National Beef Antimicrobial Research Strategy

MAY 2016



NATIONAL BEEF VALUE CHAIN ROUNDTABLE

Table of Contents:

I. Executive Summary	3
II. Background	4
III. Antimicrobial Resistance Research	10
Context:	10
5 Year Research Review:	10
Summary of Workshop Discussions:	10
Priority Research and Surveillance Outcomes for Antimicrobial Resistance	11
IV. Antimicrobial Use Research	12
Context:	12
Five-Year Research Review:	12
Summary of Workshop Discussions:	12
Priority Research and Surveillance Outcomes for Antimicrobial Use	13
V. Antimicrobial Alternatives	14
Context:	14
Five-Year Research Review:	14
Summary of Workshop Discussions:	14
Priority Research Outcomes for Antibiotic Alternatives	15
VI. Non Research Priorities	16
VII. Research Funding Priority Coordination	17
VIII. Appendix A: Target Antimicrobial Research and Surveillance Outcomes	18
IX. Appendix B: Workshop Invitees	20

I. Executive Summary

The continued effectiveness of antimicrobials as a tool to combat bacterial infections in human health has been a growing concern in recent years. Numerous international reports have noted increasing resistance to one or more antimicrobials of "last resort" in human medicine.

In addition to their clear importance in human and veterinary (food animals and companion animals) medicine, antimicrobials are used in horticulture, aquaculture, apiculture, and some household sanitizers. However, data reported in the Canadian Integrated Program for Antimicrobial Surveillance (CIPARS) indicates that approximately 80% of all medically important antimicrobials sales (total kg basis) in Canada are for livestock use.

This has led to questions about the contribution modern beef production makes to antimicrobial resistance in human medicine, pressures to reduce antimicrobial use in beef production, and a need to develop, identify and implement effective alternatives to antimicrobials for the beef industry. Research will play a critical role in each of these areas.

This strategy was developed by the Beef Cattle Research Council (BCRC) and the National Beef Value Chain Roundtable (BVCRT) following comprehensive analysis of the antimicrobial research situation relevant to the Canadian beef sector, extensive consultation and validation with all major stakeholder groups, and collaboration with funders toward coordinating and aligning funding priorities. This National Beef Antimicrobial Research Strategy identifies priority research outcomes for the Canadian beef industry and has gained the commitment from Canada's major research funders to focus on achieving these outcomes.

Research outcomes have been defined in the priority areas of:

- Antimicrobial Resistance,
- Antimicrobial Use, and
- Antimicrobial Alternatives

The National Beef Research Inventory, a comprehensive database where funding agencies share their research funding portfolios, was used to identify how and where antimicrobial related research funding has been allocated among antimicrobial resistance, use and alternatives research since January 1, 2012. Having established the current funding landscape, priority research outcomes were established through a series of breakout groups that engaged over 60 invitees representing various industry sectors (production, veterinary health, pharmaceutical, feeds), researchers and funding agencies (industry and provincial and federal government). The outcomes were further reviewed by the Science Advisory Panel for the Beef Cattle Industry Science Cluster, the National Beef Value Chain Roundtable Research Committee, and the BCRC for feedback and approval.

The outcomes for each priority area are presented in this document (Appendix A). The research priority sections include an overview of the research priority, summary of research funded over the past five years, discussions around where research focus is needed next, and the specific research outcomes that need to be achieved.

This is a dynamic document and process which is intended to continue to evolve based on stakeholder feedback and ongoing review as research outcomes are achieved and new outcomes arise. Feedback is welcome at any time and can be directed to the BCRC.

II. Background

The National Beef Value Chain Roundtable and Beef Cattle Research Council recognized the need to review the beef research situation in Canada and, starting in 2008, initiated a process that led to the development of the 2012 **National Beef Research Strategy**. The National Beef Research Strategy will be renewed in 2016.

The <u>Beef Cattle Research Council</u> (BCRC) is Canada's national industry-led funding agency for beef research, investing 18 per cent on average of every National Check-off dollar in research. The BCRC funds research and development programs focused on improving the competitiveness and sustainability of Canada's beef industry. As the national beef industry research funding body, the BCRC has a responsibility to take the lead in coordinating research, identifying research priorities and defining target industry research outcomes.

The <u>National Beef Value Chain Roundtable (BVCRT)</u> was established by the federal minister of agriculture in 2003. It is comprised of industry and government representatives representing the entire value chain and has provided leadership in addressing issues of importance to Canada's beef industry. The BVCRT identified research as a key priority and subsequently formed a working group in partnership with the BCRC to develop a National Beef Research Strategy in consultation with all stakeholders from industry, provincial governments, and the federal government through Agriculture and Agri-Food Canada (AAFC).

In light of the urgency and attention paid to antimicrobials, the BCRC and BVCRT deemed it prudent to develop a specific National Beef Antimicrobial Research Strategy for antimicrobial resistance, use and alternatives in advance of renewing the National Beef Research Strategy in 2016.

A comprehensive approach has been undertaken to develop this National Beef Antimicrobial Research Strategy including:

- Using the National Beef Research Inventory to review antimicrobial research investments relevant to cattle and beef since 2012,
- Consulting with stakeholders and a focused workshop to identify priority research outcomes for antimicrobial resistance, antimicrobial use and alternatives, and
- Collaboration with funders to ensure that research funding allocations adequately address industry research priorities, and develop a framework to work together on enhancing extension activities.

RATIONALE FOR A NATIONAL BEEF ANTIMICROBIAL RESEARCH STRATEGY

The central issue: There are serious concerns that antimicrobial resistance is threatening the effectiveness of medically important drugs, and that antimicrobial use in livestock production is contributing to this problem.

Antimicrobials have been tremendously important tools to combat bacterial infections since the use of penicillin became widespread after World War II. Antimicrobials have found valuable applications in human, pet and livestock medicine as well as horticulture (e.g. streptomycin to control fire blight in apples), aquaculture (oxytetracycline to control a variety of conditions in farmed fish and lobster), apiculture (e.g. tylosin for the control of foulbrood in honeybees), and in industrial and household chemicals (e.g. triclosan in hand sanitizers).

Antimicrobials are found in nature. Soil microorganisms produce and secrete antimicrobials as a way to compete with each other for preferred food sources and living conditions. Predictably, microorganisms have also developed counter-defences that enable them to resist antimicrobials produced by other species, so antimicrobial resistance is also a natural phenomenon.

Consequently, regardless of the antimicrobial used, or the reason for its use, exposing bacteria to antimicrobials will kill susceptible bacteria, while resistant bacteria will survive and reproduce. Over time, the frequency of antimicrobial resistance genes will increase and spread in the population.

