educational efforts specifically on the use of antimicrobials in food-producing animals.

Gaps

- There are currently no identified Canadian educational initiatives for consumers specific to AMR/AMU in food-producing animals.
- It is unclear whether the public understand “antibiotic-free” marketing strategies, and whether or how this influences their purchasing behaviour.

Related Action in the Pan-Canadian Action Plan:

- Under the Infection Prevention and Control pillar: “Foster understanding of the risks of AMR and the importance of appropriate use of antimicrobials in humans and animals amongst the public, patients, and producers through awareness/educational campaigns, feedback mechanisms and policy and regulatory initiatives.”

Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

Chapter 9:

Promising and Strategic Interventions to Further Strengthen Antimicrobial Stewardship in Food-Producing Animals in Canada

Promising and Strategic Interventions

There is compelling evidence that antimicrobial use (AMU) in food-producing animals leads to antimicrobial resistance (AMR), and that AMR can be transmitted to humans through multiple modalities (Ch. 2). Routes of transmission from animals to humans include food contamination, direct contact with food-producing animals, and the environment. AMR also is a problem in animal pathogens, and there will be no substantial new antimicrobials introduced into food-producing animal agriculture in the foreseeable future. There is also persuasive evidence both in Canada and internationally that reducing AMU in food-producing animals can have a measurable impact on reducing AMR.

The evidence presented in this report, including an evaluation of approaches used in other countries, shows that if AMS is to improve in food-producing animal agriculture, there is a need for national commitment to action, and the continued and sustained leadership of politicians, veterinarians, organized veterinary medicine, food-producing animal producers and their organizations, regulatory agencies, consumers, and food-producing animal product retailers (Chs 3, 4).

Since the 1997 Health Canada Consensus Conference in Montreal which led to the development of CIPARS, there have been unprecedented efforts to understand the dimensions of AMR in food-producing animals in Canada and to educate veterinarians, producers, governments and others about AMR and AMU (Ch. 3). Important advances have been made, including the removal of growth promoter claims and bringing all medically important AMU in food-producing animals under veterinary prescription. The CIPARS surveillance system has led to an increased understanding of AMR in Canada, and has allowed the documentation of successes in policy changes like the voluntary temporary withdrawal of in-ovo use of ceftiofur in broiler chicken hatcheries in Québec, and contributing to the development of the Chicken Farmers of Canada Responsible AMU Strategy as well as monitoring its impact (see Ch. 6). Thus, considerable progress has been made through the combined efforts of many people and groups. As identified in the key informant and virtual engagement interviews, the food-producing animal agricultural and veterinary sectors are primed and poised to make further improvements in AMS. However, as summarized in the 2023 Auditor General's report and discussed in Chapter 4, additional changes are needed for Canada to continue to make meaningful progress.

9.1 Key Findings: Topic Areas

Fifteen key findings across 7 topic areas were identified by the panel members based on an evaluation of the literature review, international case studies, and cross-Canada engagement activities. The topic areas, derived from the sponsor's questions, included:

- The current state of knowledge of AMR in food-producing animals and transmission of AMR to humans (Ch. 2),
- Antimicrobial stewardship (AMS) in food-producing animals (Ch. 3),
- Governance, policy, and regulatory approaches to support AMS (Ch. 4),
- Farm-level interventions to reduce the need for AMU (Ch. 5),
- Surveillance of AMR and AMU in food-producing animals (Ch. 6),
- Impacts of interventions to reduce AMU on AMR (Ch. 7), and
- AMR awareness and education in consumers (Ch. 8).

Detailed key findings are addressed under each respective chapter. Relevant gaps, including key gaps (i.e. gaps in knowledge, regulations, Federal-Provincial-Territorial (FPT) jurisdictional issues, and practice as compared to other countries) were also identified for each key finding.

All of the key findings in this assessment align with one or more actions identified in the PCAP (see Appendix 5 for details). The greatest area of alignment was the surveillance pillar of the PCAP (6 key findings aligned), the stewardship pillar (5 key findings aligned), the infection prevention and control pillar (5 key findings aligned), and the research and innovation pillar (5 key findings aligned). Finally, three key findings align with the leadership pillar.

9.2 Four Thematic Areas of Opportunity Encompassing All Key Findings

Based on the fifteen key findings and associated gaps, four major interconnected themes continually emerged throughout this assessment:

1. Leadership, coordination, and political commitment;
2. Supporting veterinarians and producers in keeping animals healthy;
3. Embracing antimicrobial stewardship; and

4. Enhancing surveillance of AMR in pathogens of veterinary interest and measurement of AMU in food-producing animals to meaningfully evaluate and document our successes and failures.

These four major themes encompass all of the key findings of this report. Figure 9-1 represents these thematic areas, their interconnectivity, and their linkages to one another.

The four overarching thematic areas of opportunity for impact on AMR/AMU are discussed below.

Figure 9-1. Four major thematic areas of opportunity encompassing all key findings of the assessment on AMR/AMRU in food-producing animals

1. Leadership, Coordination, and Political Commitment are Critical to Improve Antimicrobial Stewardship and Thereby Reduce AMR

Canada has been implementing changes to reduce the unnecessary use of antimicrobials. However, we lag behind some other countries. Continuing with the status quo of incremental change will not result in the meaningful reduction of AMU and enhanced AMS that is necessary to address the AMR crisis. Although AMR is a global issue with complex causation, Canada, and those involved in Canadian food production, must look for effective solutions to meet a societal imperative.

Canada is reasonably well positioned to implement meaningful changes to address AMR/AMU in food-producing animals and to operationalize the objectives of the PCAP. Canada's commodity groups are involved in many important initiatives to address AMR, ranging from voluntary actions to the removal of extra-label preventive use of Category I and II antimicrobials in broiler chicken production, to extensive research and surveillance activities on AMR/AMU. Veterinary regulatory groups are variably engaged in stewardship initiatives at the FPT levels. Collaboration from every group involved in animal production is essential to further success in addressing AMR/AMU in food-producing animals.

However, there is strong evidence from other jurisdictions that leadership and political commitment at the highest levels of government are essential to motivate all individuals and organizations involved in food animal production to reduce the use of antimicrobials to where benefits are clear and substantial and exceed the risks. Industry leadership and commitment also are essential to agree on common commodity-specific objectives for AMR/AMU, and to mobilize the necessary actions to move towards those objectives. Effective coordination of national efforts to improve stewardship and reduce AMR are the critical demonstration of leadership and political commitment.

2. Supporting Producers and Veterinarians in Keeping Animals Healthy

Preventing and controlling infections is crucial to reducing AMU. Biosecurity and evidence-based livestock management practices, effective vaccines and alternative products, and validated AMU decision-making tools are essential for keeping animals healthy so that they require fewer antimicrobials. In Canada, as in other countries, biosecurity has been a key to relying less heavily on antimicrobials and a variety of resources are available to Canadian producers, which could be developed further. Commodity groups, veterinarians, and producers support the use of these tools and approaches (Ch. 5,) but evidence-based effectiveness data are limited and there are reported regulatory barriers to accessibility and licensing of vaccines and alternative products in Canada.

3. Embracing Antimicrobial Stewardship

Antimicrobial stewardship and its many dimensions has been a critical theme throughout this assessment. The 5R's of AMS encompasses all of the principles that are needed: **responsibility to improve antimicrobial drug use**, **reducing, refining,** and **replacing** AMU when possible, and **reviewing** the impact of changes on a continuous basis. Antimicrobial stewardship is a helpful framework to bring government, industry sectors, veterinarians and producers together to work collaboratively through a holistic approach to address antimicrobial stewardship. A collaborative approach is also critical to mitigating potentially negative impacts of AMU reduction. Reduction of AMU is essential, since use drives resistance. Every sector needs to be involved in a nationally coordinated AMS approach. For example, at the federal level, by aligning Health Canada approved product labels for MIAs with stewardship principles. At the provincial veterinary level, where the use actually occurs, making AMS a standard of practice would involve veterinary regulators and veterinarians in ways that currently they are not.

4. Enhancing Measurement of AMU in Food-Producing Animals and Surveillance of AMR in Animal Pathogens

An essential cross-cutting theme is that "we cannot manage what we cannot measure". CIPARS is an important enabler to Canada's efforts to monitor AMR; however, there are major gaps that would need to be addressed to provide a clearer picture of where we are in Canada with AMR in pathogens of interest to animal health (Ch. 6). Monitoring AMR in pathogens of interest to animal health will allow temporal changes to be understood and may provide motivation for producers to engage in efforts to reduce AMR both in animals and in humans. At the national level, farm-level AMU data are restricted to mandatory reporting systems in finfish and voluntary AMU data submitted from sentinel farms for broiler chickens, grower-finisher pigs, dairy cattle, feedlot cattle, laying hens, and turkeys. Antimicrobial sales data are collected through mandatory reporting via the VASR system, jointly operated by VDD and CIPARS. Although CIPARS-VASR data can be used to track broad trends in sales, these data represent commodity-level estimates and do not provide indication for use, dose, or duration information, nor do they allow nuances of use between production stages and among farms. Farm-level data collection and farm-level benchmarking that includes reasons for use would allow collection of the critically lacking data that is needed to improve AMS and to document success.

9.3 Promising and Strategic Interventions That Could Strengthen Antimicrobial Stewardship

In this section, we describe five strategic interventions that could strengthen AMS. The potential impact of each strategic intervention spans all four thematic areas. These strategic interventions are not mutually exclusive; rather, they represent interventions that individually would have an impact but would not be enough to address AMR on their own. Collectively, these strategic interventions would tackle the areas highlighted in this assessment with potentially profound impact. Implementing these strategic interventions would involve different timeframes and entail different challenges. These interventions form the basis of the steps that could be taken to enhance AMS in food-producing animals in Canada.

Promising and Strategic Interventions:
Steps to Enhance AMS in Food Producing Animals

- Identify a governance structure to lead and coordinate implementation of the PCAP for food-producing animals
- Adopt farm-level AMU data collection and benchmarking
- Make antimicrobial stewardship the standard of practice for veterinarians
- Restrict the use of Category I antimicrobials in food-producing animals
- Support relevant targeted research to enhance knowledge on application and efficacy of strategies and products to keep animals healthy

Below, we present the five strategic interventions with the supporting evidence for their value, as well as a summary of issues that would need to be considered and possible consequences.

Strategic Intervention 1: Identify a Governance Structure to Lead and Coordinate Implementation of the PCAP for Food-Producing Animals

Supporting evidence:

Countries that have been the most successful in reducing AMU have clear governance with commitment and accountability for progress. In Canada, collaboration and discussion among relevant groups and organizations are ongoing. However, with such a complex issue and such a range of participants, full consensus of pathways forward may not always be achievable. Thus, there is a clear and compelling need for a dedicated governance structure including leadership and resources to fully coordinate and implement the next steps that are required to operationalize the PCAP.

Considerations and possible consequences:

Leadership and governance, political commitment, and accountability are key to implementing regulatory or policy approaches to support stewardship, such as changing requirements to specify duration of use on antimicrobial labels, as well as to establish, coordinate, and implement a national intersectoral and collaborative stewardship program. Two models of governance for a One Health AMR response in Canada have been proposed; a network model without one centre of control and a centre model where one organization makes changes in defined priority areas, with strong partnerships with other organizations and experts (Morris et al., 2021; Ch. 4). However, to date, these or other models have not been adopted.

Strategic Intervention 2: Adopt Farm-Level AMU Data Collection and Benchmarking

Supporting evidence:

Countries with strong AMS frameworks use farm-level AMU data as a key component in their overall approach. Without measurement of AMU, it is not possible to determine why some farms/veterinarians/commodity group /production sectors/or countries use more antimicrobials than others. Without measurement, it is impossible to evaluate whether AMS efforts are effective, or to monitor and document progress.

Considerations and possible consequences:

Benchmarking at a farm-level would focus Canada’s efforts to improve AMS in food-producing animals and would engage and motivate veterinarians and producers. It would provide producers, veterinarians and regulators with the data needed to improve AMS on individual farms and to demonstrate that efforts to improve AMS were succeeding. It would educate the entire food-producing animal system while providing the essential data needed and promoting AMS at the same time. Measurement of changes in quantity and quality of AMU, disease status, and other measures could be linked to changes in AMR in indicator bacteria and animal pathogens.

However, adopting farm-level AMU data collection and monitoring would require engagement and buy-in from commodity groups, veterinarians, and producers. We address some of the undoubted challenges and potential ways to address them in Table 7-1. There are commodity and stage of production specific logistical issues around data collection and concerns around data use (including confidentiality and competitiveness) that would need to be discussed collaboratively and resolved. This will take time and commitment to achieve and will require building trust and understanding motivations and barriers to adopting farm-level AMU data collection. Cost-benefit and proof of value assessments could provide incentives for implementation. Thus, an option would be to consider a staged approach to measurement, which could involve the following progression:

i. Collection of farm-level AMU data by producers or veterinarians by indication for use to support AMS. This already is being done by many producers, with differences in systems and intensity of data collection between commodity groups and between production sectors.

ii. Collection of farm-level AMU data by indication for use by commodity groups to allow baseline AMU to be estimated, identify areas where unnecessary use could be reduced, and monitor progress in AMS.

iii. Collection of farm-level AMU data by indication for use to allow benchmarking to compare AMU among farms and to identify farms where use is substantially higher than the average for that commodity group and production sector.

iv. Collection of farm-level AMU by indication at the national level to measure progress in AMS programs and allow comparisons to other countries.

v. Ideally, and eventually, farm-level AMU data would be needed for all commodity groups and for all stages of production. It might be reasonable to start with the production stages and commodity groups with the highest usage (overall or in feed) and potentially start with collecting AMU data on a representative sample of farms.

Strategic Intervention 3: Make Antimicrobial Stewardship the Standard of Practice for Veterinarians

Supporting evidence:

Although the federal government controls the licensing for sale of antimicrobial drugs, the actual use is controlled provincially through veterinarians (Ch. 4). A focus on the critical role of veterinarians in this provincially regulated area is not included in the PCAP. The regulatory changes implemented in Québec over the use of Category I antimicrobial drugs in food-producing animals by veterinarians show the steps required if a stewardship change such as this is to be introduced. As noted by the College of Veterinarians of Ontario (2024), standards of veterinary practice evolve over time to reflect current expectations. Examples of existing veterinary standard of practice elements include expectations related to the veterinarian-client-patient relationship, informed client consent, medical recordkeeping, prescribing and dispensing, and telemedicine. Expansion of the veterinary standard of practice to specifically include AMS, including benchmarking and restricting the use of category I antimicrobials in food-producing animals, would be an important part of a “made-in-Canada approach” to AMS (Ch. 3).

Considerations and possible consequences:

Implementing strategic intervention 3 would require changes to the current practice of veterinary medicine. Depending on how this was managed, reporting and accountability would need to be managed by provincial regulatory licensing boards, and this approach might require reporting to be a condition of maintaining individual practice accreditation, as has been done in the human hospital setting in Canada. The importance of this approach is that it would acknowledge the change in the regulations around AMU in Canada where all AMU is under the control of veterinarians, so that veterinarians are now responsible for their stewardship. Ideally, monitoring of success would be accomplished using farm-level AMU data (as discussed under Strategic intervention 2).

There could be financial repercussions to this approach for veterinarians and producers, and potentially also to veterinary colleges for education and re-education of veterinary students and veterinarians. Involving veterinary technicians and/or providing compensation to veterinarians for additional time for farm benchmarking reporting might be required, especially if there were reporting obligations by veterinarians to a central organization. Ways to encourage compliance by veterinarians would need to be considered. The potential increase in workload for veterinarians has the potential to exacerbate the shortage of large animals veterinarians and the declining proportions of new veterinarians interested in food animal practice. Therefore, incentives to adopt AMS as the standard of care would need to be evaluated and considered and the impact on access to veterinary care would need to be evaluated and monitored. A benchmarking and AMS approach to farm-level AMU analysis will become an important part of animal-farm health assessment.

Strategic Intervention 4: Restrict the Use of Category I Antimicrobials in Food-Producing Animals

Supporting evidence:

Australia and some countries in the EU have restricted the use in food-producing animals of antimicrobials essential for the treatment of human infections. In Canada, Québec has restricted the use of Category I antimicrobials; their use is no longer allowed for preventive purposes and their use for treatment is restricted to clinical cases that are not treatable with antimicrobials of less importance (Ch. 4). These restrictions resulted in documented reductions in their use in food-producing animals in Québec. Thus, a strategic intervention would be to adopt restrictions on the use of Category I antimicrobials for Canada, and then extend the restrictions across all provinces and territories. This would involve the provinces and provincial veterinary regulators in a way that the PCAP currently does not.

Considerations and possible consequences:

Several specific opportunities would enable reductions in the use of Category I antimicrobials.

Preventive uses:

i. Ban the use of all Category I antimicrobials for systemic/injectable or oral use for preventive purposes in food-producing animals. It is important to note that there are currently no label claims of Category I antimicrobials for preventive purposes, but a ban on extra label use (ELDU) for preventive purposes would emphasize the importance of maintaining the efficacy of Category I antimicrobials for human use.

ii. Implement a ban on blanket dry cow therapy with ceftiofur in dairy cows with a move to selective dry cow therapy, wherein treatment with ceftiofur would need to be explicitly justified. Evidence was presented in this review that selective dry cow therapy is associated with reduced AMU and could be implemented without negative impacts on udder health.

Therapeutic uses:

i. Ban the ELDU of Category I antimicrobials for disease treatment in food-producing animals without laboratory evidence that no other treatment option will be effective. Similar to the approach in Québec, there would be a requirement for a written veterinary protocol for use. This approach also could require a CgFARAD submission for all cases of use in all commodity groups, as is currently required in poultry.

ii. Require a written justification based on clinical or laboratory evidence and a written farm-level protocol for use (including identification of eligible cases) of all category I antimicrobials already licensed for treatment of specific conditions in food-producing animals (e.g., the treatment of BRD in cattle and swine by injection).

The additional levels of documentation required for opportunities iii and iv would result in veterinarians taking additional care in ensuring that the use of Category I antimicrobials is essential.

Making these changes would require discussion with, and action by, provincial veterinary regulators. Additionally, the application of restrictions in Category I antimicrobials in Québec was preceded by education of producers and veterinarians, so that they would be receptive to changes and understanding of the rationale. A similar approach would be warranted prior to implementing a national strategy.

Strategic Intervention 5: Support Relevant Targeted Research to Enhance Knowledge on Application and Efficacy of Strategies and Products to Keep Animals Healthy

Supporting evidence:

Key informants from countries that have implemented AMS programs and policies have stated that enhanced biosecurity, effective vaccine programs, and access to effective alternative products are among the factors important to success. However, there is limited evidence for effectiveness of these strategies and products under current commercial conditions in Canada (Ch. 5). While more research is needed, prioritizing promising biosecurity measures, vaccines, and alternative products, with rigorous replication of studies, is essential for building an evidence-based foundation to support effective AMS.

Considerations and possible consequences:

Although more research is needed to evaluate the efficacy and application of biosecurity, vaccines, and alternative products, resources would be most efficiently targeted to approaches and products that show promise in early proof-of-concept studies. Building an evidence-based knowledge base also requires replication of interventions and outcomes across multiple studies conducted with the highest level of rigor. Thus, there is a need for both more data and for better data. Biosecurity and management, vaccines, alternative products, and decision-making tools for AMU are all essential to antimicrobial stewardship. Priority research questions could be developed in consultation with commodity groups and veterinarians to ensure that they address important issues and approaches for these end-users of the research results.

Do We Need to Set Targets in Canada?

The need to set targets, and the number that might be appropriate for a target, are highly contentious issues. The UK reduced AMU in animal agriculture by 59% between 2014-2022, corresponding to 254 tons of antibiotics, using targets. In the Netherlands, a reduction in AMU in food-producing animals of 56% between 2007-2012 was achieved by setting targets and tracking progress using mandatory farm-level benchmarking data. In Canada, initial gains in supporting AMS and reducing unnecessary AMU could include resolving issues such as not having duration of use labeling. However, based on our engagement activities, it is anticipated that there would be considerable resistance to setting reduction targets from many involved parties in Canada at this time. The ultimate goal is not meeting a set target, but rather is to reduce the use of antimicrobials to where benefits are demonstrably clear and substantial and exceed the risk.

Among the concerns expressed during engagement activities was that some commodity groups already have achieved reductions, making a single target number problematic. Another issue was that targeted reductions in AMU might not achieve the desired objective and that the goals of AMU changes have not been clearly articulated. Examples of possible goals, which are not mutually exclusive, include reducing overall AMU, reducing the use of Category I antimicrobials, reductions in specific uses (e.g., dry cow therapies in dairy cattle), reductions in AMR for pathogens of importance to animals in indicator bacteria / in pathogens of concern to human health), or prevention of further increases in AMR for specific bacteria-antimicrobial combinations. Articulating and defining these goals would be a valuable first step toward defining specific objectives.

Adopting the strategic interventions identified in this assessment could, if embraced and supported throughout the food-animal production system, have the effect of reducing AMU in food-producing animals to the minimum necessary to support the needs of optimum animal health while minimizing their impact on AMR. Setting goals and objectives based on the promising strategic interventions identified by the panel could be an initial step towards identifying a “made in Canada” strategy for using as few antimicrobials as necessary. With the appropriate data, goals could be reassessed over time to determine whether objectives are being met and whether it would be appropriate to define targets in the future. The aim is to use as much antimicrobials as are needed, but no more than necessary to safeguard animal health, animal welfare, food safety and security, and ultimately human health.

Glossary

Aminoglycosides: A substance that works against many types of bacteria and includes streptomycin, gentamicin, and neomycin

Antimicrobial: "Including antibiotics, antivirals, antifungals and antiparasitics - are medicines used to prevent and treat infections in humans, animals and plants" (World Health Organization, 2024b). In this report, however, the focus is on antibiotics, specifically.

Antimicrobial resistance: "Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. AMR occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death. As a result, the medicines become ineffective and infections persist in the body, increasing the risk of spread to others" (World Health Organization, 2024b)

Antimicrobial resistance genes: "A resistance gene contains the information for the production of a protein that makes an antibiotic ineffective and results in resistance against an antibiotic to a pathogen" (German Center for Infection Research, n.d.).

Antimicrobial stewardship: "A concept relevant to and applicable by all (individuals, communities, and institutions) [scope and scale], aiming at using and prescribing antimicrobials in humans, animals and the environment in a way that ensures the availability of antimicrobials for individuals in the present day, as well as preserving antimicrobial effectiveness for current and future populations [collective and temporal responsibility]. The operationalisation of stewardship includes considerations of whether antimicrobials should be used, the ways in which antimicrobials are used, as well as the broader context within which these decisions are made [contextual contingency]" (Hibbard et al., 2024).

Antimicrobial use (veterinary context): means the administration of an antimicrobial agent to an individual or a group of animals to treat, control or prevent infectious disease:

- to treat: means to administer an antimicrobial agent to an individual or a group of animals showing clinical signs of an infectious disease;
- to control: means to administer an antimicrobial agent to a group of animals containing sick animals and healthy animals (presumed to be infected), to minimise or resolve clinical signs and to prevent further spread of the disease;

- to prevent: means to administer an antimicrobial agent to an individual or a group of animals at risk of acquiring a specific infection or in a specific situation where infectious disease is likely to occur if the drug is not administered (World Organization for Animal Health, 2020)

Avoparcin: A glycopeptide antibiotic that is an analog of vancomycin (McArthur, n.d.-a)

Ceftiofur: A third generation cephalosporin antibiotic (National Center for Biotechnology Information, 2024)

Commensal bacteria: Bacteria that act on the host's immune system to induce protective responses that prevent colonization and invasion by pathogens (Khan et al., 2019)

Horizontal gene transfer: The movement of genetic information between organisms, a process that includes the spread of antibiotic resistance genes among bacteria fueling pathogen evolution (Burmeister, 2015)

Macrolides: A class of antibiotic that includes erythromycin, roxithromycin, azithromycin and clarithromycin (Best Practice Advocacy Centre New Zealand, n.d.)

Medically important antimicrobial: Antimicrobial classes used in human medicine or those used in food-producing animals that are members of the same class as those used in human medicine and where there is the potential for these antimicrobials to select for resistance to human pathogens (World Health Organization, 2024a)

Meta-analysis: Meta-analysis is the statistical summarization of results from multiple studies; it is the analytical component of a systematic review which can be undertaken when there is a sufficient body of literature identified in the review (Sargeant & O'Connor, 2020).

Metaphylaxis: See definition for "Antimicrobial control of disease"

Narrative review: A review of the literature undertaken by one or more subject experts to describe what is known on a topic while conducting a subjective examination and critique of a body of literature (Sukhera, 2022)

Network meta-analysis: An extension of meta-analysis which allows more than 2 interventions to be compared in the same analyses, using both direct and indirect evidence. Direct evidence comes from pairwise comparisons reported in the literature, whereas indirect evidence is estimated from the data for comparisons that have not been directly compared in the literature (Hu et al., 2020).

One Health: "An integrated, unifying approach to balance and optimize the health of people, animals and the environment" (World Health Organization, 2017)

Orthosomycins: A group of experimental/veterinary orthoester and oligosaccharide antibiotics that target the 70s ribosomal subunit (McArthur, n.d.-b)

Prophylaxis: See definition for "antimicrobial prevention of disease"

Scoping review: Used to describe the volume and nature of existing literature in a topic area, to determine the feasibility of conducting a systematic review for a specific review question within a topic area, or to identify gaps in the literature on a topic (Sargeant & O'Connor, 2020). Some scoping reviews include data extraction where results are qualitatively synthesized and often do not consider risk of bias of the individual studies.

Sulfonamides: Synthetic bacteriostatic antibiotics (Werth, 2024)

Systematic review: A formal method to summarize the literature to address a specific question, which uses structured methods to identify, select, and evaluate the risk of bias for all studies that address the review question. An approach for compiling the results from multiple studies addressing the same question (Sargeant & O'Connor, 2020).

Third-generation cephalosporin: Broad-spectrum antimicrobial agents useful in a variety of clinical situations (Klein & Cunha, 1995)

Vancomycin-resistant enterococci: Strains of enterococci bacteria that are resistant to the antibiotic vancomycin (PHAC, 2010)

Appendix 1. Assessment Methods and Demographic Information of Participants in the CAHS Engagement Process

1. Academic Literature Review

Literature Review Timeframe

The timeframe for the initial literature search was limited to literature published in the past 10-years, 2013– 2023), with more recent studies included when available, and older studies included as necessary to provide historical context.

Expressed Areas of Interest to CFIA/PHAC

Reviews were gathered to address the following additional areas of interest to CFIA/PHAC:

- The networks/governance (e.g., roles & responsibilities), actions (e.g., AMU regulations/ legislation), producer and public awareness/ expectations/education initiatives, and surveillance activities of industry and government
- Major veterinary pathogen(s) of concern and extent of AMR among these animal pathogens
- Antimicrobial prescribing patterns for animal disease prevention and treatment
- The extent of transmission of AMR from animals to humans, including the impacts or patterns observed when actions were taken to decrease AMU (i.e., Did the human health burden decrease? Were there observable reductions in AMR pathogens in the hospital or other settings?)
- Availability and use of vaccines, diagnostics (e.g. screening tests to detect disease early), and other alternatives that could be beneficial to reduce dependence on medically important antimicrobials (MIAs) (best practices for prescribing patterns of AMU in animals, animal disease treatment and prevention, agricultural/farming practices (e.g., husbandry), and impact of actions taken on animal and human health)
- Impact (positive or negative) of efforts to reduce AMU in the agricultural sector on animal health and productivity (targets measuring success)
- Consumer perspective (how much consumers are aware of AMR/AMU in food producing animals), expectations on how their food is produced, gaps in education material and best practices for public education (setting, age, active/passive)

- Measurement of impact (i.e. What outcomes are available to measure success in effectiveness of antimicrobials and the possibility of reducing AMR/AMU?)

Approach to Weighting Evidence

Given the scope of the project and the timelines available for completion, a comprehensive review of all available literature addressing each of these topics was not feasible. Rather, the literature review focused on systematic review and meta-analyses, when available, as this approach has high evidentiary value. When systematic reviews were not available for a topic area, narrative reviews were used. As narrative reviews generally do not provide a quantification of results or impacts, selective searches were conducted to identify recent original research studies or grey literature (e.g., government websites) to address specific questions where this type of information was required. Given the volume of literature assessed, formal quality assessment of each study was not conducted. Rather, study methodologies corresponding to high quality evidence were preferentially selected.

