FORUM ON GENOMICS and ANTIMICROBIAL RESISTANCE

workshop REPORT

FEBRUARY 23-24, 2016
Ottawa, Ontario

GenomeCanada GenomeAlberta GenomeBritishColumbia

Canadian Food Inspection Agency / Agence canadienne d'inspection des aliments

Canada

Forum on Genomics and Antimicrobial Resistance

Workshop Report

BACKGROUND

Antimicrobial resistance (AMR) threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi.[1] Of particular concern is the dramatic increase of antibiotic resistance among bacteria. Since the discovery of penicillin, in 1941, antibiotics have been one of the biggest therapeutic successes in medicine, producing rapid and long-lasting 'miracle cures' and saving millions of lives each year. However, from the beginning antibiotics have contributed to the development of resistance in the bacterial populations that they attack — resistance that can be easily transferred between bacteria. Due to their rapid and effective mode of action, relatively low cost, high safety and ease of use, antibiotics have been both overused and misused in clinical practice and agriculture. The more an antibiotic is used and the broader its spectrum, the more widespread resistance becomes. Antibiotic resistance is complex, however, and bacteria have been discovered in hidden niches protected from human and animal exposure that are nonetheless resistant to modern-day antibiotics, suggesting that resistance is a naturally occurring and ubiquitous phenomenon.

> Antibiotics are not just used in humans (health care settings, community, travellers), but also in animals (food, companions, wildlife), aquaculture, vegetation-seed crops and fruit. All uses contribute to resistance.

The shortage of effective antibiotics is becoming a crisis in health care, threatening our ability to safely perform complex surgeries, deliver cytotoxic therapies and treat minor injuries, as well as making a major contribution to rising health care costs due to lengthened hospital stays, increased diagnostic tests and more expensive treatments. In the agri-food sector, intensive animal farming practices use antibiotics to boost productivity and enhance growth. The situation is compounded by the fact that the pharmaceutical pipeline producing new antibiotics has essentially dried up, with most of the antibiotics produced by the pharmaceutical industry during the last 40 years being minor modifications of compounds to which bacteria have already developed resistance. In the absence of a sound return on investment, industry has largely turned its attention to more lucrative areas.[3]

> In May 2015, the World Health Assembly endorsed the World Health Organization's global action plan to tackle antimicrobial resistance.[2]

Antimicrobial resistance is a global problem and many countries, including Canada, are developing strategies to address the challenge. In October 2014, the Government of Canada released its report, Antimicrobial Resistance and Use in Canada: A Federal Framework for Action,[4] which maps out a coordinated, collaborative, 'one-health' approach to overcoming the threat of antimicrobial resistance. The ensuing Federal Action Plan on Antimicrobial Resistance and Use in Canada[5] was released in March 2015. The action plan focuses federal efforts on three pillars: surveillance, stewardship and innovation, in alignment with similar plans in the United States and the United Kingdom. The design and development of diagnostic tools and preventive measures have been identified as important activities in the action plan, along with increased laboratory capacity, strengthened surveillance, and development of new treatments with a focus on monitoring, detecting and screening for antimicrobial resistance in humans, livestock and food in Canada.

WORKSHOP OBJECTIVES

Building on a number of previous national and international meetings and conferences, the February 2016 workshop was organized to bring researchers from government laboratories and academic institutions together with clinicians, representatives from industry and agri-food commodity groups, and policy makers, to focus attention on the potential role of genomics (which for this purpose includes related disciplines such as proteomics, metabolomics, epigenomics, bioinformatics etc.) in addressing the AMR challenge (see Invited Participants, Appendix 1). Specific objectives were to:

- Determine the current level of genomics based activities as they relate to AMR in the private and academic space;
- Identify priority genomics-related research topics other than activities contributing to the development of AMR-critical exposure pathways (such as Genomics R&D Initiative-funded research projects), and
- Identify opportunities to collaborate in the development of genomics tools for antimicrobial stewardship, diagnostics, monitoring and surveillance in human and animal health, and drug discovery.

While the term 'AMR' encompasses drug resistance across all microbial populations (bacteria, viruses, parasites and fungi), the workshop discussions focused primarily on one aspect of AMR — antibiotic resistance.