For many years, the regular discovery of new classes of antimicrobials with different modes of action meant that antimicrobial resistance was a relatively minor concern. The regular development of novel antimicrobials meant that antimicrobial resistant infections could still be treated with a newer drug. However, no new antimicrobial classes have been developed and commercialized since the mid 1980's. As a result, veterinary and medical practitioners are not only faced with an increasing proportion of antimicrobial resistant infections, but also a "fixed" set of antimicrobials to combat them.

Global perspective: According to the World Health Organization (WHO), antimicrobial resistance is an increasingly serious threat to global public health, which requires action (WHO 2014 <u>http://www.who.int/mediacentre/news/releases/2014/amr-report/en/</u>). The human cost of antimicrobial resistance is significant and estimated to be the primary cause of over 23,000 deaths, over 2M illnesses and up to \$20B direct costs to the economy in the USA alone (WHO 2014). A 2014 UK study estimated that up to 10M deaths due to antimicrobial resistance a year were possible by 2050 if no action is taken to prolong the effective use of antimicrobials (<u>http://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations 1.pdf</u>). As a result, the 2015 WHO Global Action plan on antibiotic resistance called on governments to enact five strategic objectives (http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763 eng.pdf?ua=1):

- 1. to improve awareness and understanding of antimicrobial resistance;
- 2. to strengthen knowledge through surveillance and research;
- 3. to reduce the incidence of infection;
- 4. to optimize the use of antimicrobial agents; and
- 5. develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

The international nature of the antimicrobial resistance issue was recently highlighted by a November 2015 report (Emergence of plasmid–mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Liu, Yi-Yun et al. 2015. The Lancet Infectious Diseases 16:161-168, <u>http://dx.doi.org/10.1016/S1473-3099(15)00424-7</u>) that reported that a gene conferring resistance to colistin (a category 1 antibiotic) previously found only on the *E. coli* chromosome had now been identified on a plasmid, allowing its transfer among different *E. coli* strains. Within weeks, the mobility and speed of antimicrobial resistance genes and the importance of travel-related antimicrobial resistance was underscored by subsequent findings of the plasmid-associated *mcr*-1 gene in Germany, Vietnam, Cambodia, Switzerland, Japan, France, Belgium and Canada.

Globally, antimicrobial use in food animals may increase by as much as 67% by 2030, with most of that increase expected to occur in China and India as their economies develop, incomes rise, and domestic livestock production grows to meet rising demand for high quality diets (van Boeckel et al. 2015. Proc. Natl. Acad. Sci, <u>http://www.pnas.org/content/112/18/5649.long</u>).

Canadian perspective: The Government of Canada released its Action Plan on Antimicrobial Resistance and Use in Canada in October 2014 (<u>http://healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/action-plan-daction-eng.php? ga=1.189027240.265955927.1454086118) that included four key actions:</u>

- 1. establish and strengthen surveillance systems to identify new threats or changing patterns in antimicrobial resistance and use, in human and animal settings,
- 2. strengthen the promotion of the appropriate use of antimicrobials in human and veterinary medicine,
- 3. work with the animal agriculture sector partners to strengthen the regulatory framework on veterinary medicines and medicated feeds, including facilitating access to alternatives and encourage the adoption of practices in order to reduce the use of antimicrobials, and
- 4. promote innovation through funding collaborative research and development efforts on antimicrobial resistance both domestically and internationally.

As part of the federal Action Plan, production (growth promotion and feed efficiency) claims for medically important antimicrobials (i.e. categorized as very high, high or medium importance in human medicine) are being removed (target date of December 2016) and increased veterinary oversight is being defined for antimicrobials used in feed or water. Regulatory changes are being developed for tighter control of imported antimicrobial products and active pharmaceutical ingredients.

Eight federal government departments and agencies (including Agriculture and Agri-Food Canada, the Canadian Food Inspection Agency, the Public Health Agency of Canada, Health Canada, and the National Research Council) are launching a 5 year (CDN\$20M) Genomics Research and Discovery Initiative (GRDI) project on critical factors that lead to antibiotic resistance and the pathways by which antimicrobial resistant bacteria reach humans. Further actions can be expected.

Surveillance is the cornerstone for planning antimicrobial resistance mitigation strategies. CIPARS is the program by which government reports antibiotic resistance in livestock, poultry and meat. As shown in Table 1, CIPARS surveillance of the hog/pork and broiler/poultry sectors is broader (on-farm use and resistance, abattoir and retail resistance) and covers a wide range of bacteria (*E. coli, Campylobacter* and *Salmonella*) than in cattle/beef (no national on-farm use or resistance component, with abattoir and retail resistance focused solely on *E. coli*). As discussed below, CIPARS data on *E. coli* isolated from the beef cattle in the abattoir have consistently shown a minor prevalence of resistance, usually limited to tetracycline and streptomycin, which have not increased significantly since CIPARS began in 2002.

Table 1: CIPARS metrics in Canadian livestock and meat					
Location	Metric	Broiler/Chicken	Swine/Pork	Cattle/Beef	
On-farm	Antimicrobial use	Yes	Yes	No	
	E. coli	Yes	Yes	No	
	Salmonella	Yes	Yes	No	
	Campylobacter	Yes	No	No	
Abattoir	E. coli	Yes	Yes	Yes	
	Salmonella	Yes	Yes	No	
	Campylobacter	Yes	Yes	Yes	
Retail meat	E. coli	Yes	Yes	Yes	
	Salmonella	Yes	No	No	
	Campylobacter	Yes	No	No	

In addition to ongoing CIPARS reports, CIPARS also provides information to the recently established Canadian Antimicrobial Resistance Surveillance System (CARSS). The most recent CIPARS report shows antimicrobial use in livestock and poultry remaining stable since 2006. In early 2016, screening genomic sequences of historical CIPARS isolates led to the discovery of the plasmid-associated *mcr*-1 gene in Canadian retail beef, though the origin of either the beef (imported or domestic) or the gene (e.g. cattle or human) could not be confirmed.

In Canada, livestock account for 79.8% of the distribution and sale of all medically important antimicrobials, with the rest going to humans (19.4%) and pets (0.7%) (CIPARS 2012 Annual Report, Chapter 4).In treating bacterial infections, human medicine relies heavily on antimicrobials of very high importance (e.g. β -lactams; 47%, fluoroquinolones; 8%), little on medium importance antimicrobials (e.g. tetracycline; 3%), and uses no antimicrobials of low medical importance (e.g. β -lactams; 9% and fluoroquinolones; < 1%), relying more on antimicrobials of medium (tetracyclines; 39%) or low medical importance (ionophores, 30%). Species-specific antimicrobial use data is not available for livestock.