2. Case Studies

A case study approach was utilized to analyze antimicrobial resistance and AMU practices in food-producing animals across eight jurisdictions, aiming to generate insights for policy development in Canada. The analysis integrated data from a comprehensive document review and key informant interviews, providing a comparative perspective on strategies, challenges, and impacts on human health associated with AMU in agriculture. Case studies were researched by Ms. Roxana Badiei.

Eight jurisdictions were selected based on their relevance, variety of approaches, and the extent of existing AMR/AMU initiatives. The chosen countries included Australia, Denmark, the European Union, France, Germany, the Netherlands, the United Kingdom, and the United States. The jurisdictions were selected by the sponsor (n=4) and Expert Panel (n=4) for their jurisdictional relevance to Canada in terms of their approach to governance, and for their activities to address AMR/AMU in food-producing animals that would enable the expert panel to respond to the sponsors' primary question. The case studies provide insights into diverse regulatory frameworks and AMU practices, facilitating an understanding of adaptable approaches for the Canadian context.

Data were gathered through a structured review of scientific and grey literature published from 2015 to 2023. The review process included:

- Manual screening of AMR/AMU policy documents, strategic plans, and regulatory initiatives from each jurisdiction.
- Analysis of relevant research articles, conference abstracts, and reports by non-governmental and civil society organizations with a focus on AMR.

- Targeted searches of resources from organizations concerned with AMU in food-producing animals to identify policy gaps and effective strategies.

This iterative review process allowed each document to inform and build upon prior findings, enhancing the overall understanding of successful AMU stewardship measures across jurisdictions.

International Key informant interviews

Twenty-three international key informants were also interviewed from across the 8 jurisdictions selected, with one to three key informants selected from each jurisdiction. Interviews were conducted by Roxana Badiei, an independent contractor with the CAHS. International key informants were identified by discussion among the panel members and selection by the Chair. Individuals in strategic positions in the chosen international organizations in the identified jurisdictions were specifically targeted (e.g. Veterinary Medical Officers, and individuals who had been involved in the development, research and/or evaluation of AMR/AMU policies in those jurisdictions). Potential names were identified in the case studies or nominated by panel members, with final selection by the Chair.

3. Cross-Canadian Engagement

A breakdown of engagement participants is presented by demographic group below, for each type of engagement.

Consumer Focus Groups

Eight focus groups were commissioned by the CAHS and conducted by Léger in July (6 focus groups) and Sep 2024 (2 focus groups) with Canadian consumers. There were 8-10 participants in each focus group, totalling 69 consumers. Participants were selected to represent a mix of genders, age, income, education, and demographic representation across Canada.

Participation was limited mainly to those who consumed animal products (limiting vegetarian or vegan participants to a maximum of two per group) and possessed limited professional knowledge of food growth and production. Each focus group was also limited to a maximum of two members aged 55 and over to ensure accommodation of diverse age groups. The intention of the qualitative focus groups was to obtain detailed information on public perceptions from a wide range of participants.

The following describes the demographics of those involved in the Cross-Canadian virtual focus groups:

	Round 1 (April 2024)	Round 2 (July 2024)
Gender	• Male (52%) • Female (46%) • Non-binary (2%)	• Male (41%) • Female (59%)
Age	• 18-34 - 20 (38%) • 35-54 – 24 (46%) • 55+ - 8 (15%)	• 18-34 - 7 (41%) • 35-54 – 8 (47%) • 55+ - 2 (12%)
Education	• High school or less – 23 (44%) • Bachelor's – 20 (38%) • Postgrad or higher – 9 (17%)	• High school or less – 5 (29%) • Bachelor's – 7 (41%) • Postgrad or higher – 5 (29%)
Income	• Less than $60,000 – 17 (33%) • $60,000 to $100,000 – 21 (40%) • $100,000 or over – 14 (27%)	• Less than $60,000 – 6 (35%) • $60,000 to $100,000 – 2 (12%) • $100,000 or over – 9 (53%)
Geographical distribution	• British Columbia - 9 • Ontario - 9 • Atlantic Canada - 7 • Prairies - 8 • Québec - 9 and 10	• British Columbia - 1 • Ontario - 2 • Atlantic Canada - 2 • Prairies - 2 • Québec - 9 • Territories - 1

Virtual Engagement Sessions

Two rounds of virtual engagement were conducted in May 2024 and Oct 2024, via Zoom. A total of 107 individuals participated. A facilitator (AMR/AMU Assessment Chair) hosted each live session and presented key content to participants, who then provided their input via the Zoom "chat" feature. A Francophone panel member addressed comments that were provided in French, and a French interpreter provided translation of the English content in real time. Participants represented multiple sectors, including educational institutions, federal and provincial governments, non-governmental organizations, professional organizations, and research centres.

The following represents the demographic of those involved in the Cross-Canadian virtual engagement sessions:

	Round 1 (May 2024)	Round 2 (Oct 2024)
Sectoral representation	• Educational institution or training facility - 7 • Government (federal) - 4 • Government (provincial/territorial) - 7 • Non-government organization (NGO) not listed here - 20 • Other - 9 • Professional association - 6 • Research centre or network - 2	• Educational institution or training facility - 9 • Government (federal) - 7 • Government (provincial/territorial) - 3 • Non-government organization (NGO) - 18 • Other - 6 • Professional association - 6 • Research centre or network - 1
Geographical representation	• Alberta - 8 • British Columbia - 2 • International - 4 • Manitoba - 2 • New Brunswick - 1 • Newfoundland and Labrador - 1 • Nova Scotia - 2 • Ontario - 9 • Other - 1 • Pan-Canadian - 17 • Prince Edward Island - 2 • Québec - 5 • Saskatchewan - 2	• Alberta - 7 • British Columbia - 2 • International - 2 • Manitoba - 2 • New Brunswick - 0 • Newfoundland and Labrador - 0 • Nova Scotia - 1 • Ontario - 9 • Other - 2 • Pan-Canadian - 18 • Prince Edward Island - 1 • Québec - 6 • Saskatchewan - 0

Commodity group representatives were self-identified as "non-government organizations (NGOs)" or "other" in the above classification.

Written Surveys

Two rounds of written surveys were conducted in May 2024 and Oct 2024. A total of 102 individuals responded to the surveys and provided input via the online survey software Alchemer or via a downloaded version submitted via email. The first round was conducted to get input on key content areas for AMR/AMU. The second round of the survey was conducted to validate key findings.

The surveys were sent to professional associations, relevant FPT government departments, research centers and organizations, commodity groups and other industry groups and private entities in the food-producing animal sectors. Participants represented a diverse range of positions and backgrounds including professionals from the food production sector (e.g. program directors and organization owners/presidents), veterinarians, researchers, and policy analysts. The second survey was also shared with the CAHS fellows.

Because survey questions differed, inclusion criteria for survey responses differed across survey rounds. Therefore, percentages (rather than numbers) are represented in the following demographics:

	Round 1 (May 2024)	Round 2 (Oct 2024)
Sectoral representation	• Professional association (10%) • Research centre or network (10%) • Government (federal) (10%) • Government (provincial/ territorial) (40%) • Industry group (10%) • Private sector (20%)	• Professional association (6%) • Educational institution or training facility (16%) • Research centre or network (6%) • Non-government organization (NGO) (6%) • Government (federal) (14%) • Government (provincial/territorial) (6%) • Industry group (32%) • Private sector (10%) • Other (4%)
Geographical representation	• Pan-Canadian (40%) • International 10%) • British Columbia (20%) • Ontario (20%) • Prince Edward Island (10%)	• Pan-Canadian (47%) • International (8%) • British Columbia (2%) • Alberta (6%) • Saskatchewan (2%) • Manitoba (2%) • Ontario (8%) • Québec (10%) • Prince Edward Island (6%) • Nova Scotia (6%) • New Brunswick (2%)

Interviews with Key Informants

ACER Consulting Ltd. was commissioned by the CAHS to conduct focus group interviews with Canadian key informants across commodity groups, food production sectors, FPT government agencies, veterinary organizations, colleges, and other professional sectors. A total of 33 interviews, some involving multiple interviewees, were conducted of approximately one hour in length each. Interviews were conducted in June-July 2024. English and French interview requests were accommodated.

The following is a breakdown of the Canadian key informants who participated in an interview, by sector and geographical location:

Canadian	Number of Canadian key informants represented
Sectoral representation	• National industry groups - 12 • Veterinary associations - 4 • Government (federal) - 6 • Government (provincial/territorial) - 7 • Other - 4
Geographical representation	• Pan-Canadian - 26 • British Columbia - 1 • Manitoba - 1 • Ontario - 1 • Québec - 1 • Nova Scotia - 1 • Prince Edward Island - 1 • Newfoundland and Labrador - 1

Written Input

Written policy documents, guidelines, and/or ongoing initiative submissions were received from 7 organizations in response to the CAHS request for written input that accompanied each survey. Several respondents shared that they do not have policies, but rather public information and guidelines.

4. Integrating Evidence From Multiple Sources

The initial panel meeting was used to introduce panel members to each other and to discuss the project charter. Thereafter, information from the various sources was presented and discussed at panel meetings, particularly in the earlier stages of the project. Each task group was asked to review the relevant information from all sources and to use this information to develop their key findings and key gaps. If the group felt that additional scientific information was required, targeted searches were conducted to identify additional research studies to supplement the literature review findings. Draft key findings and gaps were then discussed at full panel meetings.

Appendix 2. International Case Studies Key Takeaways

Australia

Australia targets several key food-producing animal sectors, including pork, chicken meat, eggs, and fish to reduce AMU/AMR. Strategies and actions in these sectors commenced early on, with strict and conservative regulation (with noted minimal AMU across the nation), while also prioritizing the promotion of infection prevention and control, the development of antimicrobial prescribing guidelines, and encouraging the use of healthy farm management practices (e.g., vaccines and biosecurity practices) to reduce the need for antimicrobials across farms.

To encourage antimicrobial stewardship activities, the Australian government has put in place several national AMR strategies and successor initiatives that set out measures to minimize the risk of AMU/AMR in both animals and humans, using a One Health framework. Specifically, this includes Australia's AMR Strategy 2020 and Beyond, Australia's Animal Sector Antimicrobial Resistance Action Plan 2023 to 2028, the One Health Master Action Plan for Australia's National Antimicrobial Resistance Strategy to 2020 and Beyond' (OHMAP), and the Animal Industries Antimicrobial Stewardship, Research, Development, and Extension Strategy (AIAS). Central to these strategies include seven key overarching objectives and targets:

1. Establishing clear governance
2. Implementing infection prevention measures
3. Raising awareness and engagement
4. Promoting appropriate usage and stewardship of antimicrobials
5. Developing integrated surveillance systems
6. Supporting collaborative research
7. Strengthening global partnerships

As demonstrated through an in-depth literature search and key informant interviews, the main and overarching components of the national strategies on AMU/AMR across Australia include:

- Robust governance structures to manage AMR/AMU initiatives
- Best practices for infection control
- Enhancing public and professional awareness about AMR/AMU

The success of the national strategies across the nation is driven by strong and conservative regulation, stakeholder engagement, cross-sectoral collaboration, and the understanding amongst food producers that 'healthy animals mean healthy food'. Additionally, many industries have quality assurance programs that include conditions to reduce AMU, including supermarkets that dictate standards, which can, in turn, influence farming practices, in the context of AMU. However, a key finding throughout this assessment, particularly highlighted through key informant interviews, has demonstrated that engagement with stakeholders can be challenging due to a lack of public and political interest in the topic (stemming from an innate natural dis-acknowledgement of ‘a problem of AMU’ across the nation), contrasting with other countries and regions, such as Europe and Canada where there is significantly more traction on AMR/AMU issues.

The desired outcomes of Australia’s AMR/AMU strategy include an ‘advocacy-based lens’ to promote practices that reduce the incidence of AMR/AMU (by reducing the need for AMU) and ensure its prudent use. Specific targets include improved data collection and reporting, enhanced public and professional awareness, and stronger regulatory frameworks. It has been noted that specific KPIs and targets are a gap across the nation, thereby leading to most strategies targeting ‘advocacy-based’ and stakeholder collaborative involvement, rather than direct data-supporting-KPIs. Specifically, such targets and stewardship activities focus on promoting responsible AMU through knowledge generation and awareness raising using guidelines, education, and training for veterinarians and farmers.

In terms of surveillance systems, the Antimicrobial Use and Resistance in Australia (AURA) system is key across the human sector; however, there is a gap in regular, systematic, and ongoing surveillance of AMU/AMR in animals. There is scope to improve the quality of prescribing in food-producing animals, but more publicly available knowledge about volumes of AMU and the disease presentations for which these antimicrobials are being used is required. With this gap in regular and systematic surveillance of AMU/AMR in animals, the key informant interviews have highlighted that it makes it challenging to engage livestock industries, which often perceive their AMU as appropriate and do not see AMU as a problem. Despite the intent to position industries for regular surveillance, the practice has not met expectations for transparent and regular government surveillance.

Key lessons learned for Canada:

- Australia’s unique context includes its biosecurity measures, geographical isolation, and regulatory frameworks that encourage active ‘advocacy-based’ involvement across all sectors in the prudent and responsible AMU. Biosecurity is emphasized as fundamental to reducing disease and AMU, with efforts to improve practices across all farms.
- Having open conversations and creating comfort around discussing AMU/AMR is critical. This is difficult due to sensitivities, as people’s livelihoods are involved, but creating space for this conversation is useful. It is particularly important for the livestock sector to own the conversation, in the interest of the industry and its participants.
- The role of the environment and wildlife is important. It is difficult to identify who to engage and who has meaningful roles in these spaces.

- Trade policies are anticipated to be a big issue in the future for Australia. Although it has not occurred yet, there is hope it will, but it needs to be founded on science and demonstrated risk, rather than taking a precautionary approach. These policies will manifest through market and regulatory signals. However, there is some anxiety about it. Recommendations to overcome anticipated trade risks include countries being able to demonstrate their AMU levels (and that it is appropriate).
- Implementing co-designed strategies and partnerships in the context of antimicrobial stewardship is key. It is important to find the people that are enthusiastic and can bring their industries along on the journey, because results will be reaped much faster and in a much simpler and less controversial way, compared to regulating.
- The availability of sustainable funding is a challenging but critical factor. Therefore, finding ways to ensure that predictable and sustainable (long-term) funding is key.
- There is a disconnect between people, working at ground level compared to the national level. Therefore, this gap needs to be bridged to allow an improved understanding of any challenges being dealt with at a national level.

Denmark

Legislation plays a crucial role in Denmark's approach to managing AMU/AMR in agriculture. Since the introduction of national surveillance in 1995 (DANMAP), legislation has increasingly shaped how farmers use antimicrobials. Key components of AMU control across the nation include national surveillance of AMU, antimicrobials exclusively prescribed by veterinarians, thresholds for maximum usage without government supervision, and limitations on the use of specified antimicrobial substances. In terms of strategic interventions, Denmark's national strategy (Danish Veterinary and Food Administration's national action plan for antibiotic resistance in production animals and food for the period 2021-2023) employs a One Health framework, with key features of the 2021-2023 plan being:

- Reduction of AMU
- Improved monitoring and surveillance through the VetStat database
- Further restrictions (from the initial action plan) on antimicrobial medicinal products

The action plan sets specific targets, including a 2% annual reduction in AMU in pigs from 2019 to 2022, and requires veterinary prescriptions for all antimicrobials used in animals to promote its responsible and prudent use. Drivers for the success of Denmark's national strategy, as demonstrated through key informant interviews and a literature search, include effective surveillance, strong stakeholder collaboration, and a culture of compliance and continuous improvement. In this context, the role of the government (and in turn political will and the prioritization of antimicrobial stewardship) is crucial, providing the regulatory framework and resources needed to implement and sustain AMU reduction efforts. Other players, such as veterinary professionals and industry organizations, contribute to the strategy's implementation and adhere (and promote) best practices by encouraging more efforts on biosecurity and "back to basics" measures to first consider the health and well-being of animals to reduce the need for AMU.

In addition to Denmark's legislation and national strategies, the Yellow Card Initiative, established in 2010, sets specific AMU thresholds, at the individual herd level. Farms exceeding these thresholds receive a Yellow Card and must reduce their AMU or face penalties, such as reduced stocking density, additional costs, and inspections. This initiative may be seen as the best proactive model and approach to managing AMU effectively and sustainably in food-producing animals, helping to ensure both animal health and public health by ensuring compliance through oversight and fines.

In terms of data and surveillance, in 1995, Denmark launched an ongoing AMR monitoring program, the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP). DANMAP tracks AMR trends across human, animal, and food sectors. Specifically, DANMAP is a surveillance system established with five main goals, including the following:

1. To assess the usage of antimicrobials in both food-producing animals and humans
2. To monitor the prevalence of AMR in bacteria from food-producing animals, animal-derived food products (like meat), and humans
3. To pinpoint areas needing further research, such as the transmission of AMR or the links between AMU and AMR
4. To provide essential data to health professionals like veterinarians and human physicians to help develop guidelines for antibiotic treatment
5. To serve as a resource for decision-makers in government, academia, and politics to support risk assessments and management strategies to prevent and control bacterial infections resistant to treatment

As key findings from the most recent DANMAP report, in 2022, the total consumption of antimicrobials in animals amounted to 86.2 tonnes of active compounds of products approved for animals, representing a 2.1% decrease compared to 2021. The report notes that AMU has shifted significantly over the past decade, with reductions in certain critical classes like cephalosporins and fluoroquinolones, and increases in macrolides, aminoglycosides, and penicillin. Meanwhile, cattle antimicrobial consumption totaled 8.2 tonnes, predominantly for older cattle, and poultry usage slightly increased (since the previous year) due to disease outbreaks, highlighting ongoing shifts in antimicrobial practices across different livestock sectors. Additionally, in Denmark, all sales of veterinary prescription medications, including those from pharmacies, private companies, feed mills, and veterinarians, are reported to

VetStat, a central database managed by the Danish Veterinary and Food Administration (DVFA). Overarchingly and captured through key informant interviews, it was highlighted that the nation's monitoring system is robust with the country retaining carcasses of tested animals and only releasing them after negative test results for residues of AMU or diseases, unlike in the Netherlands, where testing results can take up to six weeks, by which time most meat has been consumed.

In terms of alternative approaches, vaccination is referenced in the nation's One Health Approach Strategy, National Action Plan on Antibiotics in Human Healthcare, and the Danish Veterinary and Food Administration's National Action Plan for AMR in Production Animals and Foods (2021-2023). In terms of vaccination regulation, marketing drugs and vaccines directly to producers is illegal in Denmark, preventing farmers from using multiple incompatible vaccines. This ensures safer and more effective disease management.

Key lessons learned for Canada:

- Denmark's context, characterized by a well-organized agricultural sector, family-owned farms, and long-term foreign workers, facilitates a stable workforce and effective implementation of AMU strategies. With this, however, ongoing training for farmers and workers is essential. Behavioral sciences can help identify training needs and improve communication across language barriers.
- Understanding infection statuses and equal requirements for all pig producers is crucial. Consistent regulations across exporting nations are necessary for fair competition. Basic animal husbandry, proper feeding, clean water, and appropriate housing are essential for reducing AMU.
- The approach to AMR in Denmark emphasizes biosecurity, proper diagnosis, and equal regulations for all producers. The collaboration between farmers, veterinarians, and the government is key to managing and reducing AMU while maintaining animal health and welfare.
- Integrating antimicrobial strategies with broader livestock industry changes and environmental issues can provide a more comprehensive approach.
- Having data-driven approaches with objective data on consumption at the herd level is crucial. Secondly, ensuring consistency in data collection and documentation is essential. Thirdly, promoting vaccinations and better management practices, and tightening regulations on all medications, especially oral ones, are vital.

European Union (EU)

The EU comprises 27 countries and has established a comprehensive and overarching approach to promote antimicrobial stewardship activities and reduce the need for AMU in food-producing animals. The EU stands as a unique case study with the success of its initiatives driven by the collaborative efforts of the member states and various stakeholders (including farmers, food producers, veterinarians, and the agricultural sector). Specifically, key components of the EU strategies on antimicrobial stewardship include strict regulatory measures, such as Regulation (EU) 2019/6 on veterinary medicinal products and Regulation (EU) 2019/4 on medicated feed, which impose limitations on the prophylactic and metaphylactic use of antimicrobials in food-producing animals. These regulations have been designed to eliminate routine AMU and promote enhanced farm management practices to reduce the overall need for antimicrobials across member states.

Overarchingly, the EU targets key food-producing animal sectors, including cattle, pigs, chickens, and turkeys. These sectors are prioritized in data reporting and are subject to stringent measures aimed at reducing AMU. For instance, Belgium's action plans for farms in high-risk zones include biosecurity improvements and mandatory action plans overseen by recognized coaches.

In terms of surveillance and data monitoring activities, from January 2024, all EU member states are required to report data on the volume of both sales and use of antimicrobials in food-producing animals, as part of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) initiative. This initiative standardizes data collection across member states, ensuring comprehensive monitoring of AMU and helps assess and analyze trends in AMU and antimicrobial sales. The establishment of the Antimicrobial Sales and Use (ASU) Platform further supports this effort, enabling systematic data collection and reporting of data on antimicrobial medicinal products in animals from across the EU. The Farm to Fork Strategy, which is at the heart of the European Green Deal, aims for a 50% reduction in total sales of antimicrobials for farmed animals and aquaculture by 2030 compared with 2018 figures. The outcomes of these initiatives are closely monitored, with significant reductions in antimicrobial sales reported across the EU. For example, sales of antimicrobials in food-producing animals have decreased by over 50% since 2011. Specific reductions in the use of medically important antimicrobials (MIAs), such as third and fourth-generation cephalosporins and polymyxins, highlight the targeted impact of these strategies. For instance, in Italy, one of the 27 EU member states, the shift to defined daily doses (DDDs) for measuring antimicrobial treatments offers a more precise method than traditional sales metrics, though key informant interviews have highlighted that further refinement is needed to account for different animal types and conditions.

Case studies within EU

Belgium. In Belgium, the success in reducing AMU by almost 60% is attributed to a combination of training, education, and data-driven policy. The government, in collaboration with AMCRA, legislated strict criteria for the use of MIAs, such as fluoroquinolones and second-generation cephalosporins. This action, supported by robust data collection and analysis, has led to the effective management of AMU. Funding of AMCRA's projects is a mix of partners' contributions and government subsidies, demonstrating a shared commitment to prioritizing antimicrobial stewardship practices. Across Belgium, antimicrobial stewardship priorities include improved biosecurity and vaccination, with farms that are in 'higher-risk zones' required to develop action plans in consultation with veterinarians.

Italy. Italy's approach highlights the importance of precise diagnostics and strict regulatory frameworks. European legislation mandates that veterinarians diagnose and define diseases before administering antimicrobials, prohibiting metaphylaxis. This shift has significantly impacted herd management practices, emphasizing the need for improved management in the absence of routine antimicrobial treatments. Italy's experience underscores the role of financial incentives in achieving compliance and the unintended consequences of stringent regulations.

Key lessons learned for Canada:

The EU's context is unique due to its political and economic integration, which allows for harmonized regulations and coordinated actions across member states. It is essential to involve all stakeholders in discussions to avoid exclusion and opposition amongst members.

Data collection and its information on AMU usage are critical for informed decision-making. Setting quantitative goals, even if not scientifically perfect, provides clear direction. Monitoring resistance is important, but setting goals based on resistance rather than usage can be risky due to the long-term nature of the relationship between usage and resistance. Providing information and common protocols, nationwide, is crucial for tackling AMR effectively and reducing the need for AMU. A nationwide approach to AMU protocols would reduce variability and improve effectiveness.

As noted through the Italy case study, financial incentives for farmers are essential to encourage compliance with new regulations. For context, European legislation is heavily influenced by consumer demand and supermarket chains requiring antibiotic-free products, which can sometimes mislead proper AMU. For a significant change, financial incentives are, therefore, crucial. The EU provides subsidies to farmers who reduce AMU, which has proven effective in achieving reductions. However, there are no additional incentives, only penalties for non-compliance.

Trade barriers related to AMR are likely to arise, making it imperative to address this issue proactively.

France

Across France, specific measures have been undertaken for MIAs through an order published in 2013 that limits the use of 3rd- and 4th-generation cephalosporins and fluoroquinolones. Antimicrobial susceptibility testing is mandatory for veterinarians before using 3rd- and 4th-generation cephalosporins and fluoroquinolones.

As part of the country's national action plan in the context of AMU/AMR and reducing the need for AMU in food-producing animals, France has pursued actions under the Écoantibio plan, with Écoantibio 1 (2011-2017), Écoantibio 2 (2017-2022), and more recently Écoantibio 3 plan (2023-2028). The global objective of the first Écoantibio plan was to reduce animal exposure to antimicrobials by 25% in five years (which was met and further explored through consecutive plans). The first action plan combined incentive tools, such as awareness-raising campaigns aimed at professionals, and mandatory tools, such as the prohibition of discounts, rebates, and reductions (Act No. 2014-1170) with the second plan following its success.

In addition to this plan, a law published in 2014 (French Act no. 2014-1170, 13/10/2014) set a reduction target of 25 % over three years for the exposure of animals to antimicrobials that are critical for human health (including 3rd- and 4th- generation cephalosporins and fluoroquinolones). In March 2016, a Decree (2016-317, 16/03/2016) banned the use of preventive MIA which can only be used to cure animals after diagnosis, bacterial identification and antimicrobial susceptibility testing. The most recent Écoantibio plan sets the following targets:

- Maintain the dynamic of reducing current levels of exposure to antibiotics by maintaining the current levels of exposure of livestock to antibiotics and by setting a specific target of reducing dogs' and cats' exposure to antibiotics by 15% by 5 years
- Preserve the therapeutic arsenal in animals
- Strengthen the prevention of diseases that lead to the use of antimicrobials and antiparasitics
- Promote the proper use of antimicrobials and antiparasitics at the animal and herd level
- Improve understanding of antimicrobial and antiparasitic resistance
- Encourage the commitment of sectors, professionals, and citizens on AMR

The targeted food-producing animal sectors across the country include cattle, swine, poultry, and aquaculture, with specific measures tailored to each sector's unique challenges. For instance, significant reductions in AMU in poultry and pig production have been achieved through policies that limit prophylactic and metaphylactic AMU and promote alternatives like vaccination and improved biosecurity measures. Between 2011 and 2022, there was a 66%

reduction in annual sales of antimicrobials, with a 94.6% reduction in sales of MIAs like 3rd and 4th generation cephalosporins and an 84.6% reduction in fluoroquinolones.

Central to France's national strategy is the RESAPATH network, which monitors AMR in bacteria from diseased animals. More specifically, the main objectives of RESAPATH are as follows (ANSES, 2023):

- To monitor AMR in bacteria isolated from diseased animals in France
- To provide member laboratories with scientific and technical support on antimicrobial susceptibility testing methods and result interpretation
- To detect the emergence of new resistances and their dissemination within bacteria of animal origin
- To contribute to the characterization of the molecular mechanisms responsible for resistance

This network, comprising 71 veterinary diagnostic laboratories, provides critical data that informs both national policy and stewardship efforts. ANSES oversees these surveillance activities, ensuring compliance with both national and EU regulatory frameworks. The network's voluntary nature and comprehensive data collection enable France to maintain high levels of oversight and adaptability in its AMR strategies.

Overarchingly, France has demonstrated its political prioritization of reducing the need of AMU in food-producing animals through surveillance activities, strategic and regulatory measures that restrict the use of antimicrobials for disease prevention in food-producing livestock. For example, in France, data collection on antimicrobial sales (used in animals) is mandatory and the country also has strict regulations requiring prescriptions for AMU, applying to all antibiotics. Key informant interviews have also highlighted that the various surveillance programs in place across the nation assess the impact of measures, both in terms of antibiotic consumption and resistance. However, reducing AMU without compromising animal welfare was noted as a consistent challenge in commercial initiatives, such as 'antibiotic-free' labels having unintended consequences of animal protection issues.

Key lessons learned for Canada:

- A comprehensive governance and stakeholder involvement from the start (e.g., of AMU strategy development) is key.

- Integrating all stakeholders, including consumers and the food industry, from the beginning (i.e., legislative, and national action plan processes) will help avoid later tensions.