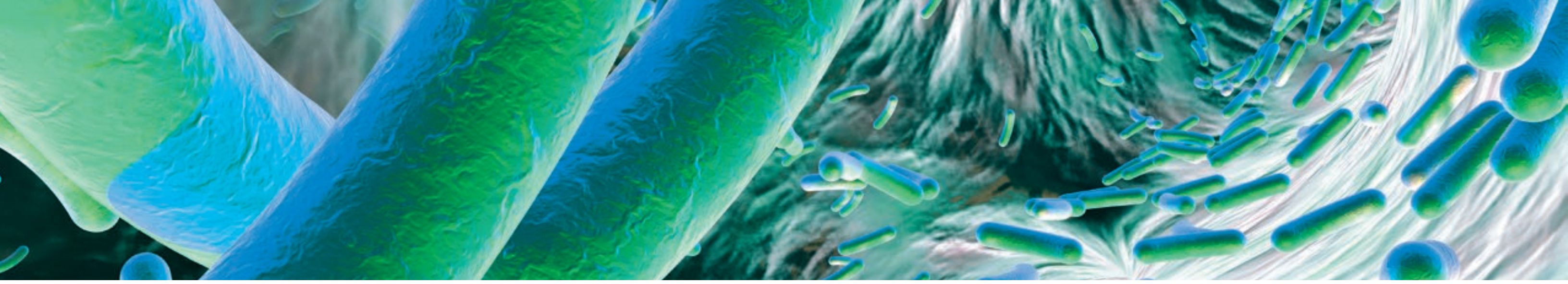
WORKSHOP FORMAT

The workshop was comprised of a blend of individual and panel presentations to set the stage, and breakout and plenary sessions to stimulate discussion and networking (see Agenda, Appendix 2). Participants exchanged ideas on how best to develop a coordinated, multidisciplinary, multi-sector strategy for tackling AMR in Canada, and explored mechanisms for the integration of genomics-based sciences within this strategy.

KEY MESSAGES FROM THE PRESENTATIONS

AMR in the Agri-food Sector

In the agri-food industry, antibiotics are routinely used as therapeutics to treat sick animals, limit the spread of disease, and prevent illness in healthy animals exposed to disease. Antibiotics are also used at sub-therapeutic levels in animal production in order to enhance growth and balance microflora.



While there is evidence that antibiotic use both in the agri-food sector and in the health care system are contributing factors to the escalating problem of AMR in modern medicine, the level that each sector contributes has not been determined.

Nevertheless, in 2014, the Canadian Animal Health Institute agreed to phase out the use of medically important antibiotics for growth promotion in livestock, and support increased veterinary oversight in therapeutic antimicrobial use. The potential downside to this approach is that reducing the use of sub-therapeutic antibiotics in livestock could lead to an increase in enteric diseases as well as productivity and mortality losses (although evidence for this is still lacking). This would potentially generate an increased need for therapeutic antibiotics, which are more likely to overlap with those used to treat infections in humans. It is clear, however, that market pressure and accumulating scientific evidence will constrain the agri-food sector's access to antibiotics in the future, and alternatives are going to be required.[6] The challenge lies in demonstrating the value and cost effectiveness of potential alternative approaches to both the livestock producers and the regulatory bodies, while at the same time maintaining the competitiveness of, and consumer confidence in, the Canadian food industry.

AMR in the Clinic

In the clinical domain, AMR continues to rise and physicians are rapidly running out of effective antibiotics for even simple infections. The situation is compounded by the fact that there have never been truly effective antibiotics for biofilm infections, which account for a significant proportion of all infections in the clinic and lead to adaptive resistance to essentially all antibiotics.[3] Antibiotic resistance in the bacterial pathogens that infect humans has now reached a crisis point. Some success in curtailing the clinical impact of AMR has been achieved through improved hospital hygiene and other public health measures, as well as the discontinued use of certain antibiotics (e.g., penicillin, fluoroquinolones), halting the increase of resistance to these specific drugs. However, it is clear that there is insufficient funding applied to this area to enable meaningful breakthroughs.