Beef industry perspective: Antimicrobials have been used to prevent, control or treat disease and improve productivity in beef cattle for more than 50 years. Depending on the situation, antimicrobials can be administered to beef cattle by individual injection or through feed or water (which will be subject to increased veterinary oversight with anticipated regulatory changes). Antimicrobials may be used to treat disease (in cattle diagnosed with illness), control disease (when illness is spreading in a herd) prevent disease (in healthy cattle that are likely to be exposed to disease), or to improve growth and feed efficiency in cattle (claims which will no longer be acceptable in medically important antimicrobials as of December 2016).

Canada's beef industry has been a leader in Canadian antimicrobial research for nearly 20 years, beginning with large-scale antimicrobial resistance studies funded under the Canada-Alberta Beef Industry Development Fund in the late 1990s. A series of subsequent industry-supported studies have included on-farm antimicrobial resistance and antimicrobial use data collection pilots in collaboration with CIPARS, and collection and comparison of genetic determinants of antimicrobial resistance in bacteria isolated from cattle and humans. Currently, large-scale research under the second Beef Science Cluster (2013-18) is examining the potential for antimicrobial resistance transmission from commercial feedlot cattle to humans through retail beef as well as environmental transmission through soil and water. All three of these large scale studies featured international collaborations between industry, provincial, and federal researchers representing both the agricultural and human medical research communities.

In addition to research investments, Canada's beef industry has closely monitored CIPARS and international antimicrobial surveillance results pertaining to cattle and beef, developed and implemented the Verified Beef Production on-farm food safety program (VBP), and made efforts to communicate the importance and science of antimicrobial resistance to producer, veterinarian, student and policy audiences.

Antimicrobial resistance and the longer-term approach to this issue have been discussed by the BVCRT. The BVCRT recommended that a workshop be held to develop a strategy and research priorities for antimicrobials that would be broadly supported by a cross-section of the industry from producers, veterinary practitioners, scientists, funding organizations and government staff. The workshop was held in Calgary, Alberta on December 10-11, 2015.

Due to the high priority placed on antimicrobial resistance and use, there is increasing awareness of, and interest expressed in increasing research funding investments related to antimicrobial resistance,

antimicrobial use and antimicrobial alternatives in livestock at both the federal and provincial level. Canada's beef industry has a responsibility and an opportunity to help guide and direct these investments to achieve the most meaningful priority outcomes relevant to both the beef industry and the Canadian public.

This approach is consistent with the Beef Cattle Industry Science Cluster concept, which has seen the largest industry and government funding agencies, BCRC and AAFC respectively, partner with other industry (Alberta Beef Producers, Beef Farmers of Ontario, Manitoba Beef Producers, Quebec Beef Producers Federation, Elanco) and government (Alberta Livestock and Meat Agency, Saskatchewan Agriculture Development Fund) organizations to deliver research addressing a set of key research outcomes. The coordination of resources and alignment of research with industry priorities as a result of the Science Cluster has led to a significantly increased level of industry research investment and leadership, capacity development in critical areas, improved research collaboration across research institutions, and a technology transfer and knowledge dissemination strategy focused on delivering applied research results to industry.

In the 2012 National Beef Research Strategy, eight target research outcomes related to antimicrobial resistance, use and alternatives were included in the Food Safety and the Animal Health and Welfare priority areas. They were:

Food Safet	y .
Outcome 1:	Improved Food Safety along the Beef Supply Chain
2018	c. Effective probiotic intervention to eliminate pathogens from beef developed.
Outcome 2:	Responsible Antimicrobial Use Demonstrated
2016	 a. On-farm data collection and food safety pathogen incidence incorporated into the Canadian Integrated Program for Antimicrobial Resistance Surveillance for beef cattle. b. Microbial genome sequencing used to investigate potential associations between pathogen incidence and antimicrobial use in cattle and the presence of pathogens and development of antimicrobial resistance in microbes found in retail beef and human
2018	 a. Statistics collected through the Canadian Integrated Program for Antimicrobial Resistance Surveillance (surveillance) demonstrate that: generic <i>E. coli</i> samples collected from <u>abattoir</u> samples demonstrate 0% resistance to five or more antimicrobials and 0% resistance to antimicrobials of very high importance in human health, and generic <i>E. coli</i> samples collected from <u>retail beef</u> demonstrate less than 2% resistance to five or more antimicrobials, and less than 1% resistance to antimicrobials of very high importance in human health.
Animal Hea	alth and Welfare
Outcome 3:	Improved Prevention of Animal Disease and Welfare Issues
2016	 a. Strategies to optimize or improve the effectiveness of existing vaccination programs identified and developed. d. Modifications to current beef production practices that reduce the need for antimicrobials to prevent or treat respiratory disease in the feedlot identified or developed (e.g. vaccination, weaning, transport and diet).
2018	b. Improved immune system function, vaccine efficacy and animal health management
	to reduce the need for Health Canada Category I and II antimicrobial drugs by 50%.
2023	a. Reduced incidence of metabolic diseases in beef feedlots without increased use of antimicrobials.

National Beef Research Inventory perspective: In preparation for the Antimicrobial Resistance, Use and Alternatives Workshop, the National Beef Research Inventory was queried for projects and funding allocations relevant to these eight outcomes. Approximately 8% of total funding (\$8.7 million out of \$104.5 million total funding recorded) was assigned to research relevant to antimicrobial resistance, use or alternatives (Figure 1).



Figure 1: 2012-15 Beef Science Cluster Funding Allocation by Priority Area

The 8% of funding allocated to antimicrobial research was further subdivided into the three areas of interest for the workshop (antimicrobial resistance, use, and alternatives) to compare investments and areas of focus within each area of interest to guide further discussion, identify gaps, and refine outstanding target research outcomes (Table 2).

Table 2: Research funding allocations across 14 Canadian funding agencies for antimicrobial resistance, use, and alternatives in beef cattle (January 1, 2012 to December 1, 2015).

	\$	%
Total Beef Research Funded	\$104,531,584	100 %
Antimicrobial Related Research Funded	\$8,748,232	8.37%
Antimicrobial Resistance	\$1,213,046	1.16%
Antimicrobial Use	\$359,374	0.34%
Antimicrobial Alternatives	\$7,175,862	6.86%

Workshop participants then divided into three breakout groups to discuss and identify research and surveillance priorities for antimicrobial resistance, antimicrobial use and antimicrobial alternatives.