- Having clear and quantified objectives, even if they are approximate estimates, at the beginning will provide direction to efforts.

- Regarding drivers of change, the veterinary sector has a key role to play, as they are mobilizable stakeholders on public health issues. Therefore, it is important to make sure they are involved and central to collaborative efforts.
- A very successful approach for France was the governance of the Écoantibio plans. These plans were not 'just documents', but were strongly associated with tight governance, supervision, support, and involvement across various sectors. The plans are a unique format (where it is not just the ministry that unfolds its plan), but instead, the ministry involves the actors in piloting the various actions of the plan. As such, the Ministry of Agriculture gives responsibilities to each stakeholder to pilot, in a way, a delegation of the ministry's action, which has the virtue of involving them.
- For the French system, an incentive-based plan with communication and practical research has worked. Communication reached the main stakeholders, correcting public misconceptions. Involving science, not relying solely on communication, and funding practical research projects have been crucial. This means focusing on the tripod of: science, communication, and funding has been the most effective lessons learned from France.

Germany

Germany has implemented a national strategy to reduce the need for AMU in food-producing animals, emphasizing a One Health framework that integrates human, animal, and environmental health. Specific interventions in the food-producing animal sector involve the implementation of guidelines for the prudent use of veterinary antimicrobial drugs, mandatory reporting of antimicrobial sales volumes, and benchmarking systems to monitor and reduce AMU on farms. Specifically, farms must submit all AMU data for each half-year period and are benchmarked against moving benchmarks (which are always in comparison with other benchmarks). The median of all farms is benchmarked with the worst 50% of farms required to create a plan and take action to improve their antimicrobial stewardship practices. The worst 25% of farms must take strict measures and send their AMU action plans to the authorities.

The German Antimicrobial Resistance Strategy (DART), developed by the Federal Ministry of Health, the Federal Ministry of Food and Agriculture, and the Federal Ministry of Education and Research, is central to Germany's efforts to reduce the need for AMU. This strategy involves multi-sectoral cooperation and international collaboration to address the global challenge of AMU. Specifically, the key components of Germany's AMU/AMR strategy include:

- Promoting prudent AMU
- Raising awareness about AMR among medical and veterinary professionals
- Improving infection prevention
- Enhancing surveillance and monitoring
- Supporting research and development

Additionally, one of the main measures in DART (2020) in the field of veterinary medicine was the establishment of a system for the nationwide minimization of AMU in livestock for specific fattening animals (cattle, swine, chickens, turkeys). With the 16th Act to Amend the Medicinal Products Act (16th AMG Amendment) which came into force on 1 April 2014, a system of this kind was established for the first time in Germany. The Antibiotics Minimization Concept, as part of the 16th amendment (sections 58a to 58d AMG) pursued three goals, namely (Federal Ministry of Food and Agriculture, 2019):

- Goal 1: To reduce the use of antibiotic veterinary medicinal products in certain fattening animals
- Goal 2: To promote prudent and responsible AMU in the treatment of diseased animals in order to limit the risk of the emergence and spread of AMR
- Goal 3: To facilitate effective task performance by competent authorities, particularly on livestock farms

The outcomes of these strategies are monitored through various surveillance systems, with significant reductions in antimicrobial sales volumes observed since the implementation of these measures. The impact is evident in the improved rankings in European reports on veterinary antimicrobial consumption and the substantial decrease in AMU on farms. However, through a literature search and key informant interviews, it was not clear whether the potential impacts of such strategies on animal welfare were evaluated.

In terms of surveillance and data reporting, AMR data from food-producing animals are collected in Germany through the German Veterinary Monitoring System (GERM-VET). Additionally, AMR testing in the Zoonosis-Monitoring System (ZOMO) report includes data on zoonotic and commensal bacteria in various food chains, as well as AMR data on *Salmonella* from national control programs, which are also reported to the European Food Safety Authority (EFSA). These systems collect and analyze data on AMU/AMR and provide essential information to guide interventions. Joint analyses are reported in the GERMAP reports, although there is a recognized need for a more harmonized approach to data collection and reporting.

Germany's strong agricultural sector, extensive use of farmland, and significant role in European and global food production has led to the country's commitment to the One Health framework and its integration of environmental considerations into AMU/AMR strategies. Government stewardship and the role of various stakeholders, including veterinarians, farmers, and consumer advocacy groups, have been critical to the success of its national strategy, DART. The government provides regulatory frameworks, funding for research, and coordination of surveillance activities, while stakeholders are engaged in implementing and adhering to guidelines and best practices. Finally, as highlighted through key informant interviews, the involvement of the quality standards company Q-S-De, which introduced AMU monitoring for its farmers, covering 90% of all farmers, also demonstrates the private sector's role in driving compliance and improving AMS practices across the nation.

Key lessons learned for Canada:

- It is important to start with low-level monitoring systems to ensure preliminary data are available.
- Implementing electronic data transfer methods to reduce farmers' workload is key, as farmers do not want extra workload burden.
- Using an indicator that is easy for farmers and veterinarians to understand is important, as this may help and encourage motivating farmers to see AMU surveillance as beneficial.
  - For example, in Germany,' 'Treatment days' data were introduced because veterinarians and farmers tend to recalculate veterinarians' AMU figures. Therefore, providing feedback (that is understandable) helps the farmers understand the calculations and its farms' contextual state of AMU.
  - In contrast, Defined Daily Doses (DDDs), which are common in other countries, are not easily calculable, leading to misunderstandings amongst farmers. Therefore, in Germany, AMU is calculated using these treatment days data to determine the average number of days with antimicrobial treatment per farm. This method relies on veterinary records rather than sales data.
- Recognize that no single solution fits all situations for enhancing prudent AMU. For example, focus on why and in which situations veterinarians decide to use antimicrobials. This approach will also consider alternative AMU methods.

The Netherlands

Historically, the Netherlands had one of the highest rates of AMU in farm livestock across Europe. This was highlighted in 2005 and 2009, when livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) and extended spectrum beta-lactamase (ESBL) producing bacteria were found in the Dutch pig industry and on poultry meat, respectively. Initially, across the country, people believed antimicrobials were necessary for animal welfare. However, this changed when the preventative use of antibiotics was no longer allowed, necessitating other methods to prevent animals from becoming sick. As a result, decreasing AMU (and its need) became a goal, and the Netherlands established a national surveillance system of AMU. The country made concentrated efforts towards antimicrobial stewardship practices, including developing the Dutch National Action Plan on AMR and a Task Force on Antibiotic Resistance as well as setting targets to reduce AMU, which was mandated by the government and supported across the livestock sectors. In response to the need for an independent body to monitor antimicrobial usage at the herd level, in 2010, the independent

Netherlands Veterinary Medicines Authority (SDa) was established to collect data on AMU on farms, establish benchmark indicators for individual major livestock sectors and analyze trends in antimicrobial consumption. The SDa is a public-private partnership between the government and stakeholders from the major livestock sectors (pigs, broilers, veal calves and dairy cattle) and the Royal Dutch Veterinary Association (KNMvD).

Strategic interventions in the Netherlands encompass both mandatory and voluntary measures. Implementing mandatory herd health plans and the requirement for periodic veterinary inspections ensure that preventive measures are prioritized over curative ones. These interventions are supplemented by educational campaigns aimed at changing perceptions and behaviours regarding AMU among farmers and veterinarians. The 'Dutch National Action Plan on AMR, although not a formal policy, integrates efforts across six sectors, including:

- Healthcare
- Animals
- Food
- International
- Science/industry
- The environment

The key components of the Dutch strategy include strict regulations on antibiotic prescriptions, compulsory health and treatment plans at the herd level, and the involvement of multiple stakeholders in the implementation process. The use of herd-level treatment plans and fostering a close, collaborative relationship between veterinarians and farmers has also been a key driver in the country's prudent use of antimicrobials. Through such a model, veterinarians and farmers jointly develop plans to optimize AMU, specifically focusing on disease prevention and maintaining animal health without relying on antibiotics. For example, at least once a year, a farmer and their veterinarian need to discuss how to optimally decrease infectious pressure and increase host resistance. Through this dialogue, the farmer and veterinarian discuss biosecurity, hygiene practices, feeding, water, and vaccination schedules annually to improve health and reduce infection pressures.

In terms of surveillance and AMU monitoring, across the Netherlands, mandatory reduction targets were defined in 2008, with total AMU in food-producing animals required to be reduced by 20% in 2011, 50% in 2013, and 70% in 2017 (as achieved). Monitoring trends in AMR and AMU in food-producing animals across the Netherlands is determined by analyzing the results generated within an annual standard monitoring program (Nethmap-MARAN). Targeted food-producing animal sectors in the Netherlands include broilers, pigs, veal calves, and dairy cattle. Each sector is subject to specific benchmarks and reduction targets, with a notable focus on minimizing the use of medically important antibiotics for human health, such as fluoroquinolones and third- and fourth-generation cephalosporins. Key informant interviews have highlighted that there are no significant gaps in data collection for AMU or AMR in the Netherlands (through the MARAN/NethMAP), although it can be improved for more detailed monitoring and it is important for all levels of government to be engaged and involved.

Comprehensively, such efforts have resulted in a significant reduction in AMU, achieving a 58% reduction from 2007 to 2012 and a 68% reduction from 2007 to 2017, with stable or decreasing resistance levels in key bacteria, such as *E. coli* and *Salmonella*. Additionally, key informant insights have highlighted that the strategic interventions in the Netherlands involved major stakeholders and multiple approaches to holistically change behaviours.

Key lessons learned for Canada:

- Although, initially, across the Netherlands, antimicrobials were considered necessary for animal welfare, this mindset shifted as preventative use of antibiotics was no longer allowed, thereby requiring other methods (e.g., biosecurity) for the prevention of sickness among animals. The establishment of a national surveillance system for AMU, where each farmer has an antibiotic usage number and a benchmark, was crucial across the Netherlands. This system provided clear goals and encouraged stakeholders, especially farmers, to change their practices. While farmers were generally more willing to change their mindset than veterinarians, the involvement and agreement of all stakeholders were essential for success.
- Cooperate: all stakeholders need to be consistent in terms of a shared objective and aligned in their messaging, especially relevant for veterinarians and farmers. A communication plan around the AMU strategy should involve shared objectives and multi-stakeholder engagement and collaboration.
- Set a goal: establish a SMART goal, both nationally and on a herd level—identify where you are and where you want to go. At a national level, take communication seriously and 'reset the mindset' by utilizing social science and communication science mechanisms through communication strategies.
- Effective change in AMU requires a sense of urgency and widespread awareness of the issue. Political will is required—all stakeholders, including the government, need to agree and be involved.
- Considering the impact of international travel and trade on AMR underscores the importance of robust monitoring systems to prevent the spread of resistant bacteria.
- Communication with stakeholders and ensuring they understand the legislation is important for compliance. Educating veterinarians to translate knowledge to farmers is also crucial (i.e., farmer vet discussions).

United Kingdom

The UK's context is unique due to its devolved agricultural policies, with distinct strategies implemented across England, Northern Ireland, Scotland, and Wales. Specifically, however, the UK has taken a different approach from many other countries when developing its system of antibiotic stewardship. Government stewardship and the role of other players, such as farmers, veterinarians, and industry associations, are critical to the success of the UK's strategy Therefore, rather than regulating, the government has worked in collaboration with farmers and veterinarians, supporting them to lead action on reducing the need for AMU. Key informant interviews have, however, highlighted that due to this voluntary approach (with farmers and veterinarians), there's little government strategic planning in terms of AMU.

Across the UK, strategic interventions began with the swine and poultry sectors, which were initially the highest users of antibiotics. Motivated by early work from the VMD, these sectors have seen significant reductions in AMU through voluntary stewardship activities driven primarily by veterinarians. SeElective dry cow therapy in the dairy sector is a notable success, demonstrating how data-driven and evidence-based approaches can effectively reduce AMU.

The key components of the UK's strategy include reducing the need for antimicrobials through improved husbandry and disease prevention measures, optimizing AMU, and investing in innovation, supply, and access to new diagnostics, therapies, and vaccines. The strategy sets specific targets for various sectors, including sheep, beef, dairy, egg, poultry meat, pig, gamebird, and fish, ensuring that tailored approaches meet the unique needs of each sector. The Responsible Use of Medicines in Agriculture (RUMA) Alliance and the Target Task Force (TTF) facilitate cross-sectoral collaboration, leading to a significant reduction in antibiotic sales for food-producing animals by half since 2014. The UK is also up-to-date in its action plans, with more recently the 2024 to 2029 action plan on AMU launched, succeeding its predecessors of the 'Tackling AMR 2019-2024: The UK's five-year national action plan' five-year national action plan which supported the UK-20 year vision for AMR.

In terms of AMU data monitoring and surveillance, published by the VMD, the UK Veterinary Antimicrobial Resistance and Sales Surveillance (VARSS) report presents veterinary antibiotic sales, usage, and resistance data from the UK. According to the VARSS report, data collected in 2021 has demonstrated that there is a continued downward trend in the use of veterinary antibiotics in the UK; specifically noting that sales of veterinary antibiotics (AMU) for food-producing animals were reduced by 55%, with the UK continuing to be one of the lowest users of veterinary antibiotics across Europe.

Additionally, launched in 2021 and under the purview of the UK Food Standards Agency, the Pathogen Surveillance in Agriculture, Food and Environment (PATH-SAFE) programme uses the latest DNA-sequencing technology and environmental sampling to improve the detection and tracking of foodborne disease (FBD) and AMR. The programme has been established as a new data platform to allow for the analysis, storage and sharing of pathogen sequence and source data, collected from multiple locations across the UK by government departments and public organizations. Specifically, the aims of the program include:

- To pilot a better national surveillance system for the monitoring and tracking of AMR in the environment and agri-food system
- To bring together and build on existing initiatives across the UK and to understand what the end-user needs to improve how they work in this space
- To provide better data to identify the prevalence, source and pathways of FBD and AMR, helping to prevent spread by enhanced targeting of interventions

However, despite such findings from the literature search, key informant interviews highlighted that ‘we don’t really have a robust surveillance system’ due to the passive and voluntary nature of data submission which inherently leads to incomplete and participant biases. The key informant interviews also noted that, in terms of targets and measuring outcomes, the emphasis has often been on activity metrics, such as participation levels in stewardship activities, rather than on robust outcome measurements. Collecting data in an automated, unbiased manner is therefore a recommendation, and crucial for accurate monitoring and assessing the true impact of these interventions.

Key lessons learned for Canada:

- The UK’s context is unique due to its devolved agricultural policies, with distinct strategies implemented across England, Northern Ireland, Scotland, and Wales. This decentralized approach allows for tailored interventions that address specific regional challenges and opportunities, contributing to the overall effectiveness of the national strategy.

- Avoid unnecessary effort (or inappropriate partitioning of limited resources).

- Work out where the key problem actually is: AMU is not the problem (AMR is), so we need to work out where this is stemming from, at a societal level. Once established, work backward, rather than make the assumption that AMU at the farm level is the only thing that needs to be ‘changed’ (which is what is occurring in the UK).

- Trade: different frameworks for monitoring AMR/AMU across countries are interesting and would be positive to motivate change and harmonization in approaches taken across countries.

- The UK is unique in terms of doing a lot with voluntary action. Good quality data is important and this is a gap in the UK.

- Key informant recommendation/idea: Despite progress, challenges remain, including the need for better linkage between AMU and AMR data and addressing other factors influencing AMR, such as diet. Alternative approaches, such as imposing a tax on antibiotics, could drive behaviour change by making AMU more expensive and promoting alternative practices.

United States of America (USA)

AMU/AMR is highly politicized across the US. Veterinarians and producers are divided on the importance of addressing AMU/AMR, and there exists a lack of political prioritization and will across the nation to address AMU/AMR.

The US has taken more of a voluntary approach to antimicrobial regulations, working closely with the FDA and pharmaceutical companies to implement changes, such as the Veterinary Feed Directive (VFD) in 2017 and moving over-the-counter antimicrobials to prescription status in 2023. In terms of strategic interventions and national action plans, the US has adopted several initiatives, including the USDA-launched Antimicrobial Resistance Action Plan (2014), the US National Strategy for Combating Antibiotic-Resistant Bacteria, the National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB), 2020-2025, and the USDA Strategy to Address Antimicrobial Resistance (USDA AMR Strategy). The US CARB National Action Plan exemplifies strong interagency collaboration across the One Health spectrum, involving various government agencies, including the FDA and USDA. As part of this work, the CARB task force, with representatives from various US agencies, has been valuable in coordinating efforts across the nation and responding to international evaluations of AMU practices.

To measure outcomes, key performance indicators, and targets of such strategies, the US has made several strides in measuring the economic and resource impact of conditions and policies. For example, across the three goals of the five-year plan Supporting Antimicrobial Stewardship in Veterinary Settings, Goals for Fiscal Years 2024-2028, the FDA tracks accomplishments per each of the three goals. Similarly, as part of the US National Action Plan for Combating Antibiotic Resistance Bacteria (CARB), key progress reports on the plan have been developed to demonstrate its achievements and progress on policy (Year 5: U.S. National Action Plan Progress Report). Despite such measures, however, key informant interviewees emphasized that measuring success in reducing AMU (and its need) is challenging. Sales data is a proxy, but more detailed farm-level data is needed to understand the impact of stewardship practices and policy changes. Finally, a gap in research and data collection on the impacts of antimicrobial stewardship activities and strategic interventions (i.e., impacts on national strategic action plans) and its link on animal welfare remains.

As part of antimicrobial stewardship activities, the USDA also works voluntarily with producers to collect data on AMU/AMR. Key informant interviews have captured that producers, especially in large operations, are generally resistant to change (in the context of AMU on-farm practices) unless financially incentivized. The primary focus for many producers is maximizing economic throughput, which can conflict with efforts to reduce AMU. Therefore, concerns about increased costs and logistical challenges hinder the adoption of new and alternative practices to AMU across the US. Across key informant interviews, it has also been noted that changing long-standing practices in AMU across food producers faces human behaviour challenges as well. Producers often believe they are already practicing good stewardship, making it difficult to implement new practices, for example.

In terms of surveillance and monitoring systems, the US has several AMU tracking networks and systems, which monitor AMU in humans, animals, and the environment. These include the National Antimicrobial Resistance Monitoring System (NARMS) which is guided by the NARMS Strategic Plan (2021-2025), the FDA's Vet-LIRN, and summary reports on antimicrobials sold or distributed for use in food-producing animals (2022 summary report). However, of note and as critiqued across studies, surveillance activities designed to generate AMU/AMR in food-producing animal data are complex, expensive, and time-consuming to implement. Specifically, key informant interviews have also highlighted that better farm-level data at a national level are required, particularly because current data collection methods include surveys and financial records, but challenges remain in obtaining consistent and comprehensive farm-level data, with this challenge further emphasized by the voluntary approach the country has taken to collect data from producers.

Key lessons learned for Canada:

The primary barrier to antimicrobial stewardship is risk aversion among veterinarians and producers. Without clear incentives and support, they are unlikely to change practices that they believe could negatively impact their operations.

- Addressing AMR requires understanding and overcoming psychological and social barriers, including producer mistrust of government and regulatory bodies.
- Support initiatives that lead to meaningful change in attitudes and practices regarding AMU to lead to a generational shift.
- Focus on decreasing the need for antibiotics rather than just reducing use numbers. Engage people within the circle of trust and use marketing and market accessibility as tools. Continue advancing science while recognizing the psychological and social barriers to change.
- To focus on reducing the need for AMU (rather than solely reducing AMU), farm management practices need to be improved with greater emphasis on animal health and welfare.

- Trade concerns could become a driver for change, but US producers are highly resistant to external mandates from international entities like the EU.
- The US collaborates with international partners through initiatives like the Quads Alliance, sharing technical information and strategies to address AMR. In addition to international collaboration, engaging industry and veterinarians is crucial for policy success. Effective communication through trusted partners is essential.
- Enhancing biosecurity and promoting effective and cost-effective vaccines are crucial for reducing the need for antimicrobials. Financial incentives and continued research investment are necessary to support these measures.

Appendix 3. Vaccines in Animals- Background

The following description of types of vaccines in animals is taken verbatim from the European Medicines Agency (EMA) and European Food Safety Authority (EFSA) Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA) (European Medicines Agency & European Food Safety Authority, 2017).

Live and modified (attenuated, or recombinant) live vaccines

- Live vaccines are commonly capable of conferring long-term immunity following a single dose or in combination with a booster dose when administered to susceptible animals, i.e. not protected by maternal immunity interfering with live vaccines or by antimicrobials preventing establishment of live bacterial vaccines.
- Risks associated with live vaccines include potential reversion to virulence in which case the vaccine will actually cause diseases.
- Thus many vaccines use DNA technology to remove several key genes from the pathogen and thus effectively have more than one attenuating modification to the pathogen (e.g. the most recent modified live virus vaccine for BVD virus II has 2 separate modifications to the virus achieved by deletion of specific genome sequences that should effectively prevent reversion).
- In addition, in cases of immune impairment the use of live vaccines is not recommended.
- Furthermore, live vaccines must normally be kept at special temperatures (2–8°C, 20°C, 196°C) to maintain efficacy.

Inactivated vaccines

- Inactivated vaccines do not carry any risk of infectious disease transmission, as they do not contain any live organisms. Most inactivated vaccines require an adjuvant formulation to activate an appropriate immune response and still generate weaker immune responses and require repeated doses to maintain immune memory compared to live vaccines.
- Subunit vaccines include only selected antigens or specific epitopes from the pathogen that elicit protection after immunization and are even more dependent on adjuvant formulation.

DIVA vaccines

- The ability to identify and selectively delete genes from a pathogen has allowed the development of 'marker vaccines' that, combined with suitable diagnostic assays, allow differentiating infected from vaccinated animals (DIVA) by distinction of antibody responses induced by infection with the wild-type virus or bacteria from those induced by the vaccine (no antibodies generated to deleted genes).
- This is an important development that will make it possible to vaccinate under regulatory control without impairing the sanitary status of the infected herd and which has proven useful.

Autogenous vaccines

- Autogenous vaccines are inactivated immunological veterinary medicinal products which are manufactured from pathogens and antigens obtained from an animal or animals from a holding and used for the treatment of that animal or the animals of the holding in the same locality.
- They are primarily used for pigs, poultry and fishes and are prepared from the pathogenic organism organisms specific to the individual herd or flock after a problem has been identified and when no registered vaccines for the pathogen or the serotype in question are available or those vaccines have been shown not to be efficacious against the particular pathogen or serotype in the locality.
- The regulations for production and use of autogenous vaccines vary considerably between EU jurisdictions, although there is an ongoing Heads of Medicines Agencies (HMA) lead initiatives to harmonize regulations.

Administration of vaccines

- Proper storage and administration of vaccines is important in obtaining the full effect of vaccination. New developments in terms of needle-free intradermal delivery of vaccines to obtain a better targeting of immune activating dendritic cells located in the epidermis appear promising, and although oral delivery of inactivated vaccines has been a target for vaccine research through decades, there are new developments in this area as well, although all registered vaccines for oral veterinary use are still live attenuated vaccines.
- Research is still needed to support development of multivalent veterinary vaccines and to investigate the optimal vaccination protocols with combined (parallel) administration of existing veterinary vaccines.

- In theory, inactivated vaccines will have no or minimal immunomodulatory effects on efficacy of other vaccines administered in parallel, while even minor immunosuppressive effects of live attenuated vaccines may influence the efficacy of other vaccinations administered at the same time or in the following weeks.

Passive immunization

- Vaccination of pregnant animals is frequently used as a means to protect the new born animal from specific diseases that occur early in life.
- Immunoglobulins form an important component of the immunological activity found in milk and colostrum and are central to the immunological link that occurs when the mother transfers passive immunity to the offspring.
- The mechanism of transfer varies among mammalian species, but access to colostrum of good quality is imperative for the vaccination of the mother to have preventive effects on the disease susceptibility of the offspring. Laying hens transfer immunoglobulins via egg yolk to their chickens. In contrast to vaccination, administration of immunoglobulins establishes instant immunity but with no induction of immunological memory.

Trained innate immunity

- All classical vaccines rely on the principle of induction of a specific adaptive immune response to the vaccine target.
- An emerging topic in vaccinology is based on the appreciation of trained immunity or innate immune memory, where cells of the innate immune system achieve a temporarily improved functional state to more efficiently combat secondary infections after a challenge by a primary infection or vaccine.
- Trained immunity has now been demonstrated in plants, invertebrates, animals and humans and has the potential to improve the health status of particularly neonates where traditional adaptive immunity is difficult to achieve by other means than passive immunization.

New technological developments in vaccine development and production

- While traditional vaccine design has most often been developed from cultivated microbial agents and isolating the protective antigens, there are a number of recent technological developments that allow vaccines to be designed from a more rational reverse vaccinology approach.
- Beyond the development of new technologies for rational antigen discovery, the advances in understanding the activation of innate and adaptive immune responses have spurred new

hope for development of adjuvant formulations with a more focused immune activation following delivery of recombinant subunit antigens. Developments in live attenuated delivery platforms based on Vaccinia virus, Adenovirus or ribonucleic acid (RNA) alpha viruses allow for new vaccines with strong immune activation and a high safety profile.

- Irrespective of any technological advances it must be remembered that vaccines are registered biological products and exchanging a component, e.g. an adjuvant or an antigen, with a superior modification cannot be done without filing a new registration for the full product to secure public and animal health. The expense and difficulty of this will inevitably keep many of the 'old' vaccines on the market for many years to come.

Appendix 4. CIPARS On-farm Antimicrobial Use and Antimicrobial Resistance Based on Data Collected from Sentinel Farms (2019-2023)

These data are presented here to provide background on farm-level AMU data in each of the major commodity sectors, in support of Ch. 6. Data presented in this appendix are based on sentinel farm data and are taken directly from the CIPARS webinar presented in Nov 2024 (PHAC, 2024a)

Poultry: Chicken and Turkey

Broiler Chicken

Overall, AMU was stable, and Salmonella resistant to ≥3 antimicrobial classes increased.

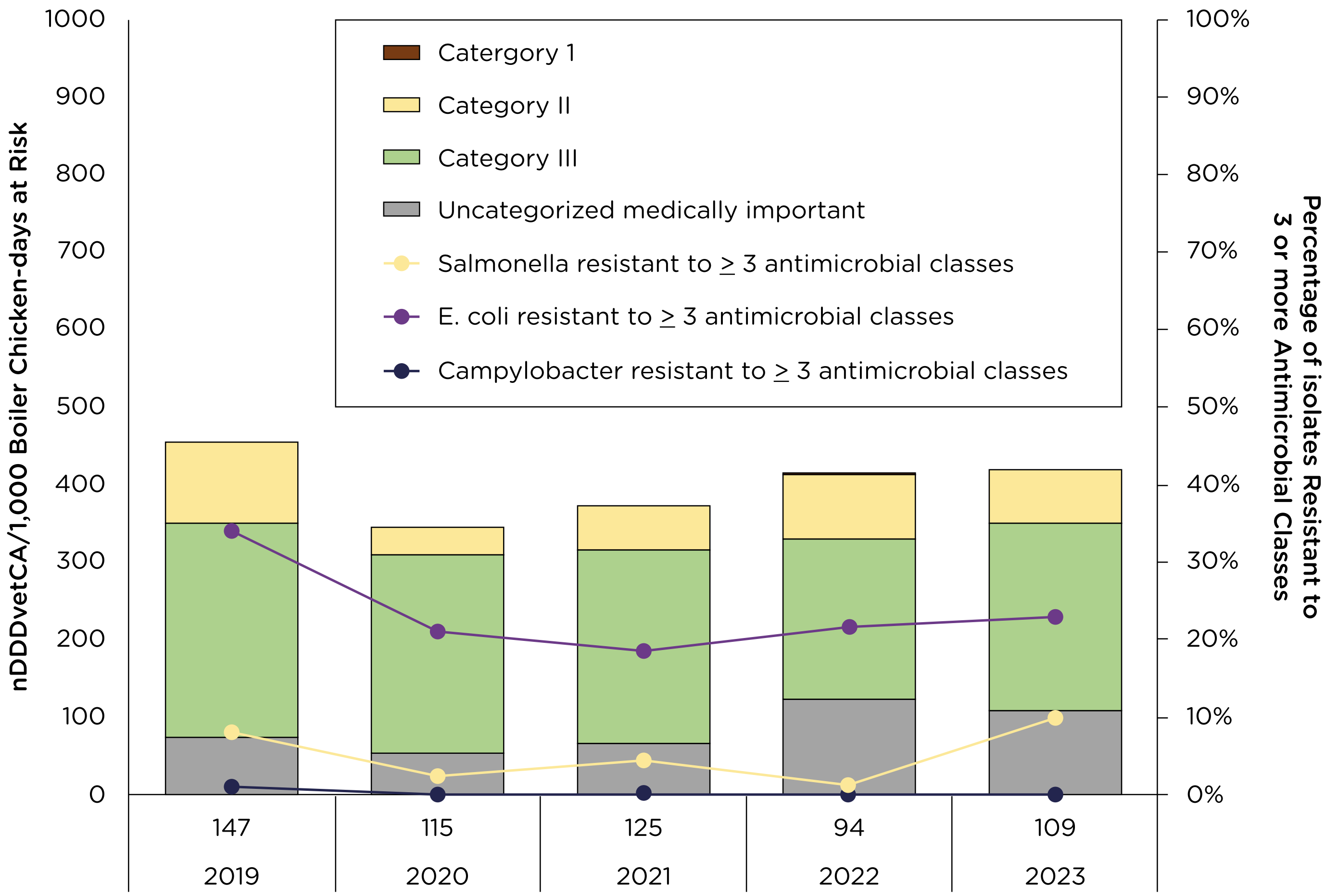


Figure 6-A. AMU and AMR in sentinel chicken flocks between 2019-2023 *(PHAC, 2024a)*

AMU. Between 2022 and 2023, the total nDDDvetCA/1,000 broiler chicken days at risk was stable (+1%). Category III use increased (+17%) while Category II (-15%) and Uncategorized antimicrobial (-12%) use decreased.