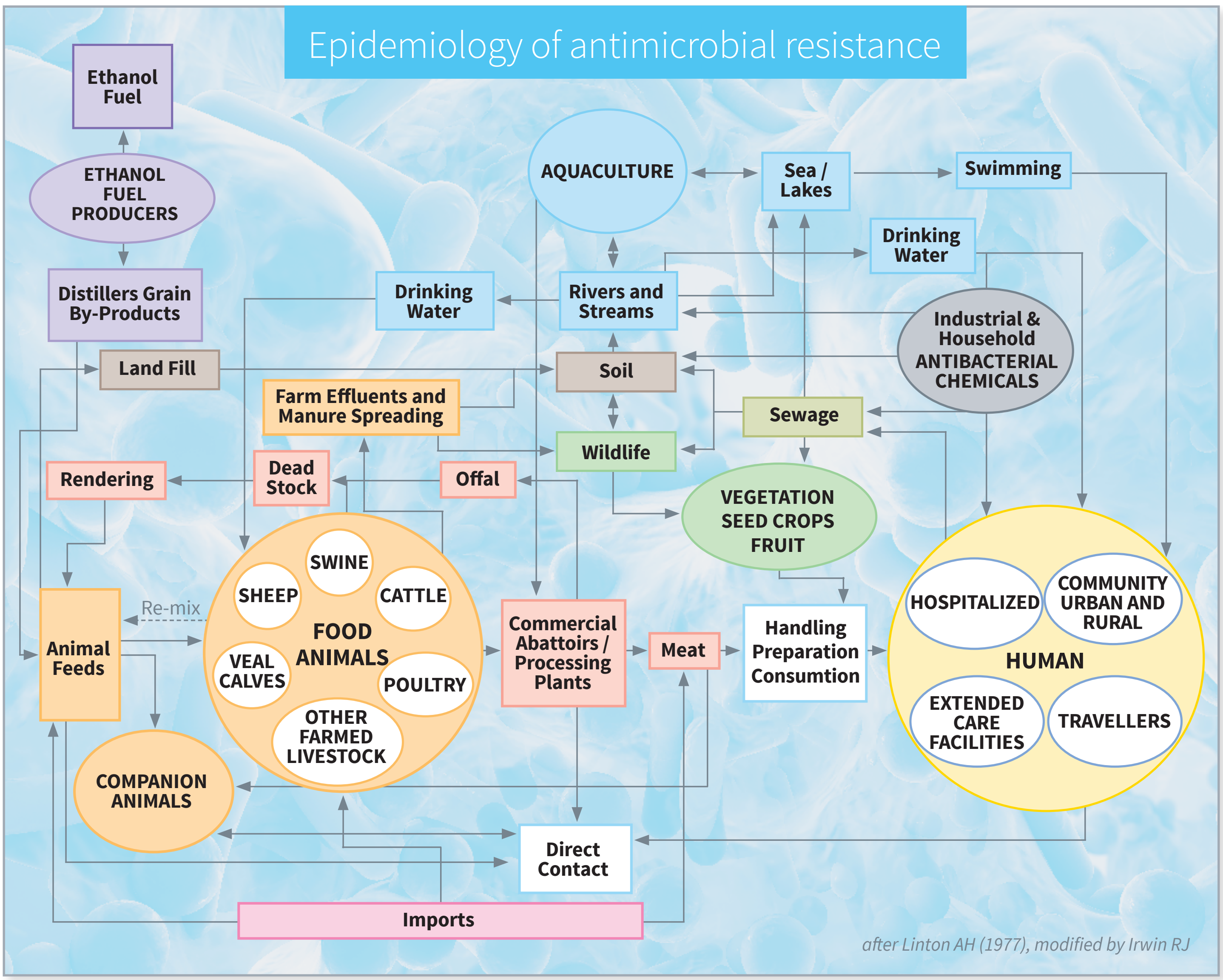
Workshop participants called for:

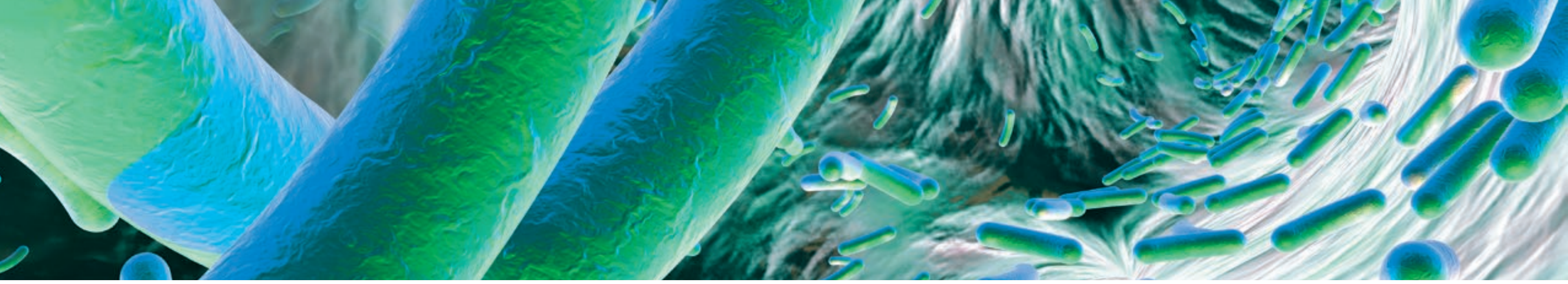
- Enhanced antibiotic stewardship practices to coordinate interventions, ensure the appropriate use of antimicrobials and optimize the use of those antibiotics that are still effective against common infections;
- Strengthened health infrastructure for surveillance;
- The evaluation and adoption into routine clinical care of rapid, sensitive point-of-care diagnostics;
- The timely development of alternatives or adjuncts to traditional antibiotics.