III. Antimicrobial Resistance Research

Context: Antimicrobial resistance research is an ever evolving field. It is increasingly recognized that antimicrobial resistance concerns and expertise can be found in both livestock and human health, opening more opportunities for collaborative research approaches than ever before. New technologies allow new antimicrobial resistance genes and transfer mechanisms to be discovered on a regular basis, and allow much more precise evaluation of the degree of relatedness between antimicrobial resistance genes and bacterial isolates collected from humans and animals. CIPARS does not conduct national onfarm antimicrobial resistance surveillance for beef or dairy cattle or bob/veal calves, although they do for broilers and swine (Table 1). CIPARS does play an important role in routine collecting and antimicrobial resistance testing of bacteria isolated from healthy feedlot finished cattle at abattoirs (*E. coli* and *Campylobacter*) and retail beef (*E. coli*).

5 Year Research Review: Of the 8% (\$8.7 million) of total national beef research funding allocated to antimicrobial related research since January 1, 2012, 1.2% (\$1.21 million) was directed towards antimicrobial resistance research (Table 2). This funding was directed towards two broad categories, antimicrobial resistance to cattle pathogens and antimicrobial resistance to indicator organisms and human pathogens.

Research into antimicrobial resistance in cattle pathogens focused on *Mycoplasma bovis*, long-term historical changes in antimicrobial sensitivity and virulence of *Histophilus somni*, the effects of pathogen prevalence and antimicrobial resistance on the incidence of bovine respiratory disease (BRD) in cattle, and surveillance screening of antimicrobial susceptibility in feedlot cattle.

One large-scale research project with a greater human health focus is examining antimicrobial resistance in *E. coli* (an indicator organism) and Enterococci (an indicator organism and potential human pathogen) in samples collected from feedlot-associated and downstream environments, including municipal water, retail beef and human clinical isolates. The scope of the sampling and collaboration involved in this trial has enabled the addition of several related projects. One of these is investigating the potential role of integrative conjugative elements in transferring antimicrobial resistance determinants among livestock species and humans; another is examining the survival and degradation of antimicrobial resistance genes and bacteria in manure, soil and water. Other One Health projects (i.e. integrated studies incorporating human-animal-environment interactions) are examining antimicrobial resistance to integrate surveillance data from human, animal, food and environmental sources to analyze and model antimicrobial resistance transmission and risks.

Summary of Workshop Discussions: The breakout groups were challenged to identify the current gaps in understanding and surveillance of antimicrobial resistance, and to establish priorities for antimicrobial resistance research.

It was noted that although research and surveillance are different activities, they are interconnected. Surveillance is the cornerstone for monitoring antimicrobial resistance, provides early indications of potential increases of antimicrobial resistance to the different classes of antimicrobials, and informs many research questions. Antimicrobial resistance is a very complex and continuously evolving issue. For instance, the 2013 CIPARS report indicated that *E coli* isolates collected from healthy beef cattle at the abattoir with resistance to 4-5 classes of antimicrobials had increased from 1% in 2012 to 8% in 2013, while resistance to category 1 antimicrobials had declined from 19% to 9% during the same time period. CIPARS conducts antimicrobial resistance surveillance in more locations and bacteria in pigs and poultry

than in beef (Table 1). Further, CIPARS reliance on *E. coli* as an indicator of antimicrobial resistance in beef cattle provides no information on macrolide resistance, because Gram-negative bacteria like *E. coli* are intrinsically resistant to macrolides. Inclusion of a Gram-positive indicator (e.g. *Enterococcus hirae*) would be beneficial. The lack of on-farm CIPARS data pertaining to antimicrobial use or resistance on beef operations is another identified gap.

CIPARS abattoir samples are collected only from healthy feedlot finished cattle. No information about antimicrobial resistance is available from dairy cows, beef cows, or bob/veal calves. CIPARS abattoir and retail surveillance also rely on indicator (*E. coli*) and zoonotic bacteria (*Campylobacter*) that seldom cause infectious disease in cattle and are not the target of antimicrobial use in beef production. Because antimicrobial use on beef operations is primarily driven by treatment for bovine respiratory disease, including one of these pathogens (e.g. *Mannheimia haemolytica*) in a CIPARS on-farm antimicrobial resistance surveillance program for beef is important. It would provide considerable relevant information to define how antimicrobial use to combat animal disease in beef operations impacts antimicrobial resistance in indicator organisms sampled in abattoir and retail meat surveillance. This would also contribute to more effective communications to veterinarians and producers at both the cow-calf and feedlot levels.

Most of the antimicrobial resistance information collected on-farm has been of a private nature and unavailable in the public domain. Apart from general surveillance of antimicrobial resistance in cattle operations there is also a need for more clinical work to determine how specific treatments using different classes of antimicrobials impact the development of antimicrobial resistance. This work is expensive to conduct, but producers and veterinary professionals need better information, particularly regarding how cow-calf, dairy and bob/veal calf production practices may impact the development of antimicrobial resistance through the beef production system. Diagnostic procedures for surveillance tend to be time consuming and expensive, so improvements in reducing the cost and time to get results would be an important step forward for the management of antimicrobial resistance. A rapid, cost-effective chute-side diagnostic test analogous to human point of care tests would have tremendous potential for refining antimicrobial use recommendations and practices in the feedlot sector. Improved coordination and standardization between animal health surveillance surveillance (CIPARS) should be strongly encouraged. Compilation of this data could provide an industry-wide perspective on antimicrobial resistance.

The use of antimicrobials at the farm level and the development of antimicrobial resistance is an important issue for veterinarians and livestock producers, but the potential transfer of this resistance to humans through animal products or the environment is of increasing concern. Thus the One Health approach to better understand how practices at the farm level impact antimicrobial resistance and human health is considered to be a high priority. The federal government's <u>Genomic Research and</u> <u>Development Initiative</u> on antimicrobials will focus on the One Health approach, consistent with the Federal Action Plan on antimicrobial resistance.

Priority Research and Surveillance Outcomes for Antimicrobial Resistance

<u>Desired Outcome</u>: Evidence-based decision making and communication to the veterinary, producer and medical communities.

• Increase CIPARS activities to encompass on-farm, abattoir and retail beef antimicrobial resistance surveillance, including *Enterococcus hirae* or other indicator organisms that are informative with regard to macrolide resistance.

- Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.
- Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.
- Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.
- Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settings.
- Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases.
- Develop methodology to evaluate, monitor and curtail the potential movement of antimicrobial resistance genes from cattle associated environments to human environments through manure, soil, food and water.