AMR. Resistant Salmonella increased (+9%), while resistance was stable among E. coli (+1%) and Campylobacter isolates

Turkey

In turkey, there were substantial increases in Category II and III antimicrobials.

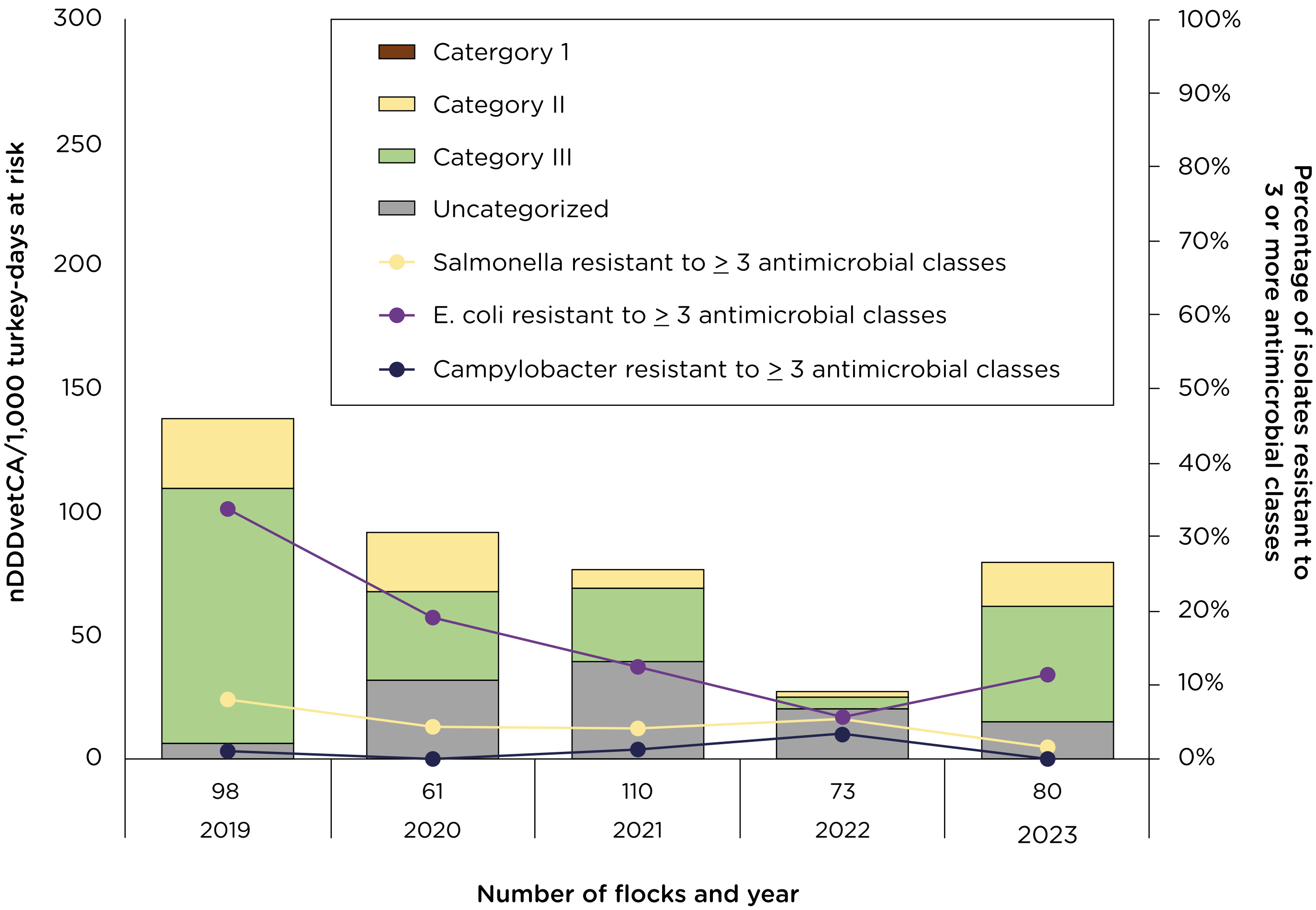


Figure 6-B. AMU and AMR in sentinel turkey flocks between 2019-2023 *(PHAC, 2024a)*

AMU. Between 2022 and 2023, the total nDDDvetCA/1,000 turkey-days at risk increased. Use of uncategorized antimicrobials decreased, while Categories II and III markedly increased. A small quantity of Category I was used (<1% of total use).

AMR. Resistance among E. coli isolates increased (+ 5%) while among Salmonella, resistance decreased (- 5%). Resistance to ≥3 antimicrobial classes was not detected among Campylobacter isolates in 2023.

Swine: Grower-Finisher Pigs

In pigs, overall AMU decreased, and resistance to ≥3 classes decreased or remained stable (Figure 6-C).

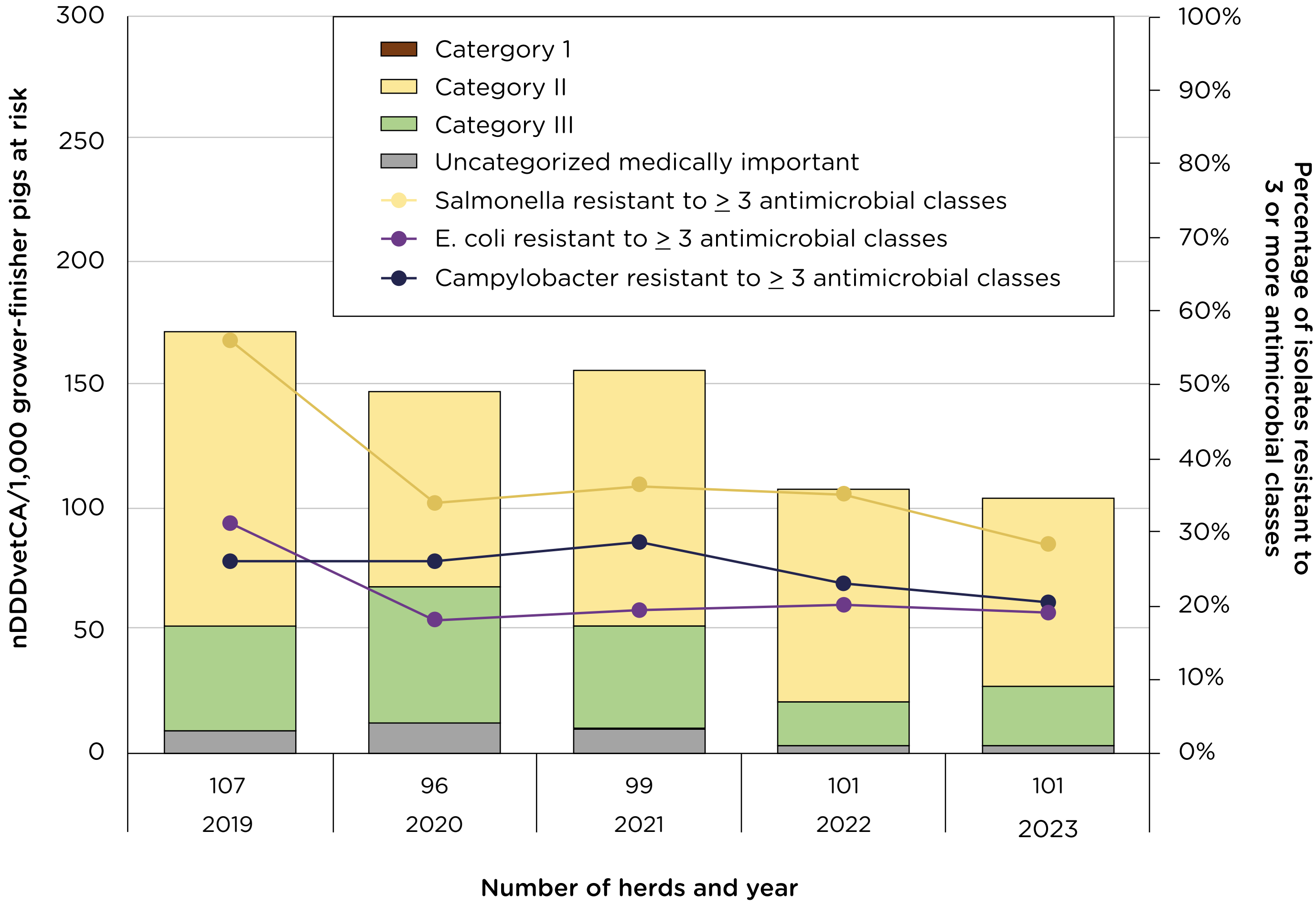


Figure 6-C. AMU and AMR in sentinel swine herds between 2019-2023 *(PHAC, 2024a)*

AMU. The quantity of AMU decreased 40% between 2019 and 2023, and 4% between 2022 and 2023.The majority of reported AMU continued to be Category II antimicrobials. Small quantities of Category I antimicrobials were used by injection each year.

AMR. In 2023, resistance decreased among Salmonella and Campylobacter isolates and remained stable among E. coli isolates.

Feedlot Cattle

Overall, AMU increased and resistance to ≥3 classes increased or remained stable.

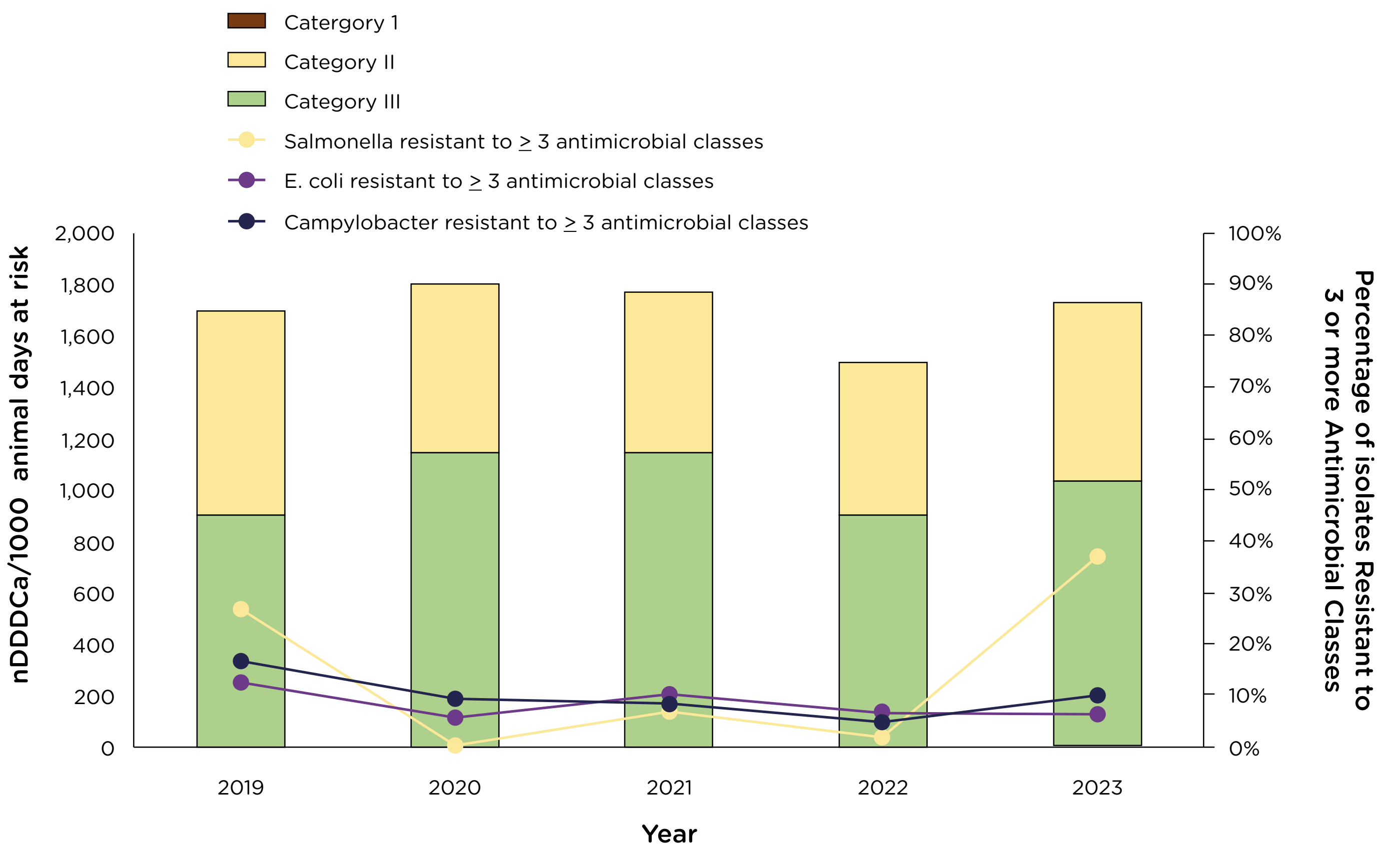


Figure 6-D. AMU and AMR in feedlot cattle between 2019-2023 *(PHAC, 2024a)*

AMU. Between 2022 and 2023, the total nDDDvetCA/1,000 cattle days at risk increased (+13%). Category III use increased (+ 13%), Category II use increased (+13%), and Category I use increased (+31%)

AMR. Between 2022 and 2023 the proportion of resistant E. coli was stable, while resistant Campylobacter increased (+5%). The proportion of resistant Salmonella was unstable due to a small number of isolates.

Dairy Cattle

Increase in Category III AMU was observed in 2021 and 2022 due to an increase in reported use of tetracyclines in both feed and water.

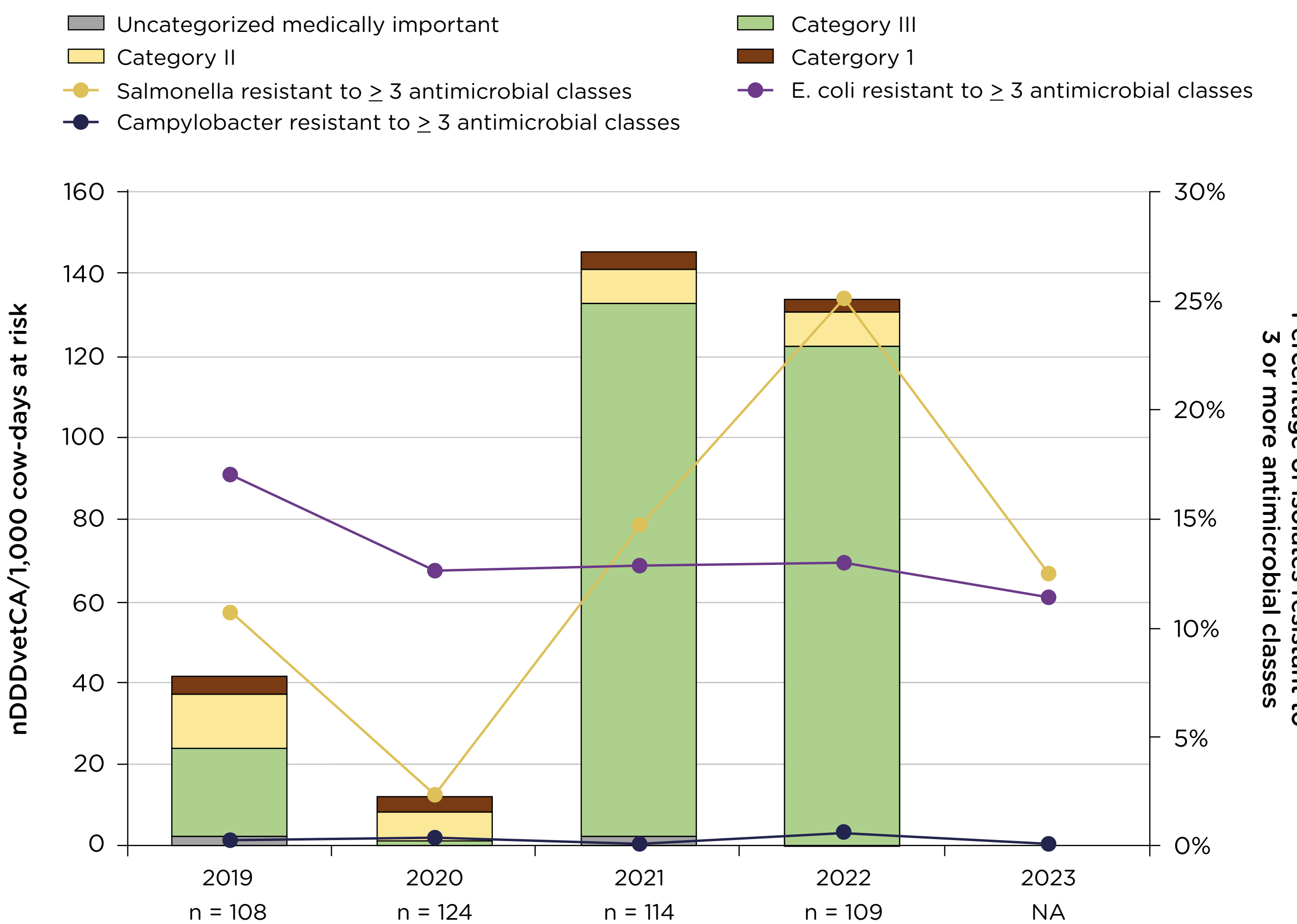


Figure 6E. AMU and AMR in dairy cattle between 2019-2023 *(PHAC, 2024a)*

AMU. An increase in Category III AMU was observed in 2021 and 2022. This was due to an increase in reported use of tetracyclines in both feed and water.

AMR. The proportion of resistant E. coli and Campylobacter isolates remains relatively low and stable. The proportion of resistant Salmonella was unstable due to the small number of isolates recovered.

Appendix 5. Alignment of Key Findings with Pan-Canadian Action Plan (PCAP) on AMR

Table 1. Alignment of key findings in the CAHS assessment of AMR/AMU in food-producing animals with the five pillars of the PCAP

Key findings	Pillars in PCAP				
	Leadership	Surveillance	Stewardship	Infection Prevention & Control	Research & Innovation
1. Antimicrobial resistant bacteria and their resistance genes in food-producing animals can transmit to humans through food-producing animal products, direct contact with food-producing animals, and the environment.		x	x	x	x
2. Development and spread of AMR in animal pathogens are important problems for animal agriculture. Antimicrobials in many commodity groups have become less effective over time because of AMR.		x			x
3. Well coordinated and integrated national AMS programs are essential to address AMR/AMU and require substantial and dedicated investment.			x		
4. Critical elements of successful governance frameworks to harmonize national efforts to reduce AMR include political (public and private sector) leadership, collaboration, coordination, regulation, integrated multi- and cross-sectoral approaches, clear delineation of responsibility for given actions, accountability, and sufficient resources to implement them.	x				
5. Government and industry regulations have been important tools for AMU reduction in Canada and worldwide, and have been most successful when based on sound science and applied in the context of collaborative engagement with commodity groups, veterinary groups, and producers.			x		

Key findings	Pillars in PCAP				
	Leadership	Surveillance	Stewardship	Infection Prevention & Control	Research & Innovation
6. An essential element to improving AMS is having evidence-informed, effective and sustainable management and biosecurity (infection prevention and control).				x	
7. Vaccines can be an important tool for disease prevention and control to be considered in addition to livestock and poultry management and biosecurity practices.				x	x
8. Alternative products could potentially reduce the need for AMU but are not replacements for antimicrobials, vaccines, good livestock and poultry management and biosecurity.				x	x
9. Validated decision tools to inform AMS protocols can be useful to refine antimicrobial usage.					x
10. The CIPARS surveillance system is and has been an asset for understanding AMR and AMU in Canada for the sectors included in the surveillance system; however, it requires sustained funding and additional resources for representativeness and additional functionalities and coverage.		x			
11. Farm-level AMU surveillance is an essential component of antimicrobial stewardship efforts.		x			
12. Interventions to reduce AMU in food-producing animals reduce AMR in animal pathogens and in surveillance indicator bacteria.	x	x			
13. Effective antimicrobial stewardship is key to avoiding or mitigating unintended consequences of AMU reduction, replacement, and refinement policies.			x		

Key findings	Pillars in PCAP				
	Leadership	Surveillance	Stewardship	Infection Prevention & Control	Research & Innovation
14. Measurement is fundamental to assessing antimicrobial stewardship in food-producing animals: If you can't measure it, you can't manage it.	x	x			
15. There is a lack of consumer knowledge and awareness about AMR/AMU in food producing animals.			x		
Please note that alignment is determined based on alignment exact wording of the **10 actions** under the PCAP. For example, Many other key findings may align with the research and innovation pillar, but they are not actioned under the PCAP.					

Table 2. Alignment of key findings (KFs) in the CAHS assessment of AMR/AMU in food-producing animals with actions identified in the PCAP

PCAP actions and respective pillars	Related KFs
Pillar 1: Research and Innovation	
Develop and implement economic and/or regulatory incentives to support innovation and facilitate sustainable access to new and existing antimicrobials, diagnostics, and alternatives to antimicrobials.	KF 7 KF 8 KF 9
Develop a One Health, national research strategy for combating AMR across all action plan pillars.	KF 1 KF 2
Pillar 2: Surveillance	
Expand sources, coverage and integration of AMR and AMU surveillance data, including the use of modern laboratory technologies and standardized reporting, to help monitor AMR/AMU across One Health sectors, with specific focus on improving data from the environment; transmission pathways between sectors; and population groups disproportionately impacted by AMR and inappropriate AMU.	KF 1 KF 2 KF 10 KF 11
Work with partners to: • establish baselines and targets for national, provincial and territorial levels of AMR and appropriate AMU in human health • establish baselines, goals and measures of progress for increasing appropriate AMU and reducing AMR in the agriculture and agri-food sectors	KF 12 KF 14

PCAP actions and respective pillars	Related KFs
Pillar 3: Stewardship	
Develop, implement and promote guidelines/standards for appropriate AMU in humans and animals through policy and regulatory initiatives, monitoring and educational interventions/accreditation requirements for health professionals and prescribers.	KF 5 KF 3 KF 13
Foster understanding of the risks of AMR and the importance of appropriate use of antimicrobials in humans and animals amongst the public, patients and producers through awareness/education campaigns, feedback mechanisms and policy and regulatory initiatives.	KF 1 KF 15
Pillar 4: Infection prevention and control	
Increase effective implementation of infection prevention measures, particularly for populations disproportionately impacted by AMR such as remote, northern and isolated communities, First Nations, Inuit and Métis populations, long-term care residents, and hospitalized patients by developing, updating and promoting uptake of guidelines/best practices for human health.	KF 1
Support the increased implementation of enhanced IPC, biosecurity, and food safety protocols across the agriculture and agri-food sectors, prioritizing sound animal husbandry, access to veterinary care, and access to additional health and nutritional aids to promote animal health.	KF 1 KF 6 KF 7 KF 8
Pillar 5: Leadership	
Build on existing One Health AMR governance structures to create a “network of networks” with inclusive representation to support action plan implementation and share progress and lessons learned within and across the 5 pillars of action, prioritizing strengthened FPT, First Nations, Inuit and Métis collaboration to co-develop AMR actions.	KF 4
Increase Canada’s contributions to global efforts to advance key bilateral and multilateral commitments by prioritizing: • generating improved data/evidence on AMR/AMU and strengthening surveillance systems and data standards • expanding efforts to support low- and middle-income countries by advancing equitable access, stewardship and IPC initiatives.	KF 12 KF 14

References

Abdallah, A., Francoz, D., Berman, J., Dufour, S., & Buczinski, S. (2022). Association Between Transfer of Passive Immunity and Health Disorders in Multisource Commingled Dairy Calves Raised for Veal or Other Purposes: Systematic Review and Meta-Analysis. *J Dairy Sci, 105*(10), 8371-8386. doi: 10.3168/jds.2021-21671

Abi Younes, J.N., Campbell, J.R., Otto, S.J.G., Gow, S.P., Woolums, A.R., Jelinski, M., Lacoste, S., & Waldner, C.L. (2024). Variation in Pen-Level Prevalence of BRD Bacterial Pathogens and Antimicrobial Resistance Following Feedlot Arrival in Beef Calves. *Antibiotics (Basel), 13*(4), 322. https://doi.org/10.3390/antibiotics13040322

Abi Younes, J.N., Campbell, J.R., Gow, S.P., Woolums, A.R., & Waldner, C.L. (2024). Association Between Respiratory Disease Pathogens in Calves Near Feedlot Arrival With Treatment for Bovine Respiratory Disease and Subsequent Antimicrobial Resistance Status. *Front Vet Sci, 11*. https://pubmed.ncbi.nlm.nih.gov/39109351/

Adam, K. E., & Bruce, A. (2023). Consumer Preferences and Attitudes towards Antibiotic Use in Food Animals. *Antibiotics*, *12*(10), 1545. https://doi.org/10.3390/antibiotics12101545

Adewusi, O.O., Waldner, C.L., Hanington, P.C., Hill, J.E., Freeman, C.N., & Otto, S.J. (2024). Laboratory Tools for the Direct Detection of Bacterial Respiratory Infections and Antimicrobial Resistance: A Scoping Review. *Journal of Veterinary Diagnostic Investigation, 36*, 400-417.

Aarestrup, F.M., Oliver Duran, C., & Burch, D.G.S. (2008). Antimicrobial Resistance in Swine Production. *Animal Health Research Reviews, 9*(2), 135-148. doi:10.1017/S1466252308001503

Aarestrup, F.M., Seyfarth, A.M., Emborg, H.D., Pedersen, K., Hendriksen, R.S., & Bager, F. (2001). Effect of Abolishment of the Use of Antimicrobial Agents for Growth Promotion on Occurrence of Antimicrobial Resistance in *Fecal Enterococci* from Food Animals in Denmark. *Antimicrob Agents Chemother, 45*(7), 2054–9.

Afifi, M., Stryhn, H., Sanchez, J., Heider, L.C., Kabera, F., Roy, J.P., Godden, S., & Dufour, S. (2023). To Seal or not to Seal Following an Antimicrobial Infusion at Dry-Off? A Systematic Review and Multivariate Meta-Analysis of the Incidence and Prevalence of Intramammary Infections Post-Calving in Dairy Cows. *Prev Vet Med, 213*, 105864. doi: 10.1016/j.prevetmed.2023.105864

Agersø, Y., & Aarestrup, F.M. (2013). Voluntary Ban on Cephalosporin use in Danish Pig Production has Effectively Reduced Extended-Spectrum *Cephalosporinase-Producing Escherichia Coli* in Slaughter Pigs. *J Antimicrob Chemother, 68,* 569.