AMR in the Environment

Antibiotic-resistant bacteria are ubiquitous in the environment and have been found in the permafrost dating back 30,000 years, in deep caves that have been sheltered from any contact with the earth's surface. The genes found in the natural metagenome represent a reservoir of antibiotic resistance readily available for mobilization into human pathogens. In addition to natural sources of AMR, human activities can significantly exacerbate the problem. As all life forms on the planet are interconnected and inextricably linked through the environment, AMR anywhere essentially means AMR everywhere. As Figure 1 shows, there are numerous potential sources of AMR and there are many pathways by which resistant microbes can enter the environment and contaminate both land and water, posing a threat to human health. The impact of the buildup of antibiotics and antibiotic-resistant organisms in the environment due to over-use and indiscriminate disposal into our water sources remains a serious and dangerous situation. This topic will be addressed as part of the $20 million, five-year federal Genomics Research and Development Initiative on AMR (GRDI-AMR), targeted for completion in 2021.

Figure 1: Epidemiology of AMR





The One-Health Approach

Speakers described AMR as a ‘wicked problem’ — a problem considered too complex for an individual person, group or discipline to address in isolation, requiring a coordinated multidisciplinary approach. Several speakers supported a one-health approach to AMR that integrates humans, animals and the environment. The one-health concept, which dates back to the mid-19th century, focuses on public health risks that come from interactions between animals, humans and the environment. It is a holistic view that requires a collaborative effort of multiple disciplines working locally, nationally and globally to attain optimum health for people, animals and the environment.

Alternatives to Antibiotics

Although antibiotics represent a major therapeutic success, albeit with the caveats described above, there are still important areas where they have never been particularly effective. Examples include sepsis, which is responsible for about five million deaths annually worldwide, chronic biofilm infections and in immunocompromised individuals. Nevertheless, a world without antibiotics would be a very different place, challenging our ability to perform major surgeries including transplantations, deliver cytotoxic therapies, manage pre-term births and treat even minor injuries. Given that both traditional and genomics-based efforts have so far failed to produce new antibiotics, the end of the antibiotic era could conceivably become a reality. It is therefore incumbent on us to look for better ways to utilize the antibiotics we have, perhaps in combination with adjuvants, and also to search for alternatives to antibiotics. A number of potential alternatives were presented that lend themselves to development by genomics methods, including manipulation of the microbiome using friendly bacteria (probiotics), bacteriophages and their lysins, immune modulation, innate defence peptides and reverse vaccinology. These approaches also lend themselves to use in the agri-food industry since they do not lead to antibiotic resistance. In human medicine they could be pursued as adjuncts to antibiotics (antibiotic adjuvants).

The Role of Genomics and Related Technologies in AMR

It was recognized that genomics has a role in the AMR field, and genomics technologies are already being applied in AMR research taking place in academic institutions and federal departments, including the eight departments and agencies involved in GRDI-AMR. Many speakers identified areas in which the application of genomics-based technologies could play a crucial role in the prevention, diagnosis and treatment of AMR as well as the identification of new therapies or alternatives, including:

- Discovering novel genes and pathways for targeted antibiotic and enzyme-target discovery;
- Advancing our understanding of the epidemiology and mode of action of AMR;
- Understanding the flow of resistance genes from animals to humans through vector-mediated transmission;
- Studying the resistome, adaptive resistance and mobile genetic elements;
- Preventing or slowing the generation of AMR by identifying bacterial infections in humans and livestock using better, faster genomics-based diagnostic tools for molecular sub-typing;
- Developing genomics-based tools to study alternative approaches, such as probiotics, therapeutic antibodies, phage, immune stimulation, reverse vaccinology, antibiotic adjuvants, antimicrobial and anti-biofilm peptides, and innate defence regulator peptides;

- Exploring the role of the respiratory and gut microbiome in the development of improved immune response in the host, and developing management (e.g., nutrition) approaches to stimulate a beneficial microbiome as part of improving animal health;
- Develop genomics-based tools to explore variation in immune responses and host susceptibility to pathogens with the objective of selecting livestock with enhanced health and thereby a reduced use of antimicrobials; and,
- Integrating genomics technologies into surveillance initiatives, leveraging existing isolate collections such as those held by the Canadian Nosocomial Infection Surveillance Program (CNISP) and the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) to monitor the emergence of resistance and the potential for transfer between livestock, humans, the environment and consumer products.

It was noted that enhanced bioinformatics support and innovative new algorithms will be needed to support the genomics effort. Furthermore, new translational tools, shared vocabularies, a resistance gene identifier and capacity building in the biocuration field are required in order to keep pace with the curation, collection, annotation and validation of the wealth of information stored in today's biological and model organism databases.

In addition, clinical data and metadata will need to be standardized and collected continuously in a way that facilitates storage and mobility, so that data can potentially be shared with multiple hospitals at the same time. In the agri-food sector, regulatory challenges with respect to genome-based interventions will also need to be addressed in addition to whether alternative therapies can be fast-tracked in this sector.

KEY MESSAGES FROM THE BREAKOUT AND PLENARY DISCUSSIONS

During the breakout and plenary discussions, participants were encouraged to share insights and experiences from their different perspectives and consider how best to coordinate Canada's efforts and overcome the traditional fragmented approach. Set within the context of Canada's inherently collaborative culture, participants felt that there is currently an opportunity to harness and coordinate AMR research expertise to support the implementation of the Federal Action Plan.