IV. Antimicrobial Use Research

Context: Antimicrobial resistance is natural, so some baseline level of resistance will always exist in bacterial populations. Increased antimicrobial use increases the prevalence of antimicrobial resistance, although the time it takes for resistance to develop is both bacteria and antibiotic-dependent. CIPARS tracks on-farm antimicrobial use in the broiler and swine sectors but not in beef, although a framework to do so has been developed. Antimicrobial use data in beef cattle is extremely limited. Some Canadian antimicrobial use data has been collected in feedlot-level pilot studies; cow-calf antimicrobial use data is much less well documented, and still less data exists for market dairy cows and bob/veal calves.

Five-Year Research Review: Of the 8% (\$8.7 million) of total national beef research funding allocated to antimicrobial research since January 1, 2012, 0.3% (\$359,374) was directed towards antimicrobial use research (Table 2). One project is examining the impact of antimicrobial use on antimicrobial resistance in BRD pathogens. A second project has surveyed cow-calf producers with questions pertaining to reasons for antimicrobial use, the class of animal antimicrobials are typically used on, the antimicrobial used, the percentage of animals treated, the typical number of treatment days per animal, attitudes towards antibiotic use, and decision making strategies for antibiotic use. Thirdly, a project (building on the large scale feedlot-associated environment antimicrobial resistance project described earlier) is evaluating how the use of both in-feed and injectable antimicrobials in different classes of feedlot cattle has changed in recent years, assessing collection logistics, and comparing different methods of quantifying antimicrobial use (e.g. number of days treated or doses given, kg active ingredient used, animal defined daily dose, population corrected units, etc.).

Summary of Workshop Discussions: The breakout groups were charged with evaluating whether Canada's beef industry needs a database to record antibiotic usage in beef cattle, what level of detail is needed to have useful data on antibiotic use in beef cattle, what level of cooperation would be required to report on antibiotic usage, which organization should take leadership in managing the database, how this data would be used and who the data would be available to.

CIPARS collects antimicrobial use data for both the poultry and pork sectors but not the beef industry due to CIPARS funding limitations. Several industry groups are positioned to facilitate the collection of

antimicrobial use data, including VBP, feedlots, veterinarians, the Canadian global Food Animal Residue Avoidance Database (CgFARAD), and feedmills. However, there is no uniform method of recording, reporting or housing this information. Appropriate use is difficult to define or defend without reliable data that describes antimicrobial use practices in beef cattle production.

An antimicrobial use database must have a clearly defined purpose, quantify what will be measured (e.g. animal category and weight, product used, dose of product given, amount of active ingredient, animal defined daily dose), describe who does the collection, and ensure data privacy will be maintained. Some of the issues with managing an antimicrobial use database are akin to those of the livestock identification program which the industry has been able to effectively manage.

An antimicrobial use database would allow the industry to be transparent about its practices and inform future research priorities. Better antimicrobial use data may increase pressure to further reduce antimicrobial use, but that pressure is inevitable. Benchmarking of antimicrobial use has had some proven value in countries where it has been used to compare differences between producers or veterinarians, and to identify where management interventions are needed. The industry would be in a much better position to define appropriate use than it is without antimicrobial use data. Industry leadership on this issue would provide objective information on antimicrobial use and may help prevent government and/or food retailers from regulating or imposing changes on industry animal health practices. There was consensus from workshop participants that an antimicrobial use database would be challenging and require a great deal of collaboration.

Several main themes were apparent. The system must be industry-led, cost-effective, user-friendly, and able to ensure the confidentiality of individual producers, operations, veterinarians and veterinary practices. Comprehensive antimicrobial use data would be ideal, but cost implications mean that a random or sentinel data collection system may be more realistic. Antimicrobial use data collection should be focused on the highest risk sectors (which have not been identified; e.g. feedlot, cow-calf, dairy, veal and bob calf operations). To provide meaningful context and value, antimicrobial use data collection and analysis must not be viewed as a standalone activity, but rather packaged and communicated with antimicrobial resistance information to drive adoption of best practices.

It was noted that tylosin and tetracycline to control liver abscesses account for the majority of antimicrobial use in the beef industry. Significantly reducing these practices would contribute to a significant reduction in overall antimicrobial use by the beef industry (discussed further under "antimicrobial alternatives").

Creating a database so baseline estimates of antimicrobial use can be determined will require a great deal of consultation and collaboration. Work in this area will likely need an industry/government committee to establish the parameters and perhaps this would be best done through the BVCRT. Together with an industry advisory board, CIPARS is well positioned to oversee and coordinate the database, given its long experience and expertise in data collection for the pork and poultry industries and its international relationships.

Priority Research and Surveillance Outcomes for Antimicrobial Use

<u>Desired Outcome</u>: Ensure that Canada's beef industry continues to have access to antimicrobials to protect animal health and welfare by developing a database to quantify and defend responsible antimicrobial use in beef production.

• Establish a working group to determine the governance, structure, potential data sources (veterinary, farm and feedlot data, CgFARAD, VBP, etc.), data collection methodology (e.g.

sentinel vs. random sampling), data reporting (e.g. kg active ingredient, animal defined daily doses, population corrected unit, etc.) and resources required to develop an antimicrobial use database for the beef industry.

- Conduct pilot projects to identify which sectors of the beef and veal industries (cow-calf, feedlot, dairy, bob/veal) pose the greatest antimicrobial use risk (classes of antimicrobials used, treatment rates, etc.).
- Develop a database to track antimicrobial use in sectors deemed to be highest risk (based on the two preceding points).
- Use the database to monitor changes in antimicrobial use over time and relate changes in antimicrobial use practices to changes in antimicrobial resistance in cattle pathogens and indicator organisms isolated from cattle, beef and cattle-associated environments.

V. Antimicrobial Alternatives

Context: A wide variety of antimicrobial alternatives have been investigated over the years. Several, including low-stress weaning, vaccination, environmental and nutritional adaptation, low stress animal handling and transportation, direct marketing to feedlots, and preconditioning have demonstrated effectiveness in applied research situations. Other alternatives, including bacteriophage, essential oils, tannins, phenolics, seaweed extracts, citrus products, organic acids, direct fed microbials, prebiotics, probiotics, bacteriocins and rapid diagnostics, have so far shown inconsistent efficacy and require further research and development.

Five-Year Research Review: Of the 8% (\$8.7 million) of total national beef research funding allocated since January 1, 2012, 6.9% (\$7.2 million) was directed towards antimicrobial alternatives research (Table 2).