Agriculture and Agri-Food Canada. (2024).*Overview of Canada's agriculture and agri-food sector.* https://agriculture.canada.ca/en/sector/overview

Agriculture and Agri-Food Canada. (2021). *Red meat and livestock slaughter and carcass weights.* https://agriculture.canada.ca/en/sector/animal-industry/red-meat-and-livestock-market-information/slaughter-and-carcass-weights

Agunos, A., Léger, D., & Carson, C. (2012). Review of antimicrobial therapy of selected bacterial diseases in broiler chickens in Canada. *Can Vet J, 53*(12), 1289-1300. https://pmc.ncbi.nlm.nih.gov/articles/PMC3500121/

Alarcón, L.V., Allepuz, A., & Mateu, E. (2021). Biosecurity in pig farms: A review. *Porc Health Manag, 7*(5). https://doi.org/10.1186/s40813-020-00181-z

Alawneh, J.I., Barreto, M.O., Moore, R.J., Soust, M., Al-harbi, H., James, A.S., Krishnan, D., & Olchowy, T.W.J. (2020). Systematic review of an intervention: The use of probiotics to improve health and productivity of calves. *Prev Vet Med, 183,* 105147. https://doi.org/10.1016/j.prevetmed.2020.105147

Alliance to Save our Antibiotics. (2020). *New European Union rules on farm antibiotic use*. https://www.saveourantibiotics.org/media/1842/2022-changes-to-european-law-farm-antibiotics.pdf

Aly, S.M. & Fathi, M. (2024). Advancing aquaculture biosecurity: A scientometric analysis and future outlook for disease prevention and environmental sustainability. *Aquac Int, 32*, 8763-8789. https://doi.org/10.1007/s10499-024-01589-y

Amalraj, A., Van Meirhaeghe, H., Lefort, A. C., Rousset, N., Grillet, J., Spaans, A., Devesa, A., Sevilla-Navarro, S., Tilli, G., Piccirillo, A., Żbikowski, A., Kovács, L., Kovács-Weber, M., Chantziaras, I., & Dewulf, J. (2024). Factors affecting poultry producers' attitudes towards biosecurity. *Animals, 14*(11), 1603. https://doi.org/10.3390/ani14111603

American Feed Industry Association. (2019). *Developing biosecurity practices for feed & ingredient manufacturing.* https://www.afia.org/pub/?id=E348BF9F-98ED-09DB-A45D-504737FE7AE2

Andres, V.M., & Davies, R.H. (2015). Biosecurity measures to control *Salmonella* and other infectious agents in pig farms: A review. *Comprehensive Reviews in Food Science and Food Safety, 14,* 317-335. https://doi.org/10.1111/1541-4337.12137

Andrés-Lasheras, S., Ha, R., Zaheer, R., Lee, C., Booker, C.W., Dorin, C., Van Donkersgoed, J., Beardon, R., Gow, S., Hannon, S.J., Hendrick, S., Anholt, M., & McAllister, T.A. (2021). Prevalence and risk factors associated with antimicrobial resistance in bacteria related to Bovine Respiratory Disease—A broad cross-sectional study of beef cattle at entry into Canadian feedlots. *Front Vet Sci, 8.* https://doi.org/10.3389/fvets.2021.692646

Andrés-Lasheras, S., Jelinski, M., Zaheer, R., & McAllister, T.A. (2022). Bovine Respiratory Disease: Conventional to culture-independent approaches to studying antimicrobial resistance in North America. *Antibiotics, 11*(4), 487. https://doi.org/10.3390/antibiotics11040487

Anedda, E., Farrell, M.L., Morris, D., & Burgess, C.M. (2023). Evaluating the impact of heavy metals on antimicrobial resistance in the primary food production environment: A scoping review. *Environmental Pollution, 320,* 121035. https://doi.org/10.1016/j.envpol.2023.121035.

Animal Industries' Antimicrobial Stewardship RD&E Strategy. (2021). *Antimicrobial stewardship in Australian livestock industries.* https://animalhealthaustralia.com.au//wp-content/uploads/dlm_uploads/2018/11/Antimicrobial-stewardship-in-Livestock-Report-2021-.pdf

Animal Nutrition Association of Canada. (2024). *Feed industry antimicrobial stewardship.* https://www.anacan.org/feed-industry/public-resources/antimicrobial-stewardship/

Aranda-Aguirre, E., Robles-Jimenez, L.E., Osorio-Avalos, J., Vargas-Bello-Pérez, E., & Gonzalez-Ronquillo, M. (2021). A systematic-review on the role of exogenous enzymes on the productive performance at weaning, growing and finishing in pigs. *Vet Anim Sci, 14,* 100195. https://www.sciencedirect.com/science/article/pii/S2451943X21000314?via%3Dihub

Autoriteit Diergeneesmidelen. (2024). *Usage of antibiotics in agricultural livestock in the Netherlands in 2023*. Netherlands Veterinary Medicines Institute. https://cdn.i-pulse.nl/autoriteitdiergeneesmiddelen/userfiles/sda%20jaarrapporten%20ab-gebruik/AB-rapport%202023/sda-rapport-incl.-cover-letter---usage-of-antibiotics-livestock-in-the-netherlands-in-2023-def.pdf

Ayrle, H., Mevissen, H., Kaske, M., Nathues, H., Gruetzner, N., Melzig, M. & Walkenhorst, M. (2016). Medicinal plants – Prophylactic and therapeutic options for gastrointestinal and respiratory diseases in calves and piglets? A systematic review. *BMC Vet Res, 12.* https://doi.org/10.1186/s12917-016-0714-8

Barlow, J. (2011). Antimicrobial resistance and the use of antibiotics in the dairy industry: Facing consumer perceptions and producer realities. In L. Doepel (Ed.), *WCDS Advances in Dairy Technology*, *23*, 47-58. https://wcds.ualberta.ca/wcds/wp-content/uploads/sites/57/wcds_archive/Archive/2011/Manuscripts/Barlow.pdf

Barrett, J. R., Innes, G. K., Johnson, K. A., Lhermie, G., Ivanek, R., Safi, A. G., & Lansing, D. (2021). Consumer perceptions of antimicrobial use in animal husbandry: A scoping review. *PloS One*, *16*(12), 0261010. https://doi.org/10.1371/journal.pone.0261010

Becker, J., Schüpbach-Regula, G., Steiner, A., Perreten, V., Wüthrich, D., Hausherr, A., & Meylan, M. (2020). Effects of the novel concept 'outdoor veal calf' on antimicrobial use, mortality and weight gain in Switzerland. *Preventive Veterinary Medicine, 176,* 104907. https://www.sciencedirect.com/science/article/pii/S0167587719304246

Beef Cattle Research Council. (2016a). *Antimicrobial use and resistance in Canadian beef production.* Fact Sheet. https://www.beefresearch.ca/files/pdf/BCRC_Fact_Sheet_Antimicrobial_Use_and_Resistance_in_Beef_Production.pdf

Beef Cattle Research Council. (2016b). *National beef antimicrobial research strategy.* https://www.beefresearch.ca/files/pdf/National_Beef_Antimicrobial_Research_Strategy.pdf

Beef Cattle Research Council. (2019a). *Antibiotic resistance.* https://www.beefresearch.ca/topics/antibiotic-resistance/

Beef Cattle Research Council. (2019b). *On-farm antimicrobial surveillance moves a step closer.* https://www.beefresearch.ca/blog/on-farm-antimicrobial-surveillance-moves-a-step-closer/

Beef Cattle Research Council. (2021). *Five-year Canadian beef research & technology transfer strategy.* Five_Year_Canadian_Beef_Research_and_Technology_Transfer_Strategy_July_2021_web-1.pdf

Beker, M., Rose, S., Lykkebo, C.A., & Douthwaite, S. (2018). Integrative and conjugative elements (ICEs) in *Pasteurellaceae* species and their detection by multiplex PCR. *Front Microbiol*, *9,*1329. https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2018.01329/full

Belcher, K. W., Germann, A. E., & Schmutz, J. K. (2007). Beef with environmental and quality attributes: Preferences of environmental group and general population consumers in Saskatchewan, Canada. *Agriculture and Human Values, 24*(3), 333–342. https://doi.org/10.1007/s10460-007-9069-x

Belay, D.G., & Jensen J.D. (2022). Quantitative input restriction and farmer's economic performance: Evidence from Denmark's yellow card Initiative on antibiotics. *Journal of Agricultural Economics, 73*(1), 155-171 https://ideas.repec.org/a/bla/jageco/v73y2022i1p155-171.html

Bengtsson-Palme, J., Abramova, A., Berendonk, T. U., Coelho, L. P., Forslund, S. K., Gschwind, R., Heikinheimo, A., Jarquín-Díaz, V. H., Khan, A. A., Klümper, U., Löber, U., Nekoro, M., Osińska, A. D., Ugarcina Perovic, S., Pitkänen, T., Rødland, E. K., Ruppé, E., Wasteson, Y., Wester, A. L., & Zahra, R. (2023). Towards monitoring of antimicrobial resistance in the environment: For what reasons, how to implement it, and what are the data needs?. *Environment international*, *178*, 108089. https://doi.org/10.1016/j.envint.2023.108089

Best Practice Advocacy Centre New Zealand. (n.d.). *The appropriate use of macrolides*. https://bpac.org.nz/bpj/2012/may/macrolides.aspx

Biosecure. (2023). *Enhancing biosecurity in livestock*. https://biosecure.eu

Blankenship, K.M., Bray, S.J., & Merson, M.H. (2000). Structural interventions in public health. *AIDS, 14*(1), 11-21. https://journals.lww.com/aidsonline/abstract/2000/06001/structural_interventions_in_public_health.3.aspx

Boerlin, P., Wissing, A., Aarestrup, F.M., Frey, J., & Nicolet, J. (2001). Antimicrobial growth promoter ban and resistance to Macrolides and Vancomycin in *Enterococci* from pigs. *J Clin Microbiol, 39*(11), 4193-5. https://journals.asm.org/doi/10.1128/jcm.39.11.4193-4195.2001

Boeters, M., Garcia-Morante, B., van Schaik, G., Segalés, J., Rushton, J., & Steeneveld, W. (2023). The economic impact of Endemic Respiratory Disease in pigs and related interventions - A systematic review. *Porcine health management*, *9*(1), 45. https://doi.org/10.1186/s40813-023-00342-w

Bondad-Reantaso, M.G., MacKinnon, B., Karunasagar, I., Fridman, S., Alday-Sanz, V., Brun, E., Le Groumellec, M., Li, A., Surachetpong, W., Karunasagar, I. and Hao, B. (2023). Review of alternatives to antibiotic use in aquaculture. *Reviews in Aquaculture, 15*, 1421-1451. https://doi.org/10.1111/raq.12786

Booker, C.W. (2021). Bovine Respiratory Disease treatment failure: Definition and impact. *Animal Health Research Reviews, 21*(2), 172-174. https://www.cambridge.org/core/journals/animal-health-research-reviews/article/abs/bovine-respiratory-disease-treatment-failure-definition-and-impact/ECB76DDED1A15F4676322E6E9C4BEB7F

Booker, C.W., & Lubbers, B.V. (2020). Bovine Respiratory Disease treatment failure: Impact and potential causes. *Vet Clin North Am Food Anim Pract, 36*(2), 487-496. https://pubmed.ncbi.nlm.nih.gov/32451037/

Bosman, A.L., Uhland, F., Agunos, A., & Carson, C.A. (2024). One Health surveillance of antimicrobial resistance and use by the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). *Can Vet J, 65*(10), 1081-1085. https://pmc.ncbi.nlm.nih.gov/articles/PMC11411476

Bourdonnais, E., Le Bris, C., Brauge, T., & Midelet, G. (2024). Tracking antibiotic resistance indicator genes in wild flatfish from the English Channel and the North Sea area: A One Health concern. *Environmental Pollution, 343,* 123274. https://doi.org/10.1016/j.envpol.2023.123274

Bourne, J. E., Ginis, K. A. M., Buchholz, A. C., & Jung, M. E. (2018). Strategies for public health initiatives targeting dairy consumption in young children: A qualitative formative investigation of parent perceptions. *Maternal and Child Nutrition, 14*(2). https://doi.org/10.1111/mcn.12587

Brault, S.A., Hannon, S.J., Gow, S.P., Warr, B.N., Withell, J., Song, J., Williams, C.M., Otto, S.J.G., Booker, C.W., & Morley, P.S. (2019). Antimicrobial use on 36 beef feedlots in Western Canada: 2008-2012. *Front Vet Sci, 6,* 329. https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2019.00329/full

British Columbia Society for the Prevention of Cruelty to Animals (BC SPCA). (2024a). *Policy platform, 2024 British Columbia provincial election. https://spca.bc.ca/wp-content/uploads/2024/05/BC-SPCA_2024-Provincial-Platform-Recommendations.pdf*

British Columbia Society for the Prevention of Cruelty to Animals (BC SPCA). (2024b, March 27). *Recommendations to improve the welfare and protections of farmed animals in B.C. presented to the Ministry of Agriculture and Food*. https://spca.bc.ca/news/fawac-recommendations/

Bueno, I., J. Williams-Nguyen, H. Hwang, J.M. Sargeant, A.J. Nault, and R.S. Singer. (2017). Impact of point sources on antibiotic resistance genes in the natural environment: A systematic review of the evidence. *Animal health research reviews*, *18*, 112-127. https://www.cambridge.org/core/journals/animal-health-research-reviews/article/impact-of-point-sources-on-antibiotic-resistance-genes-in-the-natural-environment-a-systematic-review-of-the-evidence/9291877383591315C22B65608B373642

Bueno, I., J. Williams-Nguyen, H. Hwang, J.M. Sargeant, A.J. Nault, and R.S. Singer. (2018). Systematic review: Impact of point sources on antibiotic-resistant bacteria in the natural environment. *Zoonoses and public health*, *65*(1), 162-184. https://onlinelibrary.wiley.com/doi/10.1111/zph.12426

Buller, H., Adam, K., Bard, A., Bruce, A., Ray Chan, K.W., Hinchliffe, S., Morgans, L., Rees, G., & Reyher, K.K. (2020). Veterinary diagnostic practice and the use of rapid tests in antimicrobial stewardship on UK livestock farms. *Front Vet Sci, 7,* 569545. https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2020.569545/full

Burmeister, A.R. (2015). Horizontal gene transfer. *Evolution, Medicine, and Public Health,* 193-194. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4536854/

Burns, M.J., & O'Connor, A.M. (2008). Assessment of methodological quality and sources of variation in the magnitude of vaccine efficacy: A systematic review of studies from 1960 to 2005 reporting immunization with *Moraxella Bovis* vaccines in young cattle. *Vaccine, 26*(2), 144-52. https://www.sciencedirect.com/science/article/abs/pii/S0264410X07011590?via%3Dihub

Cai, H.Y., McDowall, R., Parker, L., Kaufman, E.I., & Caswell, J.L. (2019). Changes in antimicrobial susceptibility profiles of *Mycoplasma bovis* over time. *Can J Vet Res*, *83*(1), 34-41. https://pmc.ncbi.nlm.nih.gov/articles/PMC6318825/

Canada Pork. (2025). *On-farm food safety & quality assurance.* https://canadapork.com/canadian-advantage/the-canadian-pork-commitment/on-farm-food-safety-quality-assurance/

Canadian Animal Health Institute. (2014, April 11). *Canadian Animal Health Institute (CAHI) member companies agree to phase-out uses of medically important antibiotics for growth promotion and support increased veterinary oversight of medically important antibiotics used in animal feed and water.* https://cahi-icsa.ca/wp-content/uploads/2024/04/cahi_press_release_veterinary_antimicrobials_april_11.pdf

Canadian Animal Health Institute. (2024). *Veterinary shortage.* https://cahi-icsa.ca/animal-health-issue/veterinary-shortage

Canadian Animal Health Surveillance System. (n.d.). *Cross-Canada surveillance snapshot: Antimicrobial resistance and antimicrobial use surveillance.* https://cahss.ca/CAHSS/Assets/Documents/AMR%20Surveillance%20Snapshot%20NEW.pdf

Canadian Animal Health Surveillance System. (2023, November 20). *Bovine Respiratory Disease (BRD) pathogen antimicrobial resistance (AMR) update 2022*. https://cahss.ca/cahss-tools/document-library/Bovine-Respiratory-Disease-BRD-Pathogen-Antimicrobial-Resistance-AMR-Update-2022

Canadian Aquaculture Industry Alliance. (2023). *Food quality & safety.* https://aquaculture.ca/food-quality-and-safety

Canadian Aquaculture Industry Alliance. (2024). *Advocacy*. https://nationalsheepnetwork.com/advocacy-english-1

Canadian Broadcasting Corporation (CBC). (2011, February 10). *Supermarket chicken harbours superbugs: CBC.* https://www.cbc.ca/news/supermarket-chicken-harbours-superbugs-cbc-1.1039548

Canadian Cattle Association. (2024). *Health management.* https://www.cattle.ca/resources/producer-resources/animal-care/health-management

Canadian Cattle Feeders' Association. (2015, April 29). *Canadian cattle feeders committed to prudent use of antimicrobials.* https://nationalcattlefeeders.ca/canadian-cattle-feeders-committed-to-prudent-use-of-antimicrobials/

Canadian Council of Chief Veterinary Officers (CCVO) Antimicrobial Use in Animal Agriculture Committee. (2016). *Non-human antimicrobial use surveillance in Canada: Surveillance objectives and options.* https://cahss.ca/cahss-tools/document-library/Non-human-antimicrobial-use-surveillance-in-Canada-Surveillance-Objectives-and-Options

Canadian Feedlot AMU/AMR Surveillance Program (CFAASP). (n.d.). *Home.* https://cfaasp.ca

Canadian Feedlot AMU/AMR Surveillance Program. (2023). *AMU AMR surveillance feedlot cattle in Canada.* https://cfaasp.ca/resources/cfaasp-resources/amu-amr-surveillance-feedlot-cattle-in-canada

Canadian Food Inspection Agency. (2017). *Fact sheet on antimicrobial resistance.* https://inspection.canada.ca/en/science-and-research/our-research-and-publications/science-fact-sheet-antimicrobial-resistance

Canadian Food Inspection Agency. (2022). *VICH-The international cooperation on harmonization of technical requirements for the registration of veterinary medicinal products.* https://inspection.canada.ca/en/animal-health/veterinary-biologics/guidelines-forms/vich

Canadian Food Inspection Agency. (2023a). *VB-GL-3.13: Autogenous veterinary biologics.* https://inspection.canada.ca/en/animal-health/veterinary-biologics/guidelines-forms/3-13e

Canadian Food Inspection Agency. (2023b). *Antimicrobial resistance: What we are doing.* https://inspection.canada.ca/en/animal-health/antimicrobial-resistance/what-we-are-doing

Canadian Hatching Egg Producers. (2024). *Animal care program*. https://chep-poic.ca/animal-care-program/

Canadian Pork Council. (2024). *Vaccine and drug use policy.* https://www.cpc-ccp.com/drug-use-policy

Canadian Sheep Federation. (2024). *Animal owner FAAST sheets.* https://www.cansheep.ca/resources

Canadian Veterinary Medical Association. (2024a). *Antimicrobial stewardship resources.* https://www.canadianveterinarians.net/veterinary-resources/antimicrobial-stewardship-resources/

Canadian Veterinary Medical Association. (2024b). *Veterinary oversight of antimicrobial use: A pan-Canadian framework of professional standards for veterinarians.* https://www.canadianveterinarians.net/media/kdgn4tex/pan-canadian-framework.pdf

Canali, M., Aragrande, M., & Beber, C.L.. (2024) The 2030 veterinary antimicrobial sales reduction target in Europe: Where are we? *EuroChoices.* https://www.researchgate.net/publication/384760906_The_2030_Veterinary_Antimicrobial_Sales_Reduction_Target_in_Europe_Where_Are_We

Caneschi, A., Bardhi, A., Barbarossa, A., & Zaghini, A. (2023). The use of antibiotics and antimicrobial resistance in veterinary medicine, a complex phenomenon: A narrative review. *Antibiotics (Basel, Switzerland), 12*(3), 487. https://doi.org/10.3390/antibiotics12030487

Capik, S.F., Moberly, H.K., & Larson, R.L. (2021). Systematic review of vaccine efficacy against *Mannheimia Haemolytica, Pasteurella Multocida*, and *Histophilus Somni* in North American cattle. *The Bovine Practitioner, 55*(2), 125-33. https://ksubci.org/wp-content/uploads/2024/03/Bov-Pract_55_2021_Systematic-review-vax_Capik.pdf

Carson, C., Li, X-Z., Agunos, A., Loest, D., Chapman, B., Finley, R., Mehrotra, M., Sherk, L.M., Gaumond, R., & Irwin, R. (2019). *Ceftiofur-resistant Salmonella Enterica Serovar Heidelberg* of poultry origin- A risk profile using the Codex framework. *Epidemiol Infect, 147*, 296. https://www.cambridge.org/core/journals/epidemiology-and-infection/article/ceftiofurresistant-salmonella-enterica-serovar-heidelberg-of-poultry-origin-a-risk-profile-using-the-codex-framework/D1FDDDF4DBDF04238D7AF3CC3AED4237

Castelo Taboada, A.C., & Pavic, A. (2022). Vaccinating meat chickens against *Campylobacter* and *Salmonella*: A systematic review and meta-analysis. *Vaccines, 10*, 1936. https://doi.org/10.3390/vaccines10111936

Ceric, O., Tyson, G.H., Goodman, L.B., Mitchell, P.K., Zhang, Y., Prarat, M., Cui, J., Peak, L., Scaria, J., Antony, L., Thomas, M., Nemser, S.M., Anderson, R., Thachil, A.J., Franklin-Guild, R.J., Slavic, D., Bommineni, Y.R., Mohan, S., Sanchez, S.,...Reimschuessel, R. (2019). Enhancing the One Health initiative by using whole genome sequencing to monitor antimicrobial resistance of animal pathogens: Vet-LIRN collaborative project with veterinary diagnostic laboratories in the United States and Canada. *BMC Veterinary Research*, *15*(1), 130. https://doi.org/10.1186/s12917-019-1864-2

CgFARAD. (2023). *CgFARAD™ protecting animals and our food supply.* https://www.chickenfarmers.ca/wp-content/uploads/2023/05/CgFARAD-Newsletter-Spring-2023.pdf

Chakraborty, S., Dhama, K., Tiwari, R., Iqbal Yatoo, M., Khurana, S.K., Khandia, R., Munjal, A., Munuswamy, P., Kumar, M.A., Singh, M., Singh, R., Gupta, V.K., & Chaicumpa, W. (2019). Technological interventions and advances in the diagnosis of intramammary infections in animals with emphasis on bovine population-A review. *Vet Q, 39*(1), 76-94. https://www.tandfonline.com/doi/full/10.1080/01652176.2019.1642546

Chatterjee, A., Modarai, M., Naylor, N. R., Boyd, S. E., Atun, R., Barlow, J., Holmes, A. H., Johnson, A., & Robotham, J. V. (2018). Quantifying drivers of antibiotic resistance in humans: A systematic review. *The Lancet Infectious diseases*, *18*(12), 368–378. https://doi.org/10.1016/S1473-3099(18)30296-2

Chen, C., & Wu, F. (2021). Livestock-associated *methicillin-resistant Staphylococcus Aureus (LA-MRSA)* colonisation and infection among livestock workers and veterinarians: A systematic review and meta-analysis. *Occupational and Environmental Medicine*, *78*(7), 530-540. https://doi.org/10.1136/oemed-2020-106418

Chen, S-Y., Bernardino, P.N., Fausak, E., Van Noord, M. & Maier, G. (2022). Scoping review on risk factors and methods for the prevention of Bovine Respiratory Disease applicable to cow–calf operations. *Animals, 12*(3), 334. https://doi.org/10.3390/ani12030334

Chicken Farmers of Canada. (n.d.). *Standing committee on health.* https://www.ourcommons.ca/Content/Committee/421/HESA/Brief/BR10594145/br-external/ChickenFarmersOfCanada-e.pdf

Chicken Farmers of Canada. (2021). *On-farm food safety program manual.* https://www.producteursdepoulet.ca/wp-content/uploads//2021/10/Raised-by-a-Canadian-Farmer-OFFSP-Manual-2021.pdf

Chicken Farmers of Canada. (2024a). *Canadian chicken industry further reducing antimicrobial use.* https://www.chickenfarmers.ca/media-room/canadian-chicken-industry-further-reducing-antimicrobial-use/

Chicken Farmers of Canada. (2024b). *Responsible antimicrobial use strategy*. https://www.chickenfarmers.ca/antibiotics/

Chicken Farmers of Canada. (2024c). *What is CgFARAD and why it matters.* https://www.chickenfarmers.ca/wp-content/uploads/2024/04/What-is-CgFARAD-spring-2024.pdf

Chicken Farmers of Canada. (2025). *How are you enforcing your antimicrobial usage policy?* https://www.chickenfarmers.ca/faq/how-are-you-enforcing-your-antimicrobial-usage-policy/

Cobo-Angel, C., Leblanc, S.J., Roche, S.M., & Ritter, C. (2021). A focus group study of Canadian dairy farmers' attitude and social referents on antimicrobial use and antimicrobial resistance. *Front Vet Sci, 8.* https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2021.645221/full

College of Veterinarians of Ontario. (2024). *Standards and the role of the regulator.* https://www.cvo.org/getmedia/9f5bb33b-09d3-4b08-a17e-823825a9d2a0/Standards-and-the-Role-of-the-Regulator.pdf

Collineau, L., Chapman, B., Bao, X., Sivapathasundaram, B., Carson, C. A., Fazil, A., Reid-Smith, R. J., & Smith, B. A. (2020). A farm-to-fork quantitative risk assessment model for *Salmonella Heidelberg* resistant to third-generation *cephalosporins* in broiler chickens in Canada. *International Journal of Food Microbiology*, *330*, 108559. https://doi.org/10.1016/j.ijfoodmicro.2020.108559

Commonwealth of Australia. (2023). *Australia's animal sector antimicrobial resistance: Action plan 2023-2028*. Department of Agriculture, Fisheries and Forestry. https://www.agriculture.gov.au/sites/default/files/documents/australias-animal-sector-amr-action-plan-2023-2028.pdf

Cooke, R.F. (2017). Nutritional and management considerations for beef cattle experiencing stress-induced inflammation. *Applied Animal Science, 33*(1), 1-11. https://doi.org/10.15232/pas.2016-01573

Costa, M. M., Cardo, M., Ruano, Z., Alho, A. M., Dinis-Teixeira, J., Aguiar, P., & Leite, A. (2023). Effectiveness of antimicrobial interventions directed at tackling antimicrobial resistance in animal production: A systematic review and meta-analysis. *Preventive Veterinary Medicine*, 106002. https://doi.org/10.1016/j.prevetmed.2023.106002

Council of Canadian Academies. (2019). *When antibiotics fail.* https://www.cca-reports.ca/wp-content/uploads/2023/05/Updated-AMR-report_EN.pdf

Cusack, P. (2024). Alternatives to conventional antibiotics for the prevention and treatment of commonly occurring diseases in feedlot cattle. *Aust Vet J, 102*(5), 229-241. https://doi.org/10.1111/avj.13314

Dairy Farmers of Canada. (n.d.-a). *ProAction: About. https://www.dairyfarmers.ca/proaction*

Dairy Farmers of Canada. (n.d.-b). *ProAction: How it works.* https://www.dairyfarmers.ca/proaction/how-it-works/food-safety#:~:text=Ensuring%20the%20Safe%20Use%20of%20Antibiotics&text=Farmers%20work%20closely%20with%20veterinarians,on%2Dfarm%20in%20permanent%20records

Dairy Farmers of Canada. (2020). *How and when we use antibiotics to treat cows.* https://dairyfarmersofcanada.ca/en/our-commitments/animal-care/treat-cows-antibiotics

Dairy Farmers of Canada. (2024). *Animal health, biosecurity and antimicrobial stewardship.* https://dairyfarmersofcanada.ca/en/dairy-research/research-projects/animal-health-biosecurity-and-antimicrobial-stewardship

da Silva, N., Carriquiry, A., O'Neill, K., Opriessnig, T., & O'Connor, A.M. (2014). Mixed treatment comparison meta-analysis of *Porcine Circovirus Type 2 (PCV2)* vaccines used in piglets. *Prev Vet Med, 117*, 413-424. https://doi.org/10.1016/j.prevetmed.2014.10.006