The open dialogue among participants from the biomedical, clinical, agri-food and industry sectors revealed enthusiasm for combining complementary strengths, expertise and resources to form new partnerships and collaborations. Many areas of potential alignment and collaboration were discovered among researchers from academic institutions, federal departments and agencies. There was strong support for a coordinated one-health approach that would build on Canadian unique strengths and core competencies, including existing infrastructures and networks (Table 1) to produce made-in-Canada solutions to the AMR challenge on a global level. It was suggested that the agri-food sector might be a good experimental platform, as it is possible to apply genomics technologies in Canada, especially in the beef, pork and poultry industries, in ways that cannot be done in other jurisdictions, such as the US and EU. One suggestion was that for a one-health approach it might be more appropriate for veterinary science to take the lead, rather than clinical science, to potentially fast-track the development of new therapeutics for humans. Another recommendation was to not duplicate efforts in other countries dedicated towards traditional antibiotic development but pursue a Canadian-led strategy on antibiotic adjuvants and alternatives to antibiotics.

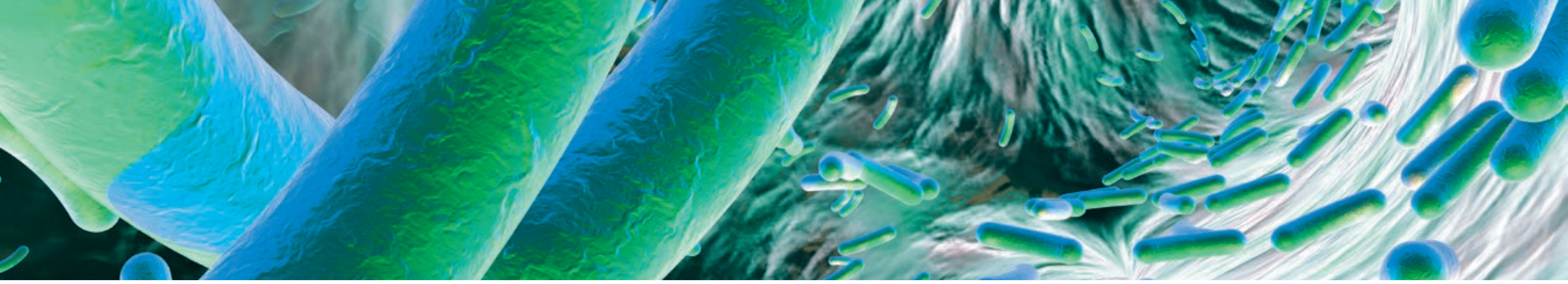


Table 1: Building on Canadian Strengths: Examples of Core Infrastructures and Networks

The Public Health Agency of Canada's National Microbiology Laboratory (NML) in Winnipeg has lab-based reference and research capabilities.
The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) tracks selected bacteria in the intestinal tract of people and animals to probe trends in antimicrobial resistance.
The Canadian Nosocomial Infection Surveillance Program (CNISP) is the infection prevention and control network that reports on rates and trends of health care-associated infections at Canadian health care facilities.
Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was created in 2009 to improve cooperation between the US and EU, and Canada is a member.
Genomics R&D Initiative (GRDI) coordinates federal science departments and agencies in the field of genomics research.
The Comprehensive Antibiotic Resistance Database (CARD), McMaster University, integrates disparate molecular and sequence data, provides a unique organizing principle in the form of the Antibiotic Resistance Ontology (ARO) and can quickly identify putative antibiotic resistance genes in new unannotated genome sequences, bridging antibiotic resistance concerns in health care, agriculture and the environment.
Western Canadian Microbiome Centre, University of Calgary (opening 2017) will be the site of a germ-free lab with embedded microscopy, plus the capability to do genomic studies on the microbiome in health and disease. There will be number of research themes with a focus on chronic inflammatory diseases, infectious diseases of animals and humans, antibiotic resistance, food production and the search for alternative energy sources.
FoodNet Canada is a sentinel surveillance system made up of integrated local networks of public health units, public health and private laboratories, farms and retail food outlets. FoodNet Canada gathers and analyzes data to better understand the links between these enteric pathogens and illness.
Genome Canada and the provincial Genome Centres support strong genomic and bioinformatics resources in Canada.
Centre for Drug Research and Development provides expertise across the drug development continuum to support transition of therapies and diagnostics from the bench to pre-clinical development.