The majority of these funds (56%) were directed toward vaccine-related research (antigen characterization, vaccine development, vaccine delivery studies), and focused primarily on common production limiting diseases pathogen (e.g. BVD, *Mannheimia haemolytica, Mycoplasma bovis, Histophilus somni*). Research focused on nasal and oral pre/pro/synbiotics to combat respiratory pathogens or replace antimicrobial growth promoters accounted for 13% of antimicrobial alternative funding. A total of 12% of funding was directed to studies of management practices to reduce antimicrobial use (e.g. reducing nutritional, physiological and behavioral stress). Diagnostic tests to identify bacterial and viral respiratory pathogens in live cattle or to identify sick cattle received 2% of funding. The remaining 17% of antimicrobial alternative funds was directed towards studies examining the effectiveness of alternative disease treatments (e.g. essential oils, nitric oxide, bacteriophage) immunomodulators (β -defensins and other host defence peptides, antimicrobial peptides, nanoparticles), and animal genetics for disease resistance.

Summary of Workshop Discussions: The breakout groups discussed whether there are gaps in available management techniques that would reduce antimicrobial use, new technologies that could provide products to replace antibiotics, and to identify the most important priorities for developing alternative products with similar efficacy to (treatment) or reduce the need for (e.g. prevention) antibiotics.

Access to effective and affordable antimicrobials has hindered the adoption of antimicrobial alternatives. However, effective alternatives would be exceedingly important in the event that

antimicrobials become less accessible, effective or affordable. While the efficacies of some alternatives (e.g. vaccination and preconditioning) are well-established and can reduce antimicrobial use, costeffectiveness in practice and market structure have hindered widespread adoption. Preconditioning is often difficult to do, difficult to verify and complicated by marketing practices and the desire of feedlot managers to fill pens which usually requires co-mingling of calves from different sources. It was considered by several workshop participants that there was a gap in evidence-based risk assessments on various management practices to determine the real value of preconditioned calves. Better diagnostic tools to predict the onset of disease before the visual symptoms become apparent was also considered an area that needs more work.

The efficacy of other alternatives is less clear. Pre-, pro- and synbiotic products have so far failed to live up to their potential in ruminants, partly due to lack of knowledge, and partly due to the complexity of the rumen microbiome. More knowledge is required on both the gut and respiratory microbiomes to better understand disease and immunity. For example, immunostimulants are under development and have been licensed in the US (e.g. Zelnate) although little information is available on their efficacy. Nutritional deficiencies were also mentioned as having a potential role in increasing susceptibility of cattle to disease.

Re-investment in vaccine development was considered to be a priority. Canada's beef industry is very small compared to the U.S., so many vaccine antigens in U.S. vaccines are derived from American isolates and may not be appropriate or fully protective against Canadian pathogen strains. Several participants also indicated that multi-valent vaccines may cause ineffective immune responses to all antigens. Improving immune status in feeder calves by reducing stress during weaning, marketing and transport were discussed extensively. Modified nutritional strategies that reduce the need for tylosin or tetracycline to control liver abscesses in feedlot cattle would have significant value for the industry. In the longer term, a better understanding of genetic resistance to disease could potentially be exploited through genomic selection. Gene editing was also discussed but thought to be a long term approach as there would be significant hurdles to overcome.

It was noted that some strategies intended to improve animal health (e.g. mineral supplementation) may have unintended negative consequences with regards to antimicrobial resistance (e.g. linkage of copper resistance and antimicrobial resistance genes in bacterial plasmids).

Priority Research Outcomes for Antibiotic Alternatives

Desired Outcome: Development of a broader toolbox for disease management.

- Evidence-based risk-assessment of the cost-effectiveness of alternative production practices (e.g. preconditioning, methods of reducing stress in weaned calves).
- Develop rapid, accurate, cost-effective chute-side diagnostic tests to evaluate whether cattle have been effectively vaccinated against specific pathogens.
- Develop rapid, accurate, cost-effective diagnostic tools to detect disease before symptoms become apparent.
- Develop cost-effective nutritional and other management strategies to effectively reduce the need for antimicrobials to control liver abscesses.
- Re-invest in vaccine development, with a specific focus on pathogens associated with bovine respiratory disease in Canada (e.g. *Mycoplasma spp, Mannheimia haemolytica, Histophilus somni, Pasteurella multocida*, bovine herpesvirus, bovine respiratory syncytial virus, bovine viral diarrhea virus, bovine coronavirus), liver abscesses (e.g. *Fusobacterium necrophorum*,

Trueperella pyogenes), footrot (e.g. F. necrophorum) and digital dermatitis (e.g. Treponema spp.).

- Investigate and develop simple, cost-effective alternative vaccine delivery methods to improve vaccination rates in the cow-calf sector.
- Develop a better understanding of the respiratory and gut microbiomes, their establishment and development in the neonate, and their relation to immunity and disease.
- Investigate the impact of animal genetics on disease susceptibility and resistance (long term).
- Investigate combination therapies incorporating antimicrobials and non-antimicrobial alternatives to improve treatment success, reduce antimicrobial use, and reduce antimicrobial resistance.
- Develop cost-effective non-antimicrobial products to prevent, treat and control disease.

VI. Non Research Priorities

A number of important recurring non-research themes also arose during the breakout sessions.

- Regulation, programs and industry / government policies need to be evidence-based.
- Regulatory modernization is required to remove barriers to innovation and product registration (e.g. there is currently no regulatory pathway for some feed additives and health claims). The regulatory system needs to be appropriately resourced to ensure adequate staff is available to review and approve submissions in a timely manner.
- Ongoing assessment of whether policies aimed at restricting antimicrobial use in beef cattle production impact animal health, animal welfare, animal nutrition, food safety, human health and industry sustainability.
- There is a need to standardize sample collection and laboratory procedures with regard to antimicrobial susceptibility and resistance.
- Both research and surveillance capacity need to be maintained, reinforced and reinvigorated in the areas of antimicrobial resistance, assessing and monitoring antimicrobial use and development of antimicrobial alternatives.
- Encourage a One Health approach to determine the impact of livestock use of antimicrobials on human health.
- More effective communication between the beef industry, researchers, veterinarians and the medical community is needed to ensure that there is mutual understanding of respective concerns, scientific evidence, opportunities for collaboration and efforts being made to combat antimicrobial resistance.
- Animal health is closely intertwined with animal welfare and food safety. This needs to be considered in discussions regarding access to effective antimicrobials or alternatives.
- As antimicrobial resistance, antimicrobial use and antimicrobial alternatives are receiving worldwide attention, there are valuable opportunities to communicate with and learn from

other countries, jurisdictions and livestock sectors. This will help allocate research resources more strategically and effectively in Canada, and help avoid repeating previous errors.