Davedow, T., Narvaez-Bravo, C., Zaheer, R., Sanderson, H., Rodas-Gonzalez, A., Klima, C., Booker, C. W., Hannon, S. J., Bras, A. L., Gow, S., & McAllister, T. (2020). Investigation of a reduction in *Tylosin* on the prevalence of liver abscesses and antimicrobial resistance in *Enterococci* in feedlot cattle. *Frontiers in veterinary science*, *7*, 90. https://doi.org/10.3389/fvets.2020.00090

Dec, M., Wernicki, A., & Urban-Chmiel, R. (2020). Efficacy of experimental phage therapies in livestock. *Anim Health Res Rev, 21*(1), 69-83. https://www.cambridge.org/core/journals/animal-health-research-reviews/article/efficacy-of-experimental-phage-therapies-in-livestock/4E894D15E6701C95CFCC911C3DA9C193

De Greeff, S. C., Kolwijck, E., Schoffelen, A., & Verduin, C. (2022). NethMap 2022. Consumption of antimicrobial agents and antimicrobial resistance among medically important bacteria in the Netherlands in 2021 / MARAN 2022. Monitoring of antimicrobial resistance and antibiotic usage in animals in the Netherlands in 2021. *National Institute for Public Health and the Environment, Ministry of Health, Welfare and Sport.* https://rivm.openrepository.com/handle/10029/625885

de Jong, E., Creytens, L., De Vliegher, S., McCubbin, K.D., Baptiste, M., Leung, A.A., Speksnijder, D., Dufour, S., Middleton, J.R., Ruegg, P.L., Lam, T.J.G.M., Kelton, D.F., McDougall, S., Godden, S.M., Lago, A., Rajala-Schultz, P.J., Orsel, K., Krömker, V., Kastelic, J.P., & Barkema, H.W. (2023). Selective treatment of nonsevere Clinical Mastitis does not adversely affect cure, somatic cell count, milk yield, recurrence, or culling: A systematic review and meta-analysis. *J Dairy Sci, 106*(2), 1267-1286. https://doi.org/10.3168/jds.2022-22271

de Jong, E., McCubbin, K.D., Speksnijder, D., Dufour, S., Middleton, J.R., Ruegg, P.L., Lam, T.J.G.M., Kelton, D.F., McDougall, S., Godden, S.M., Lago, A., Rajala-Schultz, P.J., Orsel, K., De Vliegher, S., Krömker, V., Nobrega, D.B., Kastelic, J.P., & Barkema, H.W. (2023). Invited review: selective treatment of Clinical Mastitis in dairy cattle. *J Dairy Sci, 106*(6), 3761-3778. https://doi.org/10.3168/jds.2022-22826

de Jongh, E. (2024). Antimicrobial stewardship in British Columbia farmed finfish: Linking antimicrobial use and resistance in the context of yellow mouth disease. [Master's thesis]. University of Alberta. https://era.library.ualberta.ca/items/3288fa79-e211-4fc9-9312-1156a26fba0a/view/252c0592-f615-4f4b-84e2-86bfddba41f9/de_Jongh_Etienne_J_202409_MSc.pdf

Delabbio, J.L., Johnson, G.R., Murphy, B.R., Hallerman, E., Woart, A., & McMullin, S.L. (2005). Fish disease and biosecurity: Attitudes, beliefs, and perceptions of managers and owners of commercial finfish recirculating facilities in the United States and Canada. *Journal of Aquatic Animal Health, 17*(2), 153-159 https://doi.org/10.1577/H04-005.1

de la Cruz, M. L., Conrado, I., Nault, A., Perez, A., Dominguez, L., & Alvarez, J. (2017). Vaccination as a control strategy against *Salmonella* infection in pigs: A systematic review and meta-analysis of the literature. *Research in Veterinary Science*, *114*, 86-94. https://doi.org/10.1016/j.rvsc.2017.03.005

de Lagarde, M., Fairbrother, J.M., Archambault, M., Dufour, S., Francoz, D., Massé, J., Lardé, H., Aenishaenslin, C., Paradis, M.-È., & Roy, J.-P. (2022). Impact of a regulation restricting critical antimicrobial usage on prevalence of antimicrobial resistance in *Escherichia Coli* isolates from fecal and manure pit samples on dairy farms in Québec, Canada. *Front Vet Sci, 9*, 838498. https://doi.org/10.3389/fvets.2022.838498

Deng, Q., Odhiambo, J.F., Farooq, U., Lam T., Dunn, S.M., Ametaj, B.N. (2015). Intravaginal lactic acid bacteria modulated local and systemic immune responses and lowered the incidence of uterine infections in periparturient dairy cows. *PLoS One, 10*(4), 0124167. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0124167

Denis-Robichaud, J., Kelton, D.F., Bauman, C.A., Barkema, H.W., Keefe, G.P., & Dubuc J. (2019). Biosecurity and herd health management practices on Canadian dairy farms. *J Dairy Sci, 102*(10), 9536-9547. https://www.journalofdairyscience.org/article/S0022-0302(19)30632-0/fulltext

Denmark Ministry of Health. (2017). *Denmark: National action plan on antibiotics in human health care.* https://www.who.int/publications/m/item/denmark-one-health-strategy-against-antimicrobial-resistance

Department of Fisheries and Oceans Canada. (2022). *Use of therapeutants.* https://www.pac.dfo-mpo.gc.ca/aquaculture/reporting-rapports/therapeut/index-eng.html

de Toledo, T. D. S., Roll, A. A. P., Rutz, F., Dallmann, H. M., Dai Pra, M. A., Leite, F. P. L., & Roll, V. F. B. (2020). An assessment of the impacts of litter treatments on the litter quality and broiler performance: A systematic review and meta-analysis. *PLoS One*, *15*(5), e0232853. https://doi.org/10.1371/journal.pone.0232853

Desiree, K., Mosimann, S., & Ebner, P. (2021). Efficacy of phage therapy in pigs: Systematic review and meta-analysis. *Journal of Animal Science, 99,* 157. https://doi.org/10.1093/jas/skab157

Despotovic, M., de Nies, L., Busi, S. B., & Wilmes, P. (2023). Reservoirs of antimicrobial resistance in the context of One Health. *Current Opinion in Microbiology*, *73*, 102291. https://doi.org/10.1016/j.mib.2023.102291

Dewulf, J. (2019). General principles of biosecurity in animal production and veterinary medicine. In F. Van Immerseel (Ed.), *Biosecurity in Animal Production and Veterinary Medicine: From Principles to Practice*. CABI. https://www.cabidigitallibrary.org/doi/book/10.1079/9781789245684.0000

Dhaka, P., Chantziaras, I., Vijay, D., Bedi, J.S., Makovska, I., Biebaut, E., & Dewulf, J. (2023). Can improved farm biosecurity reduce the need for antimicrobials in food animals? A scoping review. *Antibiotics, 12*(5), 893. https://www.mdpi.com/2079-6382/12/5/893

Diraviyam, T., Zhao, B., Wang, Y., Schade, R., Michael, A., & Zhang, X. (2014). Effect of chicken egg yolk antibodies (IgY) against diarrhea in domesticated animals: A systematic review and meta-analysis. *PLoS ONE, 9*(5), 97716. https://doi.org/10.1371/journal.pone.0097716

Dorado-García, A., Graveland, H., Bos, M.E., Verstappen, K.M., Van Cleef, B.A., Kluytmans, J.A., Wagenaar,J.A., & Heederik, D.J. (2015). Effects of reducing antimicrobial use and applying a cleaning and disinfection program in veal calf farming: Experiences from an intervention study to control livestock-associated MRSA. *PLoS One*, *10*(8), 0135826. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0135826

Dufour, S., Wellemans, V., Roy, J.-P., Lacasse, P., Ordonez-Iturriaga, A., & Francoz, D. (2019). Non-antimicrobial approaches at drying-off for treating and preventing intramammary infections in dairy cows. Part 1. Meta-analyses of efficacy of using an internal teat sealant without a concomitant antimicrobial treatment. *Animal Health Research Reviews, 20*(1), 86–97. https://www.cambridge.org/core/journals/animal-health-research-reviews/article/abs/nonantimicrobial-approaches-at-dryingoff-for-treating-and-preventing-intramammary-infections-in-dairy-cows-part-1-metaanalyses-of-efficacy-of-using-an-internal-teat-sealant-without-a-concomitant-antimicrobial-treatment/189B022D9972B920CABCCB94590D9A8F

Dupont, N., Diness, L.H., Fertner, M., Kristensen, C.S., & Stege, H. (2017). Antimicrobial reduction measures applied in Danish pig herds following the introduction of the "Yellow Card" antimicrobial scheme. *Prev Vet Med, 138,* 9-16. https://www.sciencedirect.com/science/article/abs/pii/S0167587716307383?via%3Dihub

Dutil, L., Irwin, R., Finley, R., Ng, L. K., Avery, B., Boerlin, P., Bourgault, A. M., Cole, L., Daignault, D., Desruisseau, A., Demczuk, W., Hoang, L., Horsman, G. B., Ismail, J., Jamieson, F., Maki, A., Pacagnella, A., & Pillai, D. R. (2010). Ceftiofur resistance in *Salmonella Enterica Serovar Heidelberg* from chicken meat and humans, Canada. *Emerging Infectious Diseases*, *16*(1), 48–54. https://doi.org/10.3201/eid1601.090729

Earnscliffe Strategy Group. (2024). *Public opinion research for the animal business line: 2023-2024 Research report*. Canadian Food Inspection Agency. https://epe.lac-bac.gc.ca/100/200/301/pwgsc-tpsgc/por-ef/canadian_food_inspection_agency/2024/108-23-e/POR108-23-report.pdf

Economou, V., & Gousia, P. (2015). Agriculture and food animals as a source of antimicrobial-resistant bacteria. *Infection and Drug Resistance*, *8*, 49–61. https://doi.org/10.2147/IDR.S55778

Edelman. (2019). *2019 Edelman trust barometer: Canada.* https://www.edelman.ca/trust-barometer/trust-barometer-2019

Edelman. (2021). *2021 Edelman trust barometer: Country report trust in Canada.* https://www.edelman.ca/trust-barometer/edelman-trust-barometer-2021

Edelman. (2023). *2023 Edelman trust barometer Canada report*. https://www.edelman.ca/trustbarometer/2023-edelman-trust-barometer

Egg Farmers of Canada. (2019). *Sustainability report 2019.* https://www.eggfarmers.ca/wp-content/uploads/2020/11/2020-11-18_Egg-Farmers-of-Canada_Sustainability-Report-2019.pdf

Elbers, A.R., de Koeijer, A.A., Scolamacchia, F., & van Rijn, P.A. (2010). Questionnaire survey about the motives of commercial livestock farmers and hobby holders to vaccinate their animals against *Bluetongue Virus Serotype 8* in 2008-2009 in the Netherlands. *Vaccine*, *28*(13), 2473-81. https://www.sciencedirect.com/science/article/abs/pii/S0264410X10000903?via%3Dihub

Environics. (2023). *Confidence in leaders*. https://www.environicsinstitute.org/docs/default-source/default-document-library/cot_cover-confidence-in-leaders5f77a9f8d8f24682b4dbcdb2b552c1a2.pdf?sfvrsn=4a85efd8_0

European Commission. (n.d.). *The European Green Deal: Striving to be the first climate-neutral continent.* European Union. https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/european-green-deal_en

European Commission (2020a). *A farm to fork strategy for a fair, healthy and environmentally-friendly food system*. European Union. https://food.ec.europa.eu/system/files/2020-05/f2f_action-plan_2020_strategy-info_en.pdf

European Commission: Directorate-General for Research and Innovation. (2020). *Horizon 2020: European Green Deal call*. Publications Office of the European Union. https://data.europa.eu/doi/10.2777/200559

European Environment Agency. (2024). *Veterinary antimicrobials in Europe's environment: A One Health perspective.* https://www.eea.europa.eu/publications/veterinary-antimicrobials-in-europes-environment

European Medicines Agency. (2023, November 20). *Sales of veterinary antimicrobial agents in 31 European countries in 2022: Trends from 2010 to 2022 thirteenth ESVAC report.* https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2022-trends-2010-2022-thirteenth-esvac-report_en.pdf

European Medicines Agency (EMA) & European Food Safety Authority (EFSA). (2017). EMA and EFSA joint scientific opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA). *EFSA Journal, 15*(1). https://doi.org/10.2903/j.efsa.2017.4666

European Union. (2022). *Commission implementing regulation (EU) 2022/1255 of 19 July 2022 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with regulation (EU) 2019/6 of the European Parliament and of the Council (Text with EEA relevance).* https://eur-lex.europa.eu/eli/reg_impl/2022/1255/oj

Farinacci, P., Mevissen, M., Ayrle, H., Maurer, V., Dalgaard, T.S., Melzig, M.F., & Walkenhorst, M. (2022). Medicinal plants for Prophylaxis and therapy of common infectious diseases in poultry–A systematic review of *in vivo* studies. *Planta medica, 88*(03/04), 200-217. https://www.thieme-connect.de/products/ejournals/abstract/10.1055/a-1543-5502

Farm biosecurity. (n.d.). *About.* https://www.farmbiosecurity.com.au/about/

Farmtario. (2020, July 10). *Regional vaccine helps manage Swine Influenza.* https://farmtario.com/livestock/regional-vaccine-helps-manage-swine-influenza/

Farmtario Staff. (2023). *New cost-share offering for biosecurity enhancement.* https://farmtario.com/news/new-cost-share-offering-for-biosecurity-enhancement/

Federal Ministry of Food and Agriculture. (2019). *Report of the Federal Ministry of Food and Agriculture on the evaluation of the antibiotics minimisation concept introduced with the 16th Act to amend the Medicinal Products Act (16th AMG Amendment).* https://www.bmel.de/SharedDocs/Downloads/EN/_Animals/Report-16thAMGAmendment.pdf?__blob=publicationFile&v=4

Federation of Veterinarians of Europe. (2024). *Animal health visits: Updated full report and poster.* https://fve.org/fve-publishes-full-report-and-poster-on-situation-regarding-animal-health-visits/

Fonseca, M., Heider, L. C., Léger, D., Mcclure, J. T., Rizzo, D., Dufour, S., Kelton, D. F., Renaud, D., Barkema, H. W., & Sanchez, J. (2022). Canadian dairy network for antimicrobial stewardship and resistance (CaDNetASR): An on-farm surveillance system. *Frontiers in Veterinary Science*, *8*, 799622. https://doi.org/10.3389/fvets.2021.799622

Food and Agriculture Organization of the United Nations, United Nations Environment Programme, World Health Organization, & World Organization for Animal Health. (n.d). *Global database for tracking antimicrobial resistance (AMR): Country self- assessment survey (TrACSS).* https://tinyurl.com/87kmcn3t

Fossen, J.D., Erickson, N., Gow, S.P., Campbell, J.R., Wilhelm, B.J., & Waldner, C.L. (2023). Producer attitudes regarding antimicrobial use and resistance in Canadian cow-calf herds. *Can Vet J*, *64*(11), 1035-1043. https://pubmed.ncbi.nlm.nih.gov/37915784/

Francoz, D., Wellemans, V., Dupré, J.P., Roy, J.P., Labelle, F., Lacasse, P., & Dufour, S. (2017). Invited review: A systematic review and qualitative analysis of treatments other than conventional antimicrobials for Clinical Mastitis in dairy cows. *J Dairy Sci, 100*(10), 7751-7770. https://doi.org/10.3168/jds.2016-12512

Galyean, M.L., Duff, G.C., & Rivera, J.D. (2022). Galyean appreciation club review: Revisiting nutrition and health of newly received cattle-What have we learned in the last 15 years? *J Anim Sci, 100*(4). https://doi.org/10.1093/jas/skac067

George, P.B.L., Rossi, F., St-Germain, M-W., Amato, P., Badard, T., Bergeron, M.G., Boissinot, M.,...Duchaine, C. (2022). Antimicrobial resistance in the environment: Towards elucidating the roles of Bioaerosols in transmission and detection of antibacterial resistance genes. *Antibiotics, 11*(7). https://www.mdpi.com/2079-6382/11/7/974

German Center for Infection Research. (n.d.). *Resistance gene.* https://www.dzif.de/en/glossary/resistance-gene

Gilbert, N. (2024). *US pressure weakens global commitments on antimicrobial resistance.* https://usrtk.org/factory-farming/us-pressure-weakens-global-commitments-on-antimicrobial-resistance/

Glass-Kaastra, S., Dougherty, B., Nesbitt, A., Viswanathan, M., Ciampa, N., Parker, S., Nadon, C., MacDonald, D., & Thomas, M. K. (2022). Estimated reduction in the burden of Nontyphoidal *Salmonella* illness in Canada circa 2019. *Foodborne Pathogens and Disease*, *19*(11), 744–749. https://doi.org/10.1089/fpd.2022.0045

Global Quality Systems and Global Strategic Sourcing Food. (2017, August 16). *McDonald's global vision for antibiotic stewardship in food animals ("VAS"). P-GSCS-001. Version 2.1.* https://corporate.mcdonalds.com/content/dam/sites/corp/nfl/pdf/McDonalds-Global-Vision-for-Antimicrobial-Stewardship-in-Food.pdf

Goddard, E., Muringai, V., & Robinson, A. (2017). Consumer interest in a natural designation in food choice. *IDEAS Working Paper Series from RePEc.* https://search.proquest.com/docview/2083125333?accountid=10267

Golding, G.R., Bryden, L., Levett, P.N., McDonald, R.R., Wong, A., Wylie, J., Graham, M.R., Tyler, S., Van Domselaar, G., Simor, A.E., Gravel, D., & Mulvey, M.R. (2010). Livestock-associated *Methicillin-Resistant Staphylococcus Aureus Sequence Type 398* in humans, Canada. *Emerging Infectious Diseases, 16*(4), 587-594. https://doi.org/10.3201/eid1604.091435

Gomez, D. E., Arroyo, L. G., Poljak, Z., Viel, L., & Weese, J. S. (2017). Implementation of an algorithm for selection of antimicrobial therapy for diarrhoeic calves: Impact on antimicrobial treatment rates, health and faecal microbiota. *The Veterinary Journal*, *226*, 15–25. https://doi.org/10.1016/j.tvjl.2017.06.009

Government of Alberta. (2024). *Alberta's One Health antimicrobial resistance framework for action*. Alberta Health. https://open.alberta.ca/dataset/784c1297-a9c1-4b67-968f-e7e30db1411e/resource/fb92cc3b-4784-4a89-878e-c3a8bd04dfb0/download/hlth-albertas-one-health-antimicrobial-resistance-framework-for-action-2024.pdf

Government of British Columbia. (2024). *Disease surveillance and investigation.* https://www2.gov.bc.ca/gov/content/industry/agriculture-seafood/animals-and-crops/animal-health/office-of-the-chief-veterinarian/26527

Government of Canada. (2023a). *Canada and Manitoba invest $2 million to enhance capacity of rural veterinary services districts.* https://www.canada.ca/en/agriculture-agri-food/news/2023/06/canada-and-manitoba-invest-2-million-to-enhance-capacity-of-rural-veterinary-services-districts.html

Government of Canada. (2023b). *Governments investing in innovation to strengthen Ontario's agri-food sector.* https://www.canada.ca/en/agriculture-agri-food/news/2024/09/governments-investing-in-innovation-to-strengthen-ontarios-agri-food-sector.html

Government of Canada. (2024). *Government of Canada announces funding to improve animal health and welfare.* https://www.canada.ca/en/agriculture-agri-food/news/2024/10/government-of-canada-announces-funding-to-improve-animal-health-and-welfare.html

Government of Manitoba. (2024). *Animal health.* https://www.gov.mb.ca/agriculture/animal-health-and-welfare/animal-health/index.html

Government of the Netherlands. (2022). *National action plan for the strengthening of the zoonotic disease policy.* https://www.government.nl/documents/reports/2022/07/06/national-action-plan-for-the-strengthening-of-the-zoonotic-disease-policy#:~:text=The%20aim%20of%20the%20action,transmitted%20from%20animals%20to%20humans

Government of New Brunswick. (2024). *Veterinary services.* https://www2.gnb.ca/content/gnb/en/departments/10/agriculture/content/livestock/veterinary_services.html

Government of Newfoundland and Labrador. (2024). *Animal health and welfare*. https://www.gov.nl.ca/ffa/programs-and-funding/programs/animals/health/

Government of Nova Scotia. (2021). *Farm animal health & welfare.* https://novascotia.ca/agri/programs-and-services/farm-animal-welfare/

Government of Ontario. (2024). *Antimicrobial resistance in agriculture*. https://www.ontario.ca/page/antimicrobial-resistance-agriculture#section-0

Government of Prince Edward Island. (2023). *Antimicrobial resistance (AMR) in agriculture.* https://www.princeedwardisland.ca/en/information/agriculture/antimicrobial-resistance-amr-in-agriculture

Gouvernement du Québec. (2024). *Surveillance de l'utilisation des antibiotiques chez les animaux*. https://www.quebec.ca/agriculture-environnement-et-ressources-naturelles/sante-animale/usage-antibiotiques/surveillance

Government of Saskatchewan. (2024). *Animal health*. https://www.saskatchewan.ca/business/agriculture-natural-resources-and-industry/agribusiness-farmers-and-ranchers/livestock/animal-health-and-welfare

Gozdzielewska, L., King, C., Flowers, P., Mellor, D., Dunlop, P., & Price, L. (2020). Scoping review of approaches for improving antimicrobial stewardship in livestock farmers and veterinarians. *Preventive Veterinary Medicine*, *180*, 105025. https://doi.org/10.1016/j.prevetmed.2020.105025

Groves, J.T. (2020). Details to attend to when managing high risk cattle. *Food Animal Practice, 36*(2), 445-460. https://www.sciencedirect.com/science/article/abs/pii/S0749072020300177?via%3Dihub

Hamzaoui Essoussi L., & Zahaf, M. (2009). Exploring the decision-making process of Canadian organic food consumers: Motivations and trust issues. *Qualitative Market Research, 12*(4), 443–459. https://doi.org/10.1108/13522750910993347

Heak, C., Sukon, P., & Sornplang, P. (2018). Effect of direct-fed microbials on culturable gut microbiotas in broiler chickens: A meta-analysis of controlled trials. *Asian-Australasian Journal of Animal Sciences, 31*(11), 1781. https://www.animbiosci.org/journal/view.php?doi=10.5713/ajas.18.0009

Health Canada. (2009). *Categorization of antimicrobial drugs based on importance in human medicine.* https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/categorization-antimicrobial-drugs-based-importance-human-medicine.html

Health Canada. (2024a). *Responsible use of medically important antimicrobials in animals*. https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/actions/responsible-use-antimicrobials.html

Health Canada. (2024b).*Veterinary antimicrobial sales reporting.* https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/veterinary-antimicrobial-sales-reporting.html

Health Canada. (2024c). *Notice to stakeholders: Post-market re-evaluation of medically important antimicrobials for veterinary use with unspecified or prolonged durations of use.* https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/post-market-re-evaluation-medically-important-antimicrobials-veterinary/notice-post-market-re-evaluation-medically-important-antimicrobials.html

Health Canada. (2024d). *List A- List of certain antimicrobial active pharmaceutical ingredients.* https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/veterinary-antimicrobial-sales-reporting/list-a.html

Health Infobase. (2024a). *CIPARS-VASR: Veterinary antimicrobial sales reporting in Canada.* https://health-infobase.canada.ca/veterinary-antimicrobial-sales/

Health Infobase. (2024b). *FoodNet Canada: The integrated sentinel site surveillance network for enteric disease in Canada.* https://health-infobase.canada.ca/foodnet-canada/

Health Infobase. (2024c). *Canadian Antimicrobial Resistance Surveillance System (CARSS) antimicrobial use dashboard.* https://health-infobase.canada.ca/carss/amu/

Health Infobase. (2024d). *Canadian Antimicrobial Resistance Surveillance System (CARSS) antimicrobial resistance dashboard.* https://health-infobase.canada.ca/carss/amr/

Herati, H., Burns, K.E., Nascimento, M., Brown, P., Calnan, M., Dubé, È., Ward, P.R., Filice, E., Rotolo, B., Ike, N., & Meyer, S.B. (2023). Canadians' trust in government in a time of crisis: Does it matter? *PLoS One, 18*(9), 0290664. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0290664

Hibbard, R., Mendelson, M., Page, S.W., Pinto Ferreira, J., Pulcini, C., Paul, M.C., & Faverjon, C. (2024). Antimicrobial stewardship: A definition with a One Health perspective. *NPJ Antimicrob Resist, 2*(1), 15. https://doi.org/10.1038/s44259-024-00031-w

Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., Devriendt, D., Erlacher-Vindel, E., Goossens, E., Karaca, K., Lemirere, S., Metzner, M., Raicek, M., Collell Suriñach, M., Wong, N.M., Gay, C., & Van Immerseel, F. (2018). Vaccines as alternatives to antibiotics for food producing animals. Part 2: New approaches and potential solutions. *Vet Res, 49*, 70. https://doi.org/10.1186/s13567-018-0561-7

Hooge, D.M., Kiers, A., & Connolly, A. (2013). Meta-analysis summary of broiler chicken trials with dietary actigen (2009-2012).. *International Journal of Poultry Science, 12*(1), 01-08. https://scialert.net/abstract/?doi=ijps.2013.1.8

Hu, D., O'Connor, A.M., Wang, C., Sargeant, J.M., & Winder, C.B. (2020). How to conduct a bayesian network meta-analysis. *Front Vet Sci*, *7*, 271. https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2020.00271/full

Iannetti, L., Romagnoli, S., Cotturone, G., & Podaliri Vulpiani, M. (2021). Animal welfare assessment in antibiotic-free and conventional broiler chicken. *Animals: An Open Access Journal from MDPI*, *11*(10), 2822. https://doi.org/10.3390/ani11102822

Jackson, M.E., & Hanford, K. (2014). Statistical meta-analysis of pen trials conducted testing heat-sensitive *β-Mannanase (Hemicell)* feed enzyme in male broilers grown to market age. *Poultry Science, 93*(1), 66.