In addition to the examples listed in Table 1, Canada is home to a number of research laboratories and centres of research excellence in AMR, many of which are active internationally through contributions to the EU's Innovative Medicines Initiative and to the Joint Programming Initiative on AMR, as well as an ongoing Canada/UK partnership. Internationally, Canadian researchers are acknowledged leaders in livestock genomics especially in niche areas where Canada has a competitive edge, such as genomics of host susceptibility. Livestock Gentec is coordinating these efforts in Canada (with partnerships across Canada including with industry as well as Agriculture and Agri-Food Canada [AAFC] and academic organizations) and with international partners in Europe and the US.

Specific recommendations for moving forward included the:

- Recognition of AMR as a high priority by both the federal and provincial governments, as well as industry;
- Creation of a coordinated multi-sector, multidisciplinary coalition based on a one-health approach that differentiates Canada as a country with important strengths and assets, and is framed around the three pillars of the Canadian Federal Action Plan. The coalition would implement the strategy by integrating health, agriculture and the environment;
- Development of a strong national research strategy based on a few specific areas where Canada could play a leadership role. The strategy could focus on topics outside traditional areas and approaches to AMR, such as the integration of genomic technologies across the AMR spectrum and the use of genomic methodologies to develop new adjuvant and alternative strategies for treating antibiotic-resistant infections;
- Setting of well-defined targets and milestones to work towards, such as those developed for greenhouse gases;
- Coordination and alignment of relevant existing and emerging programs in government and academia;
- Conduct of an environmental scan and the development of an asset map of Canadian expertise in AMR to establish a baseline and encourage cross-sector collaborations;
- Engagement of regulators, policy makers and key stakeholder groups, such as the industry-based commodity groups and the pharmaceutical industry, during the early development phase as appropriate;
- Development of an evaluation strategy to assess the durability and sustainability of outcomes in terms of practice change and cost efficiencies;
- Identification of a source of sustainable, public- and private-sector funding that supports leveraging of funds among multiple government departments and academia; and,
- Identification of a committed and well-resourced champion to build and lead the coalition.

In summary, the workshop sparked a lively dialogue among representatives from multiple disciplines and sectors that led to an enthusiastic endorsement of the one-health approach to tackling AMR in Canada.

NEXT STEPS

A small working group will be convened to examine mechanisms that will support the integration of the workshop recommendations into the government-led response to the Federal Action Plan on AMR. A one-health approach is proposed that bridges the gap between animal and human health, including environmental aspects from human and animal sources, and builds on Canada's existing strengths and core competencies, including the integration of genomics technologies where applicable.

APPENDIX 1: WORKSHOP AGENDA FEBRUARY 23-24, 2016

KW Neatby Building, 960 Carling Ave, Ottawa ON

Forum on Genomics and Antimicrobial Resistance

DAY 1 – FEBRUARY 23, 2016

8:30 - 9:00 am	Security Check-in and Registration
9:00 - 9:20 am	WELCOME – Cindy Bell, Genome Canada & Martine Dubuc, CFIA • Purpose & Objectives (see Appendix 1) • Introduction of facilitator, Judith Bray • Overview of the two days

SESSION 1: AMR Challenges in the Canadian Context

9:20 - 9:50 am	Overview of the Government of Canada response to AMR (Krista Outhwaite, PHAC)
9:50 - 10:10 am	Overview of the Federal Action Plan (innovation commitments) and alignment with international efforts (Marc Ouellette, CIHR)
10:10 - 10:30 am	Federal Genomics R&D Initiative in AMR (Ed Topp, AAFC)
10:30 - 10:45 am	COFFEE BREAK
10:45 - 11:05 am	One health and AMR (John Prescott, University of Guelph, OVC)
11:05 - 11:25 am	AMR in human medicine (Allison McGeer, Mount Sinai)
11:25 - 11:45 am	AMR in agriculture and agri-food (Tim McAllister, AAFC)
11:45 - 12:05 pm	AMR in the environment (Ed Topp, AAFC)
12:05 - 12:50 pm	NETWORKING LUNCH
12:50 - 1:20 pm	**Agri-food Sector Industry Panel**: Rob McNabb (Canadian Cattlemen's Association), Emily Bond (Canadian Pork Council), Karin Scmid (Alberta Beef Producers) **Key AMR Challenges in the Agri-food Sector: Does genomics have a role to play?**
1:20 - 1:35 pm	**The US perspective on AMR and microbial genomics** (Julie Segre, US National Human Genome Research Institute)

SESSION 2: The Role of Genomics in Addressing the Challenges of AMR

1:35 - 1:55 pm	Using genomics to understand the epidemiology of AMR (Ed Taboada, PHAC)
1:55 - 2:15 pm	Bioinformatics resources for AMR (Andrew McArthur, McMaster University)

2:15 - 2:35 pm	Using genomics for identifying resistance (John Nash, PHAC)
2:35 - 2:55 pm	COFFEE BREAK

Break-out session 1: How do we harness and apply Canadian genomics expertise and resources?