- Many of the issues around antimicrobial use in veterinary medicine are under provincial regulation. This has led to program fragmentation among provinces, and potentially valuable information may not be shared optimally. An interprovincial coordinated approach to regulation is desirable.
- There is a need to develop improved communication materials for veterinarians and producers to emphasize the importance of all sectors and stakeholders in ensuring responsible preventionbased herd health management and appropriate antimicrobial use to minimize the development of antimicrobial resistance.
- Certain pharmaceutical industry marketing practices (e.g. rebates, rewards and incentives) were discussed in light of the concern or perception that these may distort veterinary antimicrobial inventory stocking and prescribing and/or producer use decisions away from vaccination/prevention to treatment, or from using antimicrobials of lower importance in human medicine towards increased use of higher importance antimicrobials.
- The conflict of interest inherent in allowing veterinarians to both prescribe and sell pharmaceuticals (in contrast to human medicine, where doctors prescribe and pharmacists dispense) is a concern, although no economically viable solutions for rural practices are evident.
- Improved resourcing for and coordination among organizations involved in surveillance (e.g. CAHSN and CIPARS) and regulation, and support for the Canadian Center for Veterinary Biologics would benefit efforts to identify and respond to antimicrobial resistance issues and improve access to effective alternatives.
- National leadership is needed to effectively integrate national, provincial, government and industry perspectives and initiatives to successfully achieve the mutually desired outcome of continued antimicrobial effectiveness in human and animal medicine.

VII. Research Funding Priority Coordination

The intent of the defined strategy is to encourage key industry and government funders at both a federal and provincial level to develop future research funding programs that are focused on achieving the specific research outcomes.

FUNDER CONSULTATION WORKSHOP

On the second day of the workshop (December 11, 2015), the BCRC and the BVCRT engaged provincial and federal government and industry funders in a discussion about current and ongoing antimicrobial research priorities. Discussion also focused on identifying opportunities to improve funding coordination and delivery of research that clearly aligns with the research priorities and outcomes identified in the first day of the workshop. See Appendix B for a list of workshop invitees.

Participating funders reviewed their research priorities related to antimicrobial resistance, use and alternatives, upcoming funding opportunities, and their processes. There was general agreement to direct beef-related antimicrobial research towards achieving the priority outcomes identified in the National Beef Antimicrobial Research strategy developed from this workshop, once the draft strategy has been circulated and reviewed by the workshop attendees.

VIII. Appendix A: Target Antimicrobial Research and Surveillance Outcomes

BEEF INDUSTRY CORE RESEARCH OBJECTIVES

- 1. To *enhance industry sustainability and reduce production costs*, priority outcomes are to enhance feed and forage production, quantify the environmental impact of Canada's beef industry, improve feed efficiency, decrease the impact of animal health issues and production limiting diseases, and ensure animal care.
- 2. To *improve beef demand and quality*, priority outcomes are to reduce food safety incidences, define quality and yield benchmarks supporting the Canadian Beef Advantage, and improve beef quality through primary production improvements and the development and application of technologies to optimize cutout values and beef demand.

OVERARCHING AIMS FOR RESEARCH PRIORITY AREAS

- Research and surveillance capacity need to be reinvigorated and maintained.
- A One Health approach to antimicrobial research is essential.
- Animal health, welfare and food safety implications of antimicrobial use, resistance and alternatives must be monitored.
- Research collaborations among researchers, research institutions, agencies, provinces, nations, livestock sectors, and the medical community must be encouraged.
- Research findings and knowledge must be effectively communicated to veterinarians and producers to encourage and ensure appropriate antimicrobial use.

TARGET ANTIMICROBIAL RESEARCH AND SURVEILLANCE OUTCOMES

Desired Outcome: Evidence-based decision making and communication to the veterinary, producer and medical communities.Increase CIPARS activities to encompass on-farm, abattoir and retail beef antimicrobial resistance surveillance, including Enterococcus hirae or other indicator organisms that are informative with regard to macrolide resistance.Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	1. Antimicrobial Resistance
and medical communities.Increase CIPARS activities to encompass on-farm, abattoir and retail beef antimicrobial resistance surveillance, including Enterococcus hirae or other indicator organisms that are informative with regard to macrolide resistance.Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	Desired Outcome: Evidence-based decision making and communication to the veterinary, producer
Increase CIPARS activities to encompass on-farm, abattoir and retail beef antimicrobial resistance surveillance, including Enterococcus hirae or other indicator organisms that are informative with regard to macrolide resistance.Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	and medical communities.
resistance surveillance, including Enterococcus hirae or other indicator organisms that are informative with regard to macrolide resistance.Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	Increase CIPARS activities to encompass on-farm, abattoir and retail beef antimicrobial
informative with regard to macrolide resistance.Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	resistance surveillance, including Enterococcus hirae or other indicator organisms that are
Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	informative with regard to macrolide resistance.
feedyards, focusing on BRD pathogens and enteric bacteria.Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	Implement ongoing surveillance of antimicrobial resistance through sampling of live animals at
Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle.Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settingsDevelop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	feedyards, focusing on BRD pathogens and enteric bacteria.
beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have concerning levels of antimicrobial resistance into ongoing CIPARS surveillance. Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle. Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settings Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	Conduct pilot projects to identify whether the prevalence of antimicrobial resistance in market
concerning levels of antimicrobial resistance into ongoing CIPARS surveillance. Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle. Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settings Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	beef cows, dairy cows and bob/veal calves differ from fed cattle, and include any found to have
Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial resistance throughout the cattle production cycle. Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settings Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	concerning levels of antimicrobial resistance into ongoing CIPARS surveillance.
resistance throughout the cattle production cycle. Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settings Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	Conduct clinical trials to confirm best antimicrobial treatment options to minimize antimicrobial
Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in production settings Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	resistance throughout the cattle production cycle.
production settings Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	Develop rapid, accurate, cost-effective technology to detect antimicrobial resistance in
Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial isolates from both healthy animals and clinical cases	production settings
isolates from both healthy animals and clinical cases	Develop and verify best practices at the farm level to reduce antimicrobial resistance in bacterial
	isolates from both healthy animals and clinical cases
Develop methodology to evaluate and monitor the potential movement of antimicrobial	Develop methodology to evaluate and monitor the potential movement of antimicrobial
resistance genes from cattle associated environments to human environments through manure,	resistance genes from cattle associated environments to human environments through manure,
soil, food and water	soil, food and water