Jelinski M., Kinnear, A., Gesy, K., Andrés-Lasheras, S., Zaheer, R., Weese, S., & McAllister, T.A. (2020). Antimicrobial sensitivity testing of *Mycoplasma bovis* isolates derived from western Canadian feedlot cattle. *Microorganisms, 8*(1), 124. https://doi.org/10.3390/microorganisms8010124

Jha, R., Das, R., Oak, S., & Mishra, P. (2020). Probiotics (Direct-Fed Microbials) in poultry nutrition and their effects on nutrient utilization, growth and laying performance, and gut health: A systematic review. *Animals (Basel), 10*(10), 1863. https://www.mdpi.com/2076-2615/10/10/1863

Kabera, F., Roy, J. P., Afifi, M., Godden, S., Stryhn, H., Sanchez, J., & Dufour, S. (2021). Comparing blanket vs. selective dry cow treatment approaches for elimination and prevention of intramammary infections during the dry period: A systematic review and meta-analysis. *Frontiers in Veterinary Science*, *8*, 688450. https://doi.org/10.3389/fvets.2021.688450

Kadykalo, S.V., Anderson, M.E., & Alsop, J.E. (2018). Passive surveillance of antimicrobial resistance in *Salmonella* and *Escherichia Coli* isolates from Ontario livestock, 2007-2015. *Can Vet J, 59*(6), 617-622. https://pubmed.ncbi.nlm.nih.gov/29910475/

Kamel, M.S., Davidson, J.L., & Verma, M.S. (2024). Strategies for Bovine Respiratory Disease (BRD) diagnosis and prognosis: A comprehensive overview. *Animals (Basel)*, *14*(4), 627. https://doi.org/10.3390/ani14040627

Karavolias, J., Salois, M. J., Baker, K. T., & Watkins, K. (2018). Raised without antibiotics: Impact on animal welfare and implications for food policy. *Translational Animal Science*, *2*(4), 337–348. https://doi.org/10.1093/tas/txy016

Kemp, J.O.G., Taylor, J., Kelly, L., & Larocque, R. (2020). Antibiotic resistance genes in the aquaculture sector: global reports and research gaps. *Environmental Reviews, 29*(2), 300-314. https://www.researchgate.net/publication/347294681_Antibiotic_resistance_genes_in_the_aquaculture_sector_global_reports_and_research_gaps

Khan, R., Petersen, F.C., & Shekhar, S. (2019). Commensal bacteria: An emerging player in defense against respiratory pathogens. *Frontiers in Immunology, 10.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6554327/

Khanna, T., Friendship, R., Dewey, C., Weese, J.S. (2008). Methicillin resistant *Staphylococcus aureus* colonization in pigs and pig farmers. *Vet Microbiol, 128*(3-4), 298-303. https://www.sciencedirect.com/science/article/abs/pii/S0378113507004932?via%3Dihub

Kim, D.-W., & Cha, C.-J. (2021). Antibiotic resistome from the One-Health perspective: understanding and controlling antimicrobial resistance transmission. *Experimental & Molecular Medicine, 53*(3), 301–309. https://www.nature.com/articles/s12276-021-00569-z

Kim, H., Kim, M., Kim, S., Lee, Y.M., & Shin, S.C. (2022). Characterization of antimicrobial resistance genes and virulence factor genes in an Arctic permafrost region revealed by metagenomics. *Environ Pollut, 294*, 118634. https://www.sciencedirect.com/science/article/abs/pii/S0269749121022168?via%3Dihub

Kimman, T.G., Cornelissen, L.A., Moormann, R.J., Rebel, J.M., & Stockhofe-Zurwieden, N. (2009). Challenges for porcine reproductive and respiratory syndrome virus (PRRSV) vaccinology. *Vaccine, 27*(28), 3704-18. https://www.sciencedirect.com/science/article/abs/pii/S0264410X09005568?via%3Dihub

Kirchner, M., Nunez-Garcia, J., Duggett, N., Gosling, R.J., & Anjum, M.F. (2024). Use of Transcriptomics and genomics to assess the effect of disinfectant exposure on the survival and resistance of *Escherichia coli O157:H7*, a human pathogen. *Front Microbiol, 15,* 1477683. https://doi.org/10.3389/fmicb.2024.1477683

Klein, N.C, & Cunha, B.A. (1995, July). *Third-generation cephalosporins. The Medical Clinics of North America.* https://pubmed.ncbi.nlm.nih.gov/7791418/#:~:text=Third%2Dgeneration%20cephalosporins%20are%20broad,of%20the%20third%2Dgeneration%20agents

Klima, C.L., Holman, D.B., Cook, S.R., Conrad, C.C., Ralston, B.J., Allan, N., Anholt, R.M., Niu, Y.D., Stanford, K., Hannon, S.J., Booker, C.W., & McAllister, T.A. (2020). Multidrug resistance in *Pasteurellaceae* associated with Bovine Respiratory Disease mortalities in North America from 2011 to 2016. *Front Microbiol, 11,* 638008. https://www.frontiersin.org/journals/microbiology/articles/10.3389/fmicb.2020.638008/full

Krehbiel, C.R. (2020). Bovine Respiratory Disease influences on nutrition and nutrient metabolism. *Veterinary Clinics: Food Animal Practice, 36*(2), 361-373. https://www.sciencedirect.com/science/article/abs/pii/S074907202030027X?via%3Dihub

Kulathunga, D.G.R.S., Harding, J.C.S., & Rubin, J.E. (2023). Antimicrobial susceptibility of Western Canadian *Brachyspira* isolates: Development and standardization of an agar dilution susceptibility test method. *PLOS One, 18*(6), 0286594. https://doi.org/10.1371/journal.pone.0286594

Kumar, P., Tiwari, S., Uguz, S., Li, Z., Gonzalez, J., Wei, L., Samuel, R.S., Zhang, Y., & Yang, X. (2024). Bioaerosols downwind from animal feeding operations: A comprehensive review. *J Hazard Mater, 480*, 135825. https://www.sciencedirect.com/science/article/abs/pii/S030438942402404X?via%3Dihub

Kurt, T., Wong, N., Fowler, H., Gay, C., Lillehoj, H., Plummer, P., Scott, H.M., & Hoelzer, K. (2019). Strategic priorities for research on antibiotic alternatives in animal agriculture-results from an expert workshop. *Front Vet Sci, 6,* 429. https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2019.00429/full

Lardé, H., Francoz, D., Roy, J.-P., Massé, J., Archambault, M., Paradis, M.-È., & Dufour, S. (2021). Comparison of quantification methods to estimate farm-level usage of antimicrobials other than in medicated feed in dairy farms from Québec, Canada. *Microorganisms, 9*(5), 1106. https://doi.org/10.3390/microorganisms9051106

Larmer, S.G., & Mallard, B.A. (2017). High immune response sires reduce disease incidence in North American large commercial dairy populations. *Cattle Pract, 25*(1). https://bestgenetics.at/static/files/immunity/Peer-Reviewed%20papers/Larmer%20et%20al%20Cattle%20Practice.pdf

Laugier, C. & Guillaume, K. (2022). *Évaluation des deux premiers plans Ecoantibio et préparation du troisième.* Ministére de l'agriculture et de la souveraineté alimentaire. https://agriculture.gouv.fr/evaluation-des-deux-premiers-plans-ecoantibio-et-preparation-du-troisieme

Lazurko, M.M., Erickson, N.E.N., Campbell, J.R., Gow, S., & Waldner, C.L. (2023). Vaccine use in Canadian cow-calf herds and opportunities for improvement. *Front Vet Sci*, *10*, 1235942. https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2023.1235942/full

Léger. (2018). *Ontario science centre Canadian science attitudes research.* https://www.ontariosciencecentre.ca/media/3319/science_literacy_report2018.pdf

Léger, D., Deckert, A., Gow, A., Agunos, A., & Reid-Smith, R.J. (2011). The Canadian Integrated Program for Antimicrobial Resistance Surveillance: An approach to building collaboration for a voluntary farm surveillance framework. *Epidemiol et sante anim, 59*(60), 348-351. https://www.cabidigitallibrary.org/doi/pdf/10.5555/20113184529

Libera, K., Konieczny, K., Witkowska, K., Żurek, K., Szumacher-Strabel, M., Cieslak, A., & Smulski, S. (2021). The association between selected dietary minerals and Mastitis in dairy cows-A review. *Animals (Basel)*, *11*(8), 2330. https://doi.org/10.3390/ani11082330

Liu, R., Han, G., Li, Z., Cun, S., Hao, B., Zhang, J., & Liu, X. (2022). Bacteriophage therapy in aquaculture: Current status and future challenges. *Folia Microbiol (Praha), 67*(4), 573-590. https://link.springer.com/article/10.1007/s12223-022-00965-6

Lloyd, D. H., & Page, S. W. (2018). Antimicrobial stewardship in veterinary medicine. *Microbiology Spectrum, 6*(3). https://doi.org/10.1128/microbiolspec.ARBA-0023-2017

Lombard, J., Urie, N., Garry, F., Godden, S., Quigley, J., Earleywine, T., McGuirk, S., Moore, D., Branan, M., Chamorro, M., Smith, G., Shivley, C., Catherman, D., Haines, D., Heinrichs, A.J., James, R., Maas, J., & Sterner, K. (2020). Consensus recommendations on calf- and herd-level passive immunity in dairy calves in the United States. *J Dairy Sci, 103*(8), 7611-7624. https://www.journalofdairyscience.org/article/S0022-0302(20)30383-0/fulltext

López-Gálvez, G., López-Alonso, M., Pechova, A., Mayo, B., Dierick, N., & Gropp, J. (2021). Alternatives to antibiotics and trace elements (copper and zinc) to improve gut health and zootechnical parameters in piglets: A review. *Animal Feed Science and Technology, 271,* 114727. https://doi.org/10.1016/j.anifeedsci.2020.114727

Luise, D., Negrini, C., Correa, F., & Trevisi, P. (2024). Effect and mode of action of different doses and sources of zinc in weaning pigs using a meta-analytical and systematic review approach. *Italian Journal of Animal Science, 23*(1), 241-258. https://doi.org/10.1080/1828051X.2023.2300810

Maier, G.U., Breitenbuecher, J., Gomez, J.P., Samah, F., Fausak, E., & Van Noord, M. (2022). Vaccination for the prevention of neonatal calf diarrhea in cow-calf operations: A scoping review. *Veterinary and Animal Science, 15,* 100238. https://www.sciencedirect.com/science/article/pii/S2451943X22000096?via%3Dihub

Makovska, I., Chantziaras, I., Caekebeke, N., Dhaka, P., & Dewulf, J. (2024). Assessment of cleaning and disinfection practices on pig farms across ten European countries. *Animals (Basel), 14*(4), 593. https://www.researchgate.net/publication/378145088_Assessment_of_Cleaning_and_Disinfection_Practices_on_Pig_Farms_across_Ten_European_Countries

Mallard, B.A., Emam, M., Paibomesai, M., Thompson-Crispi, K., & Wagter-Lesperance, L. (2015). Genetic selection of cattle for improved immunity and health. *Jpn J Vet Res, 63*(1), 37-44. https://pubmed.ncbi.nlm.nih.gov/25872325/

Martiny, H.M., Munk, P., Brinch, C., Aarestrup, F.M., Calle, M.L., & Petersen, T.N. (2024). Utilizing co-abundances of antimicrobial resistance genes to identify potential co-selection in the resistome. *Microbiol Spectr, 12*(7). https://doi.org/10.1128/spectrum.04108-23

Maulu, S., Hasimuna, O.J., Mphande, J., & Munang'andu, H.M. (2021). Prevention and control of Streptococcosis in Tilapia culture: A systematic review. *Journal of Aquatic Animal Health, 33*(3), 162-177. https://doi.org/10.1002/aah.10132

McCubbin, K. D., Anholt, R. M., de Jong, E., Ida, J. A., Nóbrega, D. B., Kastelic, J. P., Conly, J. M., Götte, M., McAllister, T. A., Orsel, K., Lewis, I., Jackson, L., Plastow, G., Wieden, H. J., McCoy, K., Leslie, M., Robinson, J. L., Hardcastle, L., Hollis, A., Ashbolt, N. J., Barkema, H. W. (2021). Knowledge gaps in the understanding of antimicrobial resistance in Canada. *Frontiers in Public Health*, *9*, 726484. https://doi.org/10.3389/fpubh.2021.726484

McCubbin, K. D., de Jong, E., Lam, T. J. G. M., Kelton, D. F., Middleton, J. R., McDougall, S., De Vliegher, S., Godden, S., Rajala-Schultz, P. J., Rowe, S., Speksnijder, D. C., Kastelic, J. P., & Barkema, H. W. (2022). Invited review: selective use of antimicrobials in dairy cattle at drying-off. *Journal of Dairy Science*, *105*(9), 7161–7189. https://doi.org/10.3168/jds.2021-21455

McEwen, S. A., Angulo, F. J., Collignon, P. J., & Conly, J. M. (2018). Unintended consequences associated with national-level restrictions on antimicrobial use in food-producing animals. *The Lancet: Planetary Health*, *2*(7), 279–282. https://doi.org/10.1016/S2542-5196(18)30138-4

McKernan, C., Benson, T., Farrell, S., & Dean, M. (2021). Antimicrobial use in agriculture: Critical review of the factors influencing behaviour. *JAC Antimicrob Resist, 3*(4), 178. https://doi.org/10.1093/jacamr/dlab178

McMullen, C.K., Sargeant, J.M., Kelton, D.F., Churchill, K.J., Cousins, K.S., & Winder, C.B. (2021). Modifiable management practices to improve udder health in dairy cattle during the dry period and early lactation: A scoping review. *J Dairy Sci, 104*(9), 10143-10157. https://doi.org/10.3168/jds.2020-19873

Mekonnen, Y.T., Savini, F., Indio, V., Seguino, A., Giacometti, F., Serraino, A., Candela, M., & De Cesare, A. (2024). Systematic review on microbiome-related nutritional interventions interfering with the colonization of foodborne pathogens in broiler gut to prevent contamination of poultry meat. *Poult Sci, 103*(5), 103607. https://www.sciencedirect.com/science/article/pii/S003257912400186X?via%3Dihub

Merrill, S.C., Moegenburg, S., Koliba, C.J., Zia, A., Trinity, L., Clark, E., Bucini, G., Wiltshire, S., Sellnow, T., Sellnow, D., & Smith, J.M. (2019). Willingness to comply with biosecurity in livestock facilities: Evidence from experimental simulations. *Front Vet Sci, 6.* https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2019.00156/full

Miccoli, A., Saraceni, P.R., & Scapigliati, G. (2019). Vaccines and immune protection of principal Mediterranean marine fish species. *Fish Shellfish Immunol, 94*, 800-809. https://www.sciencedirect.com/science/article/abs/pii/S1050464819309490?via%3Dihub

Mijar, S., van der Meer, F., Pajor, E., Hodder, A., Louden, J.M., Thompson, S., & Orsel, K. (2023). Impacts of commingling preconditioned and auction-derived beef calves on Bovine Respiratory Disease related morbidity, mortality, and weight gain. *Front Vet Sci, 10,* 1137078. https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2023.1137078/full

Millar, N., Dufour, S., Lardé, H., Roy, J. P., Belloc, C., Francoz, D., Paradis, M. È., Archambault, M., Fairbrother, J. M., & Aenishaenslin, C. (2023). Barriers and facilitators to implementing a new regulation restricting antimicrobial use in dairy production in Québec, Canada: A qualitative study. *Frontiers in Veterinary Science*, *10*, 1025781. https://doi.org/10.3389/fvets.2023.1025781

Ministère de l'Agriculture et de la Souveraineté Alimentaire. (2023). Écoantibio 3: réduire les risques d'antibiorésistance et promouvoir le bon usage des antimicrobiens en médecine vétérinaire (plan national 2023-2028). https://agriculture.gouv.fr/le-plan-ecoantibio-3-2023-2028

Ministry of Food Agriculture and Fisheries of Denmark & Danish Veterinary and Food Administration. (2021). *The Danish veterinary and food administration's national action plan for antibiotic resistance in production animals and food 2021-2023*. https://foedevarestyrelsen.dk/Media/638610430209006066/AMR-handlingsplan%202024%20web.pdf

Mondal, H., & Thomas, J. A. (2022). Review on the recent advances and application of vaccines against fish pathogens in aquaculture. *Aquacult Int, 30,* 1971–2000. https://doi.org/10.1007/s10499-022-00884-w

Morris, A., Wright, G., Barkema, H., Hillier, S., Hindmarch, S., Quach-Thanh, C., Topp, E., & Weese, J.S. (2021). *Strengthening governance of the antimicrobial resistance response across One Health in Canada.* https://d13f8eef-a372-42c9-98d7-90d5c11f99d4.usrfiles.com/ugd/d13f8e_2745ef30e7b649eb85dd75e842b40cfb.pdf

Mosimann, S., Desiree, K., & Ebner, P. (2021). Efficacy of phage therapy in poultry: A systematic review and meta-analysis. *Poultry Science, 100*(12), 101472. https://doi.org/10.1016/j.psj.2021.101472.

Muloi, D., Ward, M. J., Pedersen, A. B., Fèvre, E. M., Woolhouse, M. E. J., & van Bunnik, B. A. D. (2018). Are food animals responsible for transfer of antimicrobial-resistant *Escherichia coli* or their resistance determinants to human populations? A systematic review. *Foodborne pathogens and disease*, *15*(8), 467–474. https://doi.org/10.1089/fpd.2017.2411

Muringai, V., & Goddard, E. W. (2010). Canadian consumer concerns about food safety issues and confidence in food products: Comparison of beef and pork. *IDEAS Working Paper Series from RePEc*. https://ideas.repec.org/p/ags/aaea10/61878.html

Mzula, A., Wambura, P.N., Mdegela, R.H., & Shirima, G.M. (2019). Current State of Modern Biotechnological-Based Aeromonas Hydrophila Vaccines for Aquaculture: A Systematic Review. *BioMed Research International*. https://doi.org/10.1155/2019/3768948

Nale, J.Y., & McEwan, N.R. (2023). Bacteriophage therapy to control bovine Mastitis: A review. *Antibiotics, 12*(8), 1307. https://doi.org/10.3390/antibiotics12081307

National Cattle Feeders Association. (2023). *Canadian Feedlot Audit Guide: Instructions, Standards and Common Audit Tool.* https://nationalcattlefeeders.ca/wp-content/uploads/2024/01/Canadian-Feedlot-Audit-Program-Common-Audit-Tool-2023_EN.pdf

National Farm Animal Care Council. (2025). *Codes of practice for the care and handling of farm animals.* https://www.nfacc.ca/codes-of-practice

National Sheep Network. (2024). *Advocacy.* https://nationalsheepnetwork.com/advocacy-english-1

Nhung, N.T., Chansiripornchai, N., & Carrique-Mas, J.J. (2017). Antimicrobial resistance in bacterial poultry pathogens: A review. *Front Vet Sci, 4*(10), 126. https://doi.org/10.3389/fvets.2017.00126

Nickell, J.S., Hutcheson, J.P., Renter, D.G., & Amrine, D.A. (2021). Comparison of a traditional Bovine Respiratory Disease control regimen with a targeted program based upon individualized risk predictions generated by the Whisper On Arrival technology. *Transl Anim Sci. 5*(2). https://doi.org/10.1093/tas/txab081

Nobrega, D.B., De Buck, J., & Barkema, H.W. (2018). Antimicrobial resistance in *Non-Aureus Staphylococci* isolated from milk is associated with systemic but not intramammary administration of antimicrobials in dairy cattle. *J Dairy Sci*, *101*(8), 7425-7436. https://doi.org/10.3168/jds.2018-14540

Noyes, N.R., Slizovskiy, I.B., & Singer, R.S. (2021). Beyond antimicrobial use: A framework for prioritizing antimicrobial resistance interventions. *Annu Rev Anim Biosci, 9*, 313-332. https://doi.org/10.1146/annurev-animal-072020-080638

Nuamah, E., Okon, U.M., Jeong, E., Mun, Y., Cheon, I., Chae, B., Odoi, F.N.A., Kim. D.W., & Choi, N.J. (2024). Unlocking Phytate with Phytase: A meta-analytic view of meat-type chicken muscle growth and bone mineralization potential. *Animals (Basel), 14*(14), 2090. https://doi.org/10.3390/ani14142090

Ochs, C., Neis, B., Tahlan, K., & Sarkar, A. (2021). Canadian Aquaculture: Supporting the need to develop sentinel surveillance programs for antimicrobial resistance among Canadian marine aquaculture facilities. *ISEE Conference Abstracts, 2021*(1). https://doi.org/10.1289/isee.2021.O-TO-144

O'Connor, A. M., Hu, D., Totton, S. C., Scott, N., Winder, C. B., Wang, B., Wang, C., Glanville, J., Wood, H., White, B., Larson, R., Waldner, C., & Sargeant, J. M. (2019). A systematic review and network meta-analysis of bacterial and viral vaccines, administered at or near arrival at the feedlot, for control of Bovine Respiratory Disease in beef cattle. *Animal Health Research Reviews*, *20*(2), 143–162. https://doi.org/10.1017/S1466252319000288

Office of the Auditor General. (2023). *2023 Reports 5 to 9 of the Auditor General of Canada to the Parliament of Canada.* https://www.oag-bvg.gc.ca/internet/English/parl_oag_202310_06_e_44339.html

Ojasanya, R.A., Gardner, I.A., Groman, D.B., Saksida, S., Saab, M.E., & Thakur, K.K. (2022). Antimicrobial susceptibility profiles of bacteria commonly isolated from farmed Salmonids in Atlantic Canada (2000-2021). *Vet Sci, 9*(4), 159. https://www.mdpi.com/2306-7381/9/4/159

Okonkwo, R.I., Grant, G., Ndukwe, H., Mohammed, Z.A., & Khan, S. (2024). Assessing the appropriateness of antimicrobial prescribing in the community setting: A scoping review. *Open Forum Infect Dis*, *11*(3), 670. https://doi.org/10.1093/ofid/ofad670

Ontario Veterinary Medical Association (OVMA). (2024). *Farmed Animal Antimicrobial Stewardship Initiative (FAAST)*. https://www.amstewardship.ca/

Otto, S. J., Carson, C. A., Finley, R. L., Thomas, M. K., Reid-Smith, R. J., & McEwen, S. A. (2014). Estimating the number of human cases of *Ceftiofur-Resistant Salmonella Enterica Serovar Heidelberg* in Québec and Ontario, Canada. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, *59*(9), 1281–1290. https://doi.org/10.1093/cid/ciu496

Otto, S.J.G., Haworth-Brockman, M., Miazga-Rodriguez, M., Wierzbowski, A., & Saxinger, L.M. (2022). Integrated surveillance of antimicrobial resistance and antimicrobial use: Evaluation of the status in Canada (2014–2019). *Can J Public Health, 113*, 11-22. https://link.springer.com/article/10.17269/s41997-021-00600-w

Otto, S.J.G., Pollock, C.M., Relf-Eckstein, J.-A., McLeod, L., Waldner, C.L. (2024). Opportunities for laboratory testing to inform antimicrobial use for Bovine Respiratory Disease: Application of information quality value stream maps in commercial feedlots. *Antibiotics, 13*(9), 903. https://doi.org/10.3390/antibiotics13090903.

Page, S., Prescott, J., & Weese, S. (2014). The 5Rs approach to antimicrobial stewardship. *The Veterinary Record*, *175*(8), 207–208. https://doi.org/10.1136/vr.g5327

Partridge, S. R., Kwong, S. M., Firth, N., & Jensen, S. O. (2018). Mobile genetic elements associated with antimicrobial resistance. *Clinical Microbiology Reviews*, *31*(4), 00088-17. https://doi.org/10.1128/CMR.00088-17

Paudel, S., Apostolakos, I., Vougat Ngom, R., Tilli, G., de Carvalho Ferreira, H.C., & Piccirillo, A. (2024). A systematic review and meta-analysis on the efficacy of vaccination against *Colibacillosis* in broiler production. *PLoS ONE, 19*(3), 0301029. https://doi.org/10.1371/journal.pone.0301029

Pearce, S. D., Parmley, E. J., Winder, C. B., Sargeant, J. M., Prashad, M., Ringelberg, M., Felker, M., & Kelton, D. F. (2023). Evaluating the efficacy of internal teat sealants at dry-off for the prevention of new intra-mammary infections during the dry-period or Clinical Mastitis during early lactation in dairy cows: A systematic review update and sequential meta-analysis. *Preventive Veterinary Medicine*, *212*, 105841. https://doi.org/10.1016/j.prevetmed.2023.105841

Pig Improvement Company. (2024) *PIC PRRS-resistant pig*. https://www.pic.com/pic-prrs-resistant-pig/

Pig Progress. (2021, August 2). *Canada follows the EU, with zinc oxide.* https://www.pigprogress.net/pigs/canada-follows-the-eu-with-zinc-oxide/#:~:text=Canada%20is%20in%20the%20midst,at%20nutritional%20levels%20of%20350ppm

The Pig Site. (2023, Jan 31). *USask developing a regional Influenza vaccine for pigs.* https://www.thepigsite.com/news/2023/01/usask-developing-a-regional-influenza-vaccine-for-pigs

Pilati, G.V.T., Cadamuro, R.D., Filho, V.B., Dahmer, M., Elois, M.A., Savi, B.P., Salles, G.B.C., Muniz, E.C., & Fongaro, G. (2023). Bacteriophage-associated antimicrobial resistance genes in avian pathogenic *Escherichia coli* isolated from brazilian poultry. *Viruses, 15*(7), 1485. https://doi.org/10.3390/v15071485

Pinto Jimenez, C.E., Keestra, S., Tandon, P., Cumming, O., Pickering, A.J., Moodley, A., & Chandler, C.I.R. (2023). Biosecurity and Water, Sanitation, and Hygiene (WASH) interventions in animal agricultural settings for reducing infection burden, antibiotic use, and antibiotic resistance: A One Health systematic review. *The Lancet Planetary Health, 7*(5), 418-434. https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196(23)00049-9/fulltext

Polycarpo, G.V., Andretta, I., Kipper, M., Cruz-Polycarpo, V.C., Dadalt, J.C., Rodrigues, P.H.M., & Albuquerque, R. (2017). Meta-analytic study of organic acids as an alternative performance-enhancing feed additive to antibiotics for broiler chickens. *Poultry Science, 96*(10), 3645-3653. https://doi.org/10.3382/ps/pex178

Postma, M., Stärk, K.D.C., Sjölund, M., Backhans, A., Beilage, E.G., Lösken, S., Belloc, C., Collineau, L., Iten, D., Visschers, V., Nielsen, E.O., Dewulf, J., & MINAPIG Consortium. (2015). Alternatives to the use of antimicrobial agents in pig production: A multi-country expert-ranking of perceived effectiveness, feasibility and return on investment. *Prev Vet Med, 118*(4), 457-466. https://doi.org/10.1016/j.prevetmed.2015.01.010

Power, G.M., Renaud, D.L., Miltenburg, C., Spence, K.L., Hagen, B.N.M., & Winder, C.B. (2024). Graduate Student Literature Review: Perceptions of biosecurity in a Canadian dairy context. *J Dairy Sci, 107*(7), 4605-4615. https://www.journalofdairyscience.org/article/S0022-0302(24)00057-2/fulltext

Proof Strategies. (2023). *2023 Results report proof strategies CanTrust index.* https://proofagency.wpenginepowered.com/wp-content/uploads/2023/02/Proof-Strategies-CanTrust-Index-2023.pdf

Public Health Agency of Canada, PHAC. (2010). *Vancomycin-Resistant Enterococci (VRE). https://www.canada.ca/en/public-health/services/infectious-diseases/nosocomial-occupational-infections/vancomycin-resistant-enterococci.html#q1*

Public Health Agency of Canada, PHAC. (2022a). *Research summary: Antimicrobial use in lactating sows, suckling and nursery pigs. https://www.canada.ca/en/public-health/services/publications/drugs-health-products/research-summary-antimicrobial-use-lactating-sows-suckling-nursery-pigs.html*

Public Health Agency of Canada, PHAC. (2022b, Dec 14). *AMRNet: One Health approach to antimicrobial resistance surveillance.* https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2022-48/issue-11-12-november-december-2022/antimicrobial-resistance-network-one-health-approach-antimicrobial-resistance-surveillance.html

Public Health Agency of Canada, PHAC. (2023a). *Pan-Canadian action plan on antimicrobial resistance.* *https://www.canada.ca/en/public-health/services/publications/drugs-health-products/pan-canadian-action-plan-antimicrobial-resistance.html*

Public Health Agency of Canada, PHAC. (2023b). *Canadian Antimicrobial Resistance Surveillance System (CARSS) report 2022.* https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-antimicrobial-resistance-surveillance-system-report-2022.html

Public Health Agency of Canada, PHAC. (2024a, November 19). *The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) 2023 integrated and key findings* [Webinar]. *chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://cahss.ca/CAHSS/Assets/Documents/CIPARS%202024%20Stakeholder%20Webinar%20Integrated%20deck%20EN_FINAL.pdf*

Public Health Agency of Canada, PHAC. (2024b). *Epidemiology of antimicrobial resistance*. https://www.phac-aspc.gc.ca/cipars-picra/gfx/epi-lg-eng.png

Public Health Agency of Canada, PHAC. (2024c, February 23). *CIPARS: Antimicrobial resistance- temporal trends in antimicrobial resistance (AMR) in bacteria.* https://health-infobase.canada.ca/cipars/antimicrobial-resistance/

Public Health Agency of Canada. (2024d). *Pan-Canadian action plan on antimicrobial resistance: Year 1 progress report (June 2023 to May 2024).* https://www.canada.ca/en/public-health/services/publications/drugs-health-products/pan-canadian-action-plan-antimicrobial-resistance-year-1-progress-report-2023-2024.html

Public Health Agency of Canada, PHAC. (2024e, June 28). *About CIPARS: Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS).* https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars/about-cipars.html

Public Health Agency of Canada, PHAC. (2024f, April 18). *Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS): Design and methods.* https://publications.gc.ca/collections/collection_2023/aspc-phac/HP2-4-2019-3-eng.pdf

Public Health Agency of Canada, PHAC. (2024g Nov 6). *Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS): Data visualization* https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars/interactive-data.html

Public Health Agency of Canada, PHAC. (2024h, Mar 14). *Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) 2022 executive summary: Key and integrated findings.* https://www.canada.ca/en/public-health/services/publications/drugs-health-products/canadian-integrated-program-antimicrobial-resistance-surveillance-2022-executive-summary.html#a6

Public Health Agency of Canada, PHAC. (2024i, May 2). *Canadian Nosocomial Infection Surveillance Program (CNISP)*. https://www.canada.ca/en/public-health/programs/canadian-nosocomial-infection-surveillance-program.html

Puig, A., Ruiz, M., Bassols, M., Fraile, L., & Armengol, R. (2022). Technological tools for the early detection of Bovine Respiratory Disease in farms. *Animals, 12*(19), 2623. https://doi.org/10.3390/ani12192623

Racicot, M., Venne, D., Durivage, A., & Vaillancourt, J.P. (2011). Description of 44 biosecurity errors while entering and exiting poultry barns based on video surveillance in Quebec, Canada. *Prev Vet Med, 100*(3-4), 193-9. https://doi.org/10.1016/j.prevetmed.2011.04.011

Radke, B.R., (2023). *Use of antibiotics in BC livestock and poultry feed 2002 – 2021.* https://www2.gov.bc.ca/assets/gov/farming-natural-resources-and-industry/agriculture-and-seafood/animal-and-crops/bc_in-feed_antibiotic_report_2002-2021.pdf

Rainard, P., Gilbert, F.B., Germon, P., & Foucras, G. (2021). Invited review: A critical appraisal of Mastitis vaccines for dairy cows. *J Dairy Sci, 104*(10), 10427-10448. https://doi.org/10.3168/jds.2021-20434

Regan, Á., Burrell, A., McKernan, C., Martin, H., Benson, T., McAloon, C., Manzanilla, E. G., & Dean, M. (2023). Behaviour change interventions for responsible antimicrobial use on farms. *Irish Veterinary Journal*, *76*(1), 8. https://doi.org/10.1186/s13620-023-00236-x

Renaud, D., & Pardon, B. (2022). Preparing male dairy calves for the veal and dairy beef industry. *Veterinary Clinics: Food Animal Practice, 38*(1), 77-92. https://doi.org/10.1016/j.cvfa.2021.11.006

Responsible Use of Antibiotics in Agriculture Alliance, RUMA. (2022). *Who we are and what we do*. https://www.ruma.org.uk/

Responsible Use of Antibiotics in Agriculture Alliance. (2023). *RUMA targets task force 2: A report summarising the third year of progress against antibiotic use targets identified by the UK livestock industry's targets task force 2 (TTF2).* https://www.ruma.org.uk/wp-content/uploads/2023/10/RUMA-TTF-Report-2023-FINAL.pdf

Rhodes, L., Parrish, K.L., & Willis, M.L. (2023). Review of best practices for biosecurity and disease management for marine aquaculture in U.S. waters. *United States of America Department of Commerce.* https://doi.org/10.25923/b4qp-9e65

Richens, I.F., Hobson-West, P., Brennan, M.L., Lowton, R., Kaler, J., & Wapenaar, W. (2015). Farmers' perception of the role of veterinary surgeons in vaccination strategies on British dairy farms. *Veterinary Record, 177*(18), 465. https://doi.org/10.1136/vr.103415

Roy, J.P., Archambault, M., Desrochers, A., Dubuc, J., Dufour, S., Francoz, D., Paradis, M.-E., Rousseau, M. (2020). New Quebec regulation on the use of antimicrobials of very high importance in food animals: Implementation and impacts in dairy cattle practice. *Canadian Veterinary Journal, 61*(2), 193-196. https://pmc.ncbi.nlm.nih.gov/articles/PMC6973201/

Rudnick, W., Mukhi, S.N., Reid-Smith, R.J., German, G.J., Nichani, A., Mulvey, M.R., the Canadian Public Health Laboratory Network Antimicrobial Resistance Working Group, & the Canadian Animal Health Laboratorians Network Antimicrobial Susceptibility Testing Work Group. (2022). *Overview of Canada's Antimicrobial Resistance Network (AMRNet): A data-driven One Health approach to antimicrobial resistance surveillance. CCDR, 48.* https://www.canada.ca/content/dam/phac-aspc/documents/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2022-48/issue-11-12-november-december-2022/ccdrv48i1112a05-eng.pdf

Salois, M.J., R.A. Cady, and E.A. Heskett. (2016). The environmental and economic impact of withdrawing antibiotics from US broiler production. *Journal of Food Distribution Research. 47*(1), 79-80. https://doi.org/10.22004/ag.econ.232315.