2:55 - 3:55 pm	Break-out discussions
3:55 - 4:50 pm	Reports from break-out sessions followed by plenary discussion
4:50 - 5:00 pm	DAY 1 WRAP-UP

DAY 2 – FEBRUARY 24, 2016

8:00 - 8:15 am	WELCOME - David Bailey, Genome Alberta & David Charest, Genome BC

SESSION 3: New Approaches Towards Addressing the AMR Challenge

8:15 -8:35 am	Alternatives to antibiotics (Bob Hancock, UBC)
8.35 - 8.55 am	Diagnostics (Patrice Allibert, GenePOC)
8:55 - 9:15 am	New drug discovery (Gerry Wright, McMaster University)
9:15 - 10:15 am	**Pharmaceutical Industry Panel:** Mirela Baranci (Merck), Fiona Fitzgerald (GE Canada), Amyn Sayani (GSK) **Pharmaceutical activities in AMR: Does genomics have a role to play?** *5 mins per speaker followed by plenary discussion*
10:15 - 10:30 am	COFFEE BREAK
10.30 - 11.30 am	**Plenary Discussion: How can genomics contribute to the development of innovative approaches?**
11:30 - 12:00 pm	**WRAP UP – David Bailey** • Re-cap of discussions and recommendations from the meeting • Next steps
12:00 pm	MEETING ADJOURNMENT
12:00 - 1:00 pm	NETWORKING LUNCH

SPONSORED BY:

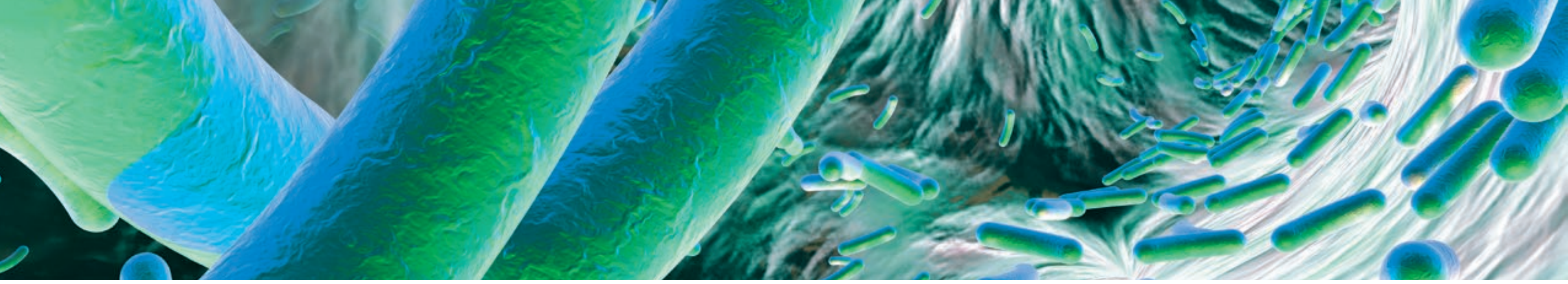
GenomeCanada GenomeAlberta GenomeBritishColumbia Canadian Food Inspection Agency / Agence canadienne d'inspection des aliments Canada

APPENDIX 2: INVITED WORKSHOP PARTICIPANTS

Forum on Genomics and Antimicrobial Resistance

Last Name	First Name	Organization
Allibert	Patrice	GenePOC
Ayoub	Micheline	Genome Quebec
Bach	Horacio	University of British Columbia
Bailey	David	Genome Alberta
Baranci	Mirela	Merck
Bell	Cindy	Genome Canada
Blais	Burton	Canadian Food Inspection Agency
Boerlin	Patrick	Ontario Veterinary College
Bond	Emily	Canada Pork Council
Bonfils	Anne-Christine	Life Sciences National Research Council
Boyd	David	Public Health Agency of Canada (PHAC)
Bray	Judith	Facilitator
Burrows	Lori	McMaster University
Charest	David	Genome British Columbia
Coklin	Tatjana	Canadian Food Inspection Agency
Conly	John	Alberta Health Services
Correa	Jorge	Canadian Meat Council
Dewar	Karen	Genome Canada
Dimitri	Aline	Canadian Food Inspection Agency
Dong	Tao	University of Calgary
Dubuc	Martine	Canadian Food Inspection Agency
Duplessis	Martin	Health Canada
Fitzgerald	Fiona	GE Canada
Gonano	Caroline	Turkey Farmers of Canada
Hamel	Marie-Andrée	Agriculture and Agri-Food Canada
Hancock	Robert	University of British Columbia
Jackson	Allison	Canadian Institutes of Health Research
Johnson	David	Canadian Food Inspection Agency
Knox	Ken	Science, Technology and Innovation Council
Kondejewski	Les	Ontario Genomics
Lambert	Dominic	Canadian Food Inspection Agency
Lepage	Marc	Genome Canada