2. Antimicrobial Use	
Outcome: Ensure that Canada's beef industry continues to have access to antimicrobials to protect	
animal health and welfare by developing a database to quantify and defend responsible antimicrobial	
use in beef production.	
Establish a working group to determine the governance, structure, potential data sources	
(veterinary, farm and feedlot data, CgFARAD, VBP, etc.), data collection methodology (e.g	
sentinel vs. random sampling), data reporting (e.g. kg active ingredient, animal defined daily	
doses, population corrected unit, etc.) and resources required to develop an antimicrobial use	
database for the beef industry.	
Conduct pilot projects to identify which sectors of the beef and veal industries (cow-calf	
feedlot, dairy, bob/veal) pose the greatest antimicrobial use risk (classes of antimicrobials used	
treatment rates, etc.).	
Develop a database to track antimicrobial use in sectors deemed to be highest risk (based on 1	
and 2).	
Use the database to monitor changes in antimicrobial use over time and relate changes ir	
antimicrobial use practices to changes in antimicrobial resistance in cattle pathogens and	
indicator organisms isolated from cattle, beef and cattle-associated environments.	
3. Antimicrobial Alternatives	
Outcome: Develop a broader toolbox for disease management.	
Evidence-based risk-assessment of the effectiveness of alternative production practices (e.g	
preconditioning, methods of reducing stress in weaned calves).	
Develop rapid, accurate, cost-effective chute-side diagnostic tests to evaluate whether cattle	
have been effectively vaccinated against specific pathogens	
Develop rapid, accurate, cost-effective diagnostic tools to detect disease before symptoms	
become apparent.	
Develop cost-effective nutritional and other management strategies to effectively reduce the	
need for antimicrobials to control liver abscesses	
Re-invest in vaccine development, with a specific focus on pathogens associated with bovine	
respiratory disease in Canada (e.g. Mycoplasma spp, Mannheimia haemolytica, Histophilus	
somni, Pasteurella multocida, bovine herpesvirus, bovine respiratory syncytial virus, bovine vira	
diarrhea virus, bovine coronavirus), liver abscesses (e.g. Fusobacterium necrophorum	
Trueperella pyogenes), footrot (e.g. F. necrophorum) and digital dermatitis (e.g. Treponemo	
spp.).	
Investigate and develop simple, cost-effective alternative vaccine delivery methods to improve	
vaccination rates in the cow-calf sector.	
Develop a better understanding of the respiratory and gut microbiomes, their establishment	
and development in the neonate, and their relation to immunity and disease.	
Investigate the impact of animal genetics on disease susceptibility and resistance (long term)	
Develop cost-effective non-antimicrobial products to prevent, treat and control disease.	

IX. Appendix B: Workshop Invitees

Trevor Alexander, Agriculture and Agri-Food Canada Lethbridge David Bailey, Genome Canada Janice Berg, Merck Animal Health Reynold Bergen, Beef Cattle Research Council Darren Bevans, Deseret Ranches / Beef Cattle Research Council Patrick Boerlin, Ontario Veterinary College, University of Guelph My-Lien Bosch, Animal Nutrition Association of Canada Andrea Brocklebank, Beef Cattle Research Council Erin Bureau, Agriculture and Agri-Food Canada Ottawa John Campbell, Western College of Veterinary Medicine, University of Saskatchewan Jorge Correa, Canadian Meat Council Miles Crandall, Boehringer Ingelheim Canada Stewart Cressman, Agricultural Research Institute of Ontario Stephen Desroches, Agriculture and Agri-Food Canada Ottawa Aline Dimitri, Canadian Food Inspection Agency Clinton Dobson, Alberta Livestock and Meat Agency Trish Dowling, Canadian global Food Animal Residue Avoidance Database Rajinder Dubb, Alberta Livestock and Meat Agency Francois Eudes, Agriculture and Agri-Food Canada Sheryl Gow, Public Health Agency of Canada, University of Saskatchewan Phil Greibel, Vaccine and Infectious Diseases Organization, University of Saskatchewan Driss Haboudane, Natural Sciences and Engineering Research Council Tom Hamilton, Ontario Ministry of Agriculture, Food and Rural Affairs Sherry Hannon, Feedlot Health Management Services Steve Hendrick, Coaldale Veterinary Clinic Marlene Huerta, Alberta Innovates Technology Futures Mike Jelinski, Veterinary Agri-Health Services Murray Jelinski, Western College of Veterinary Medicine, University of Saskatchewan Barbara Johnstone Grimmer, Canadian Sheep Federation Cornelia Kreplin, Alberta Innovates BioSolutions Thomas Lynch -Staunton, Canadian Cattlemen's Association Holly Mayer, Agriculture and Agri-Food Canada Calgary Tim McAllister, Agriculture and Agri-Food Canada Lethbridge Rob McNabb, Canadian Cattlemen's Association Steve Morgan-Jones, Amaethon Agricultural Solutions Inc. - Facilitator Noel Murray, Canadian Food Inspection Agency Tim Oleksyn, Beef Cattle Research Council Marc Oulette, Canadian Institutes of Health Research - Institute of Infection and Immunity

Tye Perrett, Feedlot Health Management Services

Gabriel Piette, Agriculture and Agri-Food Canada Ottawa Normand Plourde, Boehringer Ingelheim Canada Colleen Pollock, Merck Animal Health Ron Read, University of Calgary Faculty of Medicine Leigh Rosengren, Rosengren Epidemiology Consulting John Ross, Agriculture and Agri-Food Canada, Ottawa Richard Rusk, Medical Officer of Health, Manitoba Health Karin Schmid, Alberta Beef Producers Guy Seguin, Dairy Farmers of Canada Daniel Shock, Zoetis Canada Angie Siemens, Cargill, Incorporated Brady Stadnicki, Canadian Cattlemen's Association Jean Szkotnicki, Canadian Animal Health Institute Bryan Thiessen, Namaka Farms / Beef Cattle Research Council Edouard Timsit, University of Calgary, Faculty of Veterinary Medicine Ed Topp, Agriculture and Agri-Food Canada London Anatoliy Trokhymchuk, Prairie Diagnostic Services Inc., University of Saskatchewan Joyce van Donkersgoed, Alberta Beef Health Solutions Casey Vander Ploeg, National Cattle Feeders Association Cheryl Waldner, Western College of Veterinary Medicine, University of Saskatchewan Lee Whittington, Prairie Swine Centre Inc. Wendy Wilkins, Ministry of Agriculture, Saskatchewan Xianguin Yang, Agriculture and Agri-Food Canada Lacombe