Sanders, P., Vanderhaeghen, W., Fertner, M., Fuchs, K., Obritzhauser, W., Agunos, A., Carson, C., Høg, B.B., Andersen, V.D., Chauvin, C., Hémonic, A., Käsbohrer, A., Merle, R., Alborali, G.L., Scali, F., Stärk, K.D., Muenter, C., van Geijlswijk, I.,... Dewulf, J. (2020). Monitoring of farm-level antimicrobial use to guide stewardship: Overview of existing systems and analysis of key components and processes. *Frontiers in Veterinary Science, 7.* https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2020.00540

Santinello, M., De Marchi, M., Diana, A., Rampado, N., Hocquette, J.F., & Penasa, M. (2022). Effect of commingling animals at sorting facilities on performances and antibiotic use in beef cattle. *Italian Journal of Animal Science, 21*(1), 771-81. https://doi.org/10.1080/1828051X.2022.206376

Santman-Berends, I.M.G.A., van den Heuvel, K.W.H., Lam, T.J.G.M., Scherpenzeel, C.G.M., & van Schaik, G. (2021). Monitoring udder health on routinely collected census data: Evaluating the short- to mid-term consequences of implementing selective dry cow treatment. *J Dairy Sci, 104*(2), 2280-2289. https://doi.org/10.3168/jds.2020-18973

Sargeant, J.M., Bergevin, M.D., Churchill, K., Dawkins, K., Deb, B., Dunn, J., Hu, D., Logue, C.M., Meadows, S., Moody, C., Novy, A., O'Connor, A.M., Reist, M., Sato, Y., Wang, C., & Winder, C.B. (2019). The efficacy of litter management strategies to prevent morbidity and mortality in broiler chickens: A systematic review and network meta-analysis. *Anim Health Res Rev*, *20*(2), 247-262. https://doi.org/10.1017/S1466252319000227

Sargeant, J.M., Deb, B., Bergevin, M.D., Churchill, K., Dawkins, K., Dunn, J., Hu, D., Moody, C., O'Connor, A.M., O'Sullivan, T.L., Reist, M., Wang, C., Wilhelm, B., & Winder, C.B. (2019). Efficacy of bacterial vaccines to prevent respiratory disease in swine: A systematic review and network meta-analysis. *Anim Health Res Rev, 20*(2), 274-290. https://doi.org/10.1017/S1466252319000173

Sargeant, J. M., & O'Connor, A. M. (2020). Scoping reviews, systematic reviews, and meta-analysis: Applications in veterinary medicine. *Front Vet Sci, 7.* https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2020.00011/full

Sawford, K., Vollman, A.R., & Stephen, C. (2013). A focused ethnographic study of Alberta cattle veterinarian's decision making about diagnostic laboratory submissions and perceptions of surveillance programs. *PloS One, 8*(5), 64811. https://doi.org/10.1371/journal.pone.0064811

Scherpenzeel, C.G.M., Santman-Berends, I.M.G.A., & Lam, T.J.G.M. (2018). Veterinarians' attitudes toward antimicrobial use and selective dry cow treatment in the Netherlands. *J Dairy Sci, 101*(7), 6336-6345. https://www.journalofdairyscience.org/article/S0022-0302(18)30276-5/fulltext

Scicchitano, D., Leuzzi, D., Babbi, G., Palladino, G., Turroni, S., Laczny, C., Wilmes, P., Correa, F., Leekitcharoenphon, P., Savojardo, C., Luise, D., Martelli, P., Trevisi, P., Aarestrup, F., Candela, M., Rampelli, S. (2024). Dispersion of antimicrobial resistant bacteria in pig farms and in the surrounding environment. *Animal Microbiome, 6*(17). https://doi.org/10.1186/s42523-024-00305-8

Scott, A. M., Beller, E., Glasziou, P., Clark, J., Ranakusuma, R. W., Byambasuren, O., Bakhit, M., Page, S. W., Trott, D., & Mar, C. D. (2018). Is antimicrobial administration to food animals a direct threat to human health? A rapid systematic review. *International Journal of Antimicrobial Agents*, *52*(3), 316–323. https://doi.org/10.1016/j.ijantimicag.2018.04.005

Schwarz. S., Cavaco, L.M., Shen, J., Aerestrup, F.M. (Eds.). (2018). *Antimicrobial resistance in bacteria from livestock and companion animals*. ASM Press. https://onlinelibrary.wiley.com/doi/book/10.1128/9781555819804

Semex. 2014. *Developing disease resistant, healthier cows is simple: Start with immunity+.* https://www.semex.com/nz/i?lang=en&news=list&pg=16#:~:text=The%20research%20also%20shows%20that,less%20of%20the%20dairyman's%20time

Semex. 2013. *Disease resistant genes.* https://www.semex.com/images/immunity/ENImmunityWebsiteMar2013.pdf

Shamshirgaran, M. A., & Golchin, M. (2024). *Necrotic Enteritis* in chickens: A comprehensive review of vaccine advancements over the last two decades. *Avian Pathology, 54*(1), 1–26. https://doi.org/10.1080/03079457.2024.2398028

Silverberg, S.L., Zannella, V.E., Countryman, D., Ayala, A.P., Lenton, E., Friesen, F., & Law, M. (2017). A review of antimicrobial stewardship training in medical education. *Int J Med Educ, 8,* 353-374. https://www.ijme.net/archive/8/antimicrobial-stewardship-training-in-medical-education/

Silverio, M.P., Kraychete, G.B., Rosado, A.S., & Bonelli, R.R. (2022). *Pseudomonas Fluorescens* complex and its intrinsic, adaptive, and acquired antimicrobial resistance mechanisms in pristine and human-impacted sites. *Antibiotics (Basel)*, *11*(8), 985. https://doi.org/10.3390/antibiotics11080985

Singer, R. S., Porter, L. J., Thomson, D. U., Gage, M., Beaudoin, A., & Wishnie, J. K. (2019). Raising animals without antibiotics: U.S. producer and veterinarian experiences and ppinions. *Frontiers in Veterinary Science*, *6*, 452. https://doi.org/10.3389/fvets.2019.00452

Slifierz, M. J., Friendship, R., & Weese, J. S. (2015). Zinc oxide therapy increases prevalence and persistence of *Methicillin-Resistant Staphylococcus Aureus* in pigs: A randomized controlled trial. *Zoonoses and Public Health*, *62*(4), 301–308. https://doi.org/10.1111/zph.12150

Speksnijder, D.C., Mevius, D.J., Bruschke, C.J.M., & Wagenaar, J.A. (2014). Reduction of veterinary antimicrobial use in the Netherlands: The Dutch success model. *Zoonoses and Public Health 62*(1), 79–87. https://doi.org/10.1111/zph.12167

Speksnijder, D.C., Page, S.W., Wagenaar, J.A., & Prescott, J.F. (2025). Antimicrobial stewardship in food-producing animals. In T.M. Dowling, J.F., Prescott, K.E. Baptiste (Eds)., *Antimicrobial Therapy in Veterinary Medicine* (459-495). Oxford: John Wiley and Sons. https://onlinelibrary.wiley.com/doi/book/10.1002/9781119654629

Sri, A., Bailey, K.E., Scarborough, R., Gilkerson, J.R., Thursky, K., Browning, G.F. & Hardefeldt, L.Y. (2024). Reaching consensus amongst international experts on the use of high importance-rated antimicrobials in animals – A Delphi study. *One Health, 19,* 100883. https://doi.org/10.1016/j.onehlt.2024.100883

Statens Serum Institut. (2023). *DANMAP- The Danish Integrated Antimicrobial Resistance Monitoring and Research Programme- Report*. https://www.danmap.org/reports/2023

Steinburg, J. (2024). *Trust in Canada: Recent trends in measures of trust.* (TRuST) Scholarly Network. Trust-in-canada-recent-trends-in-measures-of-trust-april-2024.pdf

Stewardship of Antimicrobial by Veterinarians Initiative. (2024). *SAVI: The Stewardship of Antimicrobials by Veterinarians Initiative.* https://savi.canadianveterinarians.net/en/home/

Subasinghe, R., Alday-Sanz, V., Bondad-Reantaso, M.G., Jie, H., Shinn, A.P., & Sorgeloos, P. (2023). Biosecurity: Reducing the burden of disease. *World Aquaculture Society, 54*(2), 397-426. https://doi.org/10.1111/jwas.12966

Sukhera, J. (2022, August). Narrative reviews: flexible, rigorous, and practical. *Journal of Graduate Medical Education, 14*(4), 414. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9380636/

Suojala, L., Kaartinen, L., & Pyörälä, S. (2013). Treatment for bovine *Escherichia coli* Mastitis - An evidence-based approach. *J Vet Pharmacol Ther, 36*(6), 521-31. https://doi.org/10.1111/jvp.12057

Swann, D., & Romero, L. (2014). A meta-analysis on effect of a multi-enzyme solution on apparent ileal undigested starch, fat and crude protein in broilers. *Poultry Science, 93*(1), 66–67.

Sweeney, M.T., Gunnett, L.A., Kumar, D.M., Lunt, B.L., Galina Pantoja, L., Bade, D., & Machin, C. (2022). Antimicrobial susceptibility of *Actinobacillus Pleuropneumoniae*, *Bordetella Bronchiseptica, Pasteurella Multocida*, and *Streptococcus Suis* isolated from disease pigs in the United States and Canada, 2016 to 2020. *Journal of Swine Health and Production, 30*(3), 130-144. https://doi.org/10.54846/jshap/1282

Sweeney, M.T., Gunnett, L., Kumar, D.M., Lunt, B.L., Moulin, V., Barrett, M., Gurjar, A., Doré, E., Pedraza, J.R., Base, D., & Machin, C. (2024). Antimicrobial susceptibility of Mastitis pathogens isolated from North American dairy cattle, 2011-2022. *Vet Microbiol, 291,* 110015. https://doi.org/10.1016/j.vetmic.2024.110015

Tang, K. L., Caffrey, N. P., Nóbrega, D. B., Cork, S. C., Ronksley, P. E., Barkema, H. W., Polachek, A. J., Ganshorn, H., Sharma, N., Kellner, J. D., & Ghali, W. A. (2017). Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: A systematic review and meta-analysis. *The Lancet. Planetary health*, *1*(8), 316–327. https://doi.org/10.1016/S2542-5196(17)30141-9

Theurer, M. E., Larson, R. L., & White, B. J. (2015). Systematic review and meta-analysis of the effectiveness of commercially available vaccines against Bovine *Herpesvirus*, Bovine Viral Diarrhea Virus, Bovine Respiratory Syncytial Virus, and *Parainfluenza Type 3* Virus for mitigation of Bovine Respiratory Disease Complex in cattle. *Journal of the American Veterinary Medical Association*, *246*(1), 126–142. https://doi.org/10.2460/javma.246.1.126

Timsit, E., Dendukuri, N., Schiller, I., & Buczinski, S. (2016). Diagnostic accuracy of clinical illness for Bovine Respiratory Disease (BRD) diagnosis in beef cattle placed in feedlots: A systematic literature review and hierarchical Bayesian latent-class meta-analysis. *Prev Vet Med*, *135,* 67-73. https://doi.org/10.1016/j.prevetmed.2016.11.006

Todorov, S.D., Lima, J.M.S., Bucheli, J.E.V., Popov, I.V. , Tiwari, S.K., & Chikindas, M.L. (2024). Probiotics for aquaculture: Hope, truth, and reality. *Probiotics & Antimicro. Prot.* https://doi.org/10.1007/s12602-024-10290-8

Tong, B. (2011). *Canadian organic and raised without antibiotics pork consumer characteristics*. [Master's thesis, University of Guelph]. ProQuest Dissertation & Theses. https://search.proquest.com/docview/859606670?accoun

Torres-Pitarch, A., Hermans, D., Manzanilla, E.G., Bindelle, J., Everaert, N., Beckers, Y., Torrallardona, D., Bruggeman, G., Gardiner, G.E., Lawlor, P.G. (2017). Effect of feed enzymes on digestibility and growth in weaned pigs: A systematic review and meta-analysis. *Animal Feed Science and Technology, 233*, 145-159. https://doi.org/10.1016/j.anifeedsci.2017.04.024

Tóth, A.G., Csabai, I., Judge, M.F., Maróti, G., Becsei, Á., Spisák, S., & Solymosi, N. (2021). Mobile antimicrobial resistance genes in probiotics. *Antibiotics (Basel), 10*(11), 1287. https://doi.org/10.3390/antibiotics10111287

Tremblay, R. (2024). Food animal matters – A role for registered veterinary technicians in food animal practice. *Can Vet J*, *65*(2), 185–188. https://pmc.ncbi.nlm.nih.gov/articles/PMC10783579/

Tridge. (2021, Jan 9). *NETPOULSAFE: A European H2020 network to improve biosecurity compliance in the poultry industry.* https://www.tridge.com/news/netpoulsafe-a-european-h2020-network-to-improve-bi

Trinity, L., Merrill, S.C., Clark, E.M., Koliba, C.J., Zia, A., Bucini, G., & Smith, J.M. (2020). Effects of social cues on biosecurity compliance in livestock facilities: Evidence from experimental simulations. *Front Vet Sci, 7.* https://www.frontiersin.org/journals/veterinary-science/articles/10.3389/fvets.2020.00130/full

Trott, D.J., McWhorter, A., Hewson, K., Abraham, R., & Abraham, S. (2024). Antimicrobial resistance in production animals. *Microbiology Australia, 45*(2). https://www.publish.csiro.au/ma/MA24019

Turkey Farmers of Canada. (2024). *Antibiotics.* https://www.turkeyfarmersofcanada.ca/on-the-farm/antibiotics/#:~:text=Antimicrobial%20Use%20(AMU)%20Strategy&text=Antibiotics%20can%20be%20used%20to,an%20option%20for%20turkey%20farmers

UK Veterinary School Council. (2024). *A new vision for responsible antibiotic use through data safeguarding and optimisation in the UK farm livestock sectors.* Veterinary Schools Council. https://www.vetschoolscouncil.ac.uk/wp-content/uploads/2024/05/VSC-FIIA-AMR-report-lay-summary.pdf

University of Calgary. (2024). *AMR One Health consortium.* https://research.ucalgary.ca/amr/home

Uyama, T., Kelton, D.F., Winder, C.B., Dunn, J., Goetz, H.M., LeBlanc, S.J., McClure, J.T., & Renaud, D.L. (2022). Colostrum management practices that improve the transfer of passive immunity in neonatal dairy calves: A scoping review. *PLoS ONE, 17*(6), 0269824. https://doi.org/10.1371/journal.pone.0269824

Uyama, T., Renaud, D., LeBlanc, S., McClure, J., Slavic, D., Winder, C., & Kelton, D. (2022). Observational study on antimicrobial resistance in *Escherichia coli* and *Salmonella* isolates from Ontario calf samples submitted to a diagnostic laboratory from 2007 to 2020. *Can Vet J*, *63*(3), 260-268. https://pubmed.ncbi.nlm.nih.gov/35237012/

Van Goethem, M.W., Pierneef, R., Bezuidt, O.K.I., Van De Peer, Y., Cowan, D.A., & Makhalanyane, T.P. (2018). A reservoir of 'historical' antibiotic resistance genes in remote pristine Antarctic soils. *Microbiome, 6*(1), 40. https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-018-0424-5

Van Katwyk, S.R., Grimshaw, J.M., & Hoffman, S.J. (2020). Ten years of inaction on antimicrobial resistance: An environmental scan of policies in Canada from 2008 to 2018. *Healthcare Policy, 15*(4), 48-62. https://www.longwoods.com/content/26224/healthcare-policy/ten-years-of-inaction-on-antimicrobial-resistance-an-environmental-scan-of-policies-in-canada-from

van Schaik G., Dijkhuizen, A.A., Benedictus, G., Barkema, H.W., & Koole, J.L. (1998). Exploratory study on the economic value of a closed farming system on Dutch dairy farms. *Vet Rec, 142*(10), 240-242. https://doi.org/10.1136/vr.142.10.240

van Schaik, G., Schukken, Y.H., Nielen, M., Dijkhuizen, A.A., Barkema, H.W., & Benedictus, G. (2002). Probability of and risk factors for introduction of infectious diseases into Dutch SPF dairy farms: A cohort study. *Prev Vet Med, 54*(3), 279-89. https://doi.org/10.1016/S0167-5877(02)00004-1

Varga, C., Brash, M.L., Slavic, D., Boerlin, P., Ouckama, R., Weis, A., Petrik, M., Pilippe, C., Barham, M., & Guerin, M.T. (2018). Evaluating virulence-associated genes and antimicrobial resistance in avian pathogenic *Escherichia coli* isolates from broiler and broiler breeder chickens in Ontario, Canada. *Avian Dis, 62*(3), 291-299. https://doi.org/10.1637/11834-032818-Reg.1

Veeman, M.M., & Li, Y. (2007). Investigating changes in Canadian consumers' food safety concerns, 2003 and 2005. *Ideas*. https://ideas.repec.org/p/ags/ualbnp/7710.html

Verified Beef Protection Plus. (2024). *Simple, practical, trusted.* https://verifiedbeef.ca/

Verified Beef Production Plus. (2021). *About VBP+.* https://www.verifiedbeef.ca/about-vbp/current-vbp-statistics.cfm.html

Wade, J., & Weber, L. (2020). C*haracterization of Tenacibaculum Maritimum and Mouthrot to inform pathogen transfer risk assessments in British Columbia*. Fisheries and Oceans Canada publication. https://waves-vagues.dfo-mpo.gc.ca/library-bibliotheque/40952824.pdf

Wales, A.D., & Davies, R.H. (2015). Co-Selection of resistance to antibiotics, biocides and heavy metals, and its relevance to foodborne pathogens. *Antibiotics*, *4*(4), 567–604. https://doi.org/10.3390/antibiotics4040567

Waldner, M., Kinnear, A., Yacoub, E., McAllister, T., Register, K., Changxi, L., & Jelinski, M. (2022a). Genome-wide association study of *nucleotide* variants associated with resistance to nine antimicrobials in *Mycoplasma bovis*. *Microorganism, 10*(7), 1366. https://doi.org/10.3390/microorganisms10071366

Waldner, C., Wilhelm, B., Windeyer, M.C., Parker, S., & Campbell, J. (2022b). Improving beef calf health: Frequency of disease syndromes, uptake of management practices following calving, and potential for antimicrobial use reduction in Western Canadian herds. *Transl Anim Sci, 6*(4), 151. https://doi.org/10.1093/tas/txac151

Wang, H., Long, W., Chadwick, D., Zhang, X., Zhang, S., Piao, X., & Hou, Y. (2022). Dietary acidifiers as an alternative to antibiotics for promoting pig growth performance: A systematic review and meta-analysis. *Animal Feed Science and Technology, 289,* 115320. https://doi.org/10.1016/j.anifeedsci.2022.115320

Warder, L., Heider, L.C., Léger, D.F., Rizzo, D., McClure, J.T., de Jong, E., McCubbin, K.D., Uyama, T., Fonseca, M., Jaramillo, A.S., Kelton, D.F., Renaud, D.L., Barkema, H.W., Dufour., S., Roy, J., & Sánchez, J. (2023). Quantifying antimicrobial use on Canadian dairy farms using garbage can audits. *Frontiers in Veterinary. Science*, 10. https://doi.org/10.3389/fvets.2023.1185628

Weese, J.S. , Page, S. W., & Prescott, J. F. (2013). Antimicrobial stewardship in animals. In S. Giguère, J.F. Prescott, & P.M. Dowling (Eds.). *Antimicrobial Therapy in Veterinary Medicine* (117-132). Wiley-Blackwell. https://doi.org/10.1002/9781118675014.ch7

Wennekamp, T.R., Waldner, C.L., Parker, S., Windeyer, M.C., Larson, K., & Campbell, J.R. (2021). Biosecurity practices in Western Canadian cow-calf herds and their association with animal health. *Can Vet J, 62*(7), 712-718. https://pubmed.ncbi.nlm.nih.gov/34219779/

Werth, B.J. (2024). *Sulfonamides.* Merck Manual. https://www.merckmanuals.com/en-ca/professional/infectious-diseases/bacteria-and-antibacterial-medications/sulfonamides

Wiencek, I., Hartmann, M., Merkel, J., Trittmacher, S., Kreinbrock, L., & Hennig-Pauga, I. (2022). Temporal patterns of phenotypic antimicrobial resistance and coinfecting pathogens in *Glaesserella Parasuis* strains isolated from disease swine in Germany from 2006 to 2021. *Pathogens 11*(7), 721. https://doi.org/10.3390/pathogens11070721

Winder, C.B., Sargeant, J.M., Hu, D., Wang, C., Kelton, D.F., Leblanc, S.J., Duffield, T.F., Glanville, J., Wood, H., Churchill, K.J., Dunn, J., Bergevin, M.D., Dawkins, K., Meadows, S., Deb, B., Reist, M., Moody, C., & O'Connor, A.M. (2019). Comparative efficacy of teat sealants given prepartum for prevention of intramammary infections and clinical Mastitis: A systematic review and network meta-analysis. *Anim Health Res Rev*, *20*(2), 182-198. https://doi.org/10.1017/S1466252319000276

Winder, C. B., Sargeant, J. M., Kelton, D. F., Leblanc, S. J., Duffield, T. F., Glanville, J., Wood, H., Churchill, K. J., Dunn, J., Bergevin, M. D., Dawkins, K., Meadows, S., & O'Connor, A. M. (2019). Comparative efficacy of blanket versus selective dry-cow therapy: A systematic review and pairwise meta-analysis. *Animal Health Research Reviews*, *20*(2), 217–228. https://doi.org/10.1017/S1466252319000306

Wong, Z.C., Amirah Mohamad Alwie, N., Seng Lim, L., Sano, M., & Tamrin Mohamad Lal, M. (2024) Potential biocontrol for bacterial and viral disease treatment in aquaculture: A minireview. *J Microorg Control, 29*(3), 99-103. https://doi.org/10.4265/jmc.29.3_99

World Health Organization. (n.d.) *Promoting antimicrobial stewardship to tackle antimicrobial resistance.* https://www.who.int/europe/activities/promoting-antimicrobial-stewardship-to-tackle-antimicrobial-resistance

World Health Organization. (2017, September 21). *One Health.* https://www.who.int/news-room/questions-and-answers/item/one-health

World Health Organization. (2024a). *WHO list of medically important antimicrobials: A risk management tool for mitigating antimicrobial resistance due to non-human use.* https://cdn.who.int/media/docs/default-source/gcp/who-mia-list-2024-lv.pdf?sfvrsn=3320dd3d_2

World Health Organization. (2024b). *Antimicrobial resistance.* https://www.who.int/health-topics/antimicrobial-resistance

World Health Organization. (2024c). *WHO bacterial priority pathogens list, 2024: Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance.* https://www.who.int/publications/i/item/9789240093461

World Organisation for Animal Health. (2020). *OIE standards, guidelines and resolutions on antimicrobial resistance and the use of antimicrobial agents.* https://www.woah.org/app/uploads/2021/03/book-amr-ang-fnl-lr.pdf

World Veterinary Association. (2024, February 19). *Dr. Shane Renwick, part of CVMA staff, is the winner of medicine stewardship category of the WVA global veterinary awards.* https://worldvet.org/news/dr-shane-renwick-part-of-cvma-staff-is-the-winner-of-medicine-stewardship-category-of-the-wva-global-veterinary-awards/

Yang, Y., Xie, X., Tang, M., Liu, J., Tuo, H., Gu, J., Tang, Y., Lei, C., Wang, H., & Zhang, A. (2020). Exploring the profile of antimicrobial resistance genes harboring by bacteriophage in chicken feces. *Sci Total Environ, 700,* 134446. https://doi.org/10.1016/j.scitotenv.2019.134446

Yazdankhah, S., Rudi, K., & Bernhoft, A. (2014). Zinc and copper in animal feed – Development of resistance and co-resistance to antimicrobial agents in bacteria of animal origin. *Microbial Ecology in Health and Disease, 25*(1). https://pmc.ncbi.nlm.nih.gov/articles/PMC4179321/

Zamudio, R., Boerlin, P., Mulvey, M.R., Haenni, M., Beyrouthy, R., Madec, J.-Y., Schwarz, S., Cormier, A., Chalmers, G., Bonnet, R., Zhanel, G.G., Kaspar, H., & Mather, A.E. (2024). Global transmission of extended-spectrum cephalosporin resistance in *Escherichia coli* driven by epidemic plasmids. *EBioMedicine, 103,* 105097. https://doi.org/10.1016/j.ebiom.2024.105097