Last Name	First Name	Organization
Li	Xian-Zhi	Health Canada
Loughrey	Helen	Canadian Institutes of Health Research
Louie	Thomas	Alberta Health Services
McAllister	Tim	Agriculture and Agri-Food Canada
McArthur	Andrew	McMaster University
McGeer	Allison	Mount Sinai Hospital
McNabb	Rob	Canadian Cattlemen's Association
Meadows	Kimberley	Canadian Food Inspection Agency
Mehrotra	Manisha	Health Canada
Murray	Noel	Canadian Food Inspection Agency
Nash	John	Public Health Agency of Canada
Ouellette	Marc	Canadian Institutes of Health Research
Oughton	Matthew	Jewish General Hospital
Outhwaite	Krista	Public Health Agency of Canada
Pagé	Elisabeth	Canadian Institutes of Health Research
Parker	Cathy	Health Canada
Petitclerc	Denis	Agriculture and Agri-Food Canada
Plastow	Graham	University of Alberta
Pontarollo	Reno	Genome Prairie
Prescott	John	University of Guelph
Quinlan	Sean	Canadian Food Inspection Agency
Roberts	Bruce	Canadian Poultry Research Council
Roy	Paul	Université Laval
Saindon	Gilles	Agriculture and Agri-Food Canada
Sayani	Amyn	GlaxoSmithKline, Inc.
Schmid	Karin	Alberta Beef Producers
Segre	Julie	National Human Genome Research Institute
Seto	Esther	Pest Management Regulatory Agency
Siemens	Angie	Cargill
Swan	Kate	Genome Canada
Taboada	Ed	Public Health Agency of Canada
Topp	Ed	Agriculture and Agri-Food Canada
Wilkinson	David	Public Health Agency of Canada
Wilson	Caroline	Chicken Farmers of Canada
Wright	Gerry	McMaster University



REFERENCES

Forum on Genomics and Antimicrobial Resistance

1. World Health Organization. Antimicrobial resistance: Global report in surveillance 2014. Available: www.who.int/drugresistance/documents/surveillancereport/en/ (accessed Oct. 26, 2016).

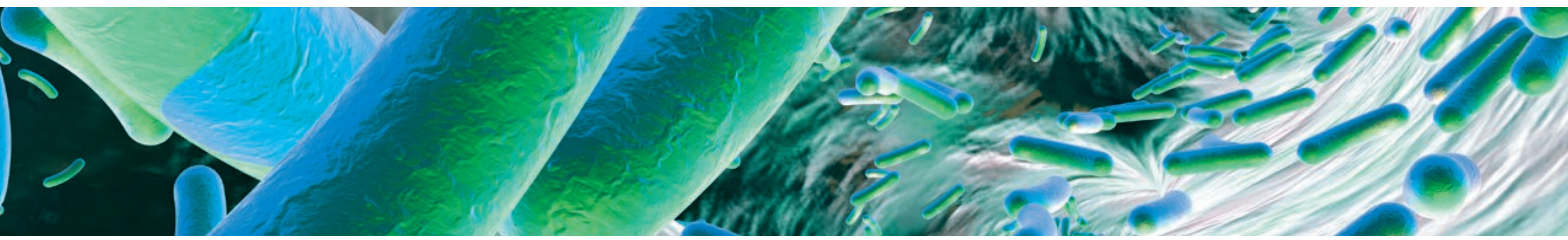
2. World Health Organization. Global Action Plan on Antimicrobial Resistance. Available: www.who.int/drugresistance/en/ (accessed Oct. 26, 2016).

3. Hancock, REW. Rethinking the Antibiotic Discovery Paradigm., EBioMedicine 2015; vol. 2, issue 7. Available: www.ebiomedicine.com/article/S2352-3964(15)00124-3/fulltext (accessed Oct. 26, 2016).

4. Government of Canada. Antimicrobial Resistance and Use in Canada: A Federal Framework for Action. Available: www.healthycanadians.gc.ca/drugs-products-medicaments-produits/buying-using-achat-utilisation/antibiotic-resistance-antibiotique/antimicrobial-framework-cadre-antimicrobiens-eng.php (accessed Oct. 31, 2016).

5. Government of Canada. Federal Action Plan on Antimicrobial Resistance and Use in Canada. Available: http://healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/action-plan-daction-eng.php (accessed Oct. 31, 2016).

6. Czaplewski L et al. Alternatives to antibiotics — a pipeline portfolio review. Lancet Infect Dis. 2016 Feb;16(2):239-51. doi: 10.1016/S1473-3099(15)00466-1. Epub 2016 Jan 13. Available: http://thelancet.com/journals/laninf/article/PIIS1473-3099(15)00466-1/fulltext (accessed Oct. 31, 2016).



GenomeCanada GenomeAlberta GenomeBritishColumbia

Canadian Food Inspection Agency
Agence canadienne d'inspection des aliments

Canada