

NON-HUMAN ANTIMICROBIAL USE SURVEILLANCE IN CANADA: SURVEILLANCE OBJECTIVES AND OPTIONS

**Prepared for:
The Canadian Council of Chief Veterinary Officers (CCVO)**

**Prepared by:
CCVO Antimicrobial Use in Animal Agriculture Committee – AMU
Surveillance Working Group**

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List of Supporting Documents

- 1. Detailed review of international AMU surveillance programs**
 - a. File: *CCVO-WG-AMU_InternationalSurveillance_v9_FINALReport_2016-03-18.xlsx*
- 2. Detailed review of Canadian AMU surveillance**
 - a. File: *CCVO-WG-AMU_CANADA_Surveillance_FINALReport_2016-03-18.xlsx*
- 3. Summary of the Gap Analysis (Canadian surveillance compared to international programs)**
 - a. File: *CCVO_AMUCommittee_Non-HumanAMUSurveillance_GapAnalysis_2016-03-18.pdf*

List of Acronyms

AMR	antimicrobial resistance
AMU	antimicrobial use
API	active pharmaceutical ingredient
CAHI	Canadian Animal Health Institute
CBSA	Canadian Border Services Agency
CCVO	Canadian Council of Chief Veterinary Officers
CMIB	Compendium of Medicating Ingredients Brochure
DCD	defined course dose
DCDA	defined course dose-animal
DDD	defined daily dose
DDDA	defined daily dose-animal
OTC	over-the-counter
OUI	own use importation
PCU	population corrected unit

List of Surveillance Programs

CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CNISP	Canadian Nosocomial Infection Surveillance Program
CARRS	Canadian Antimicrobial Resistance Surveillance System
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Program
VetSTAT	Danish register of the consumption of prescription drugs of animals
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
NARMS	National Antimicrobial Resistance Monitoring System (USA)
FDA	US Food and Drug Administration (USFDA)
SWEDRES	Swedish Antibiotic Utilisation and Resistance in Human Medicine
SVARM	Swedish Veterinary Antimicrobial Resistance Monitoring
ANSES	French Agency for Food, Environmental and Occupational Health & Safety

VARSS	Veterinary Antimicrobial Resistance and Sales Surveillance (UK)
MARAN	Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands
FINRES-Vet	Finnish Veterinary Antimicrobial Resistance Monitoring and Consumption of Antimicrobial Agents
NORM-Vet	Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway (veterinary and food production sectors)
SARIS	Surveillance of Antimicrobial Resistance in Scotland
New Zealand	
COIPARS	Columbian Integrated Surveillance Program for Antimicrobial Resistance
JVARM	Japanese Veterinary Antimicrobial Resistance Monitoring System
BelVet-SAC	Belgium Veterinary Surveillance of Antimicrobial Consumption
AURES	Resistance Report Austria
ARCH-VET	Usage of Antibiotics and Occurrence of Antibiotic Resistance in Bacteria from Humans and Animals in Switzerland
Germany	German strategy and related research (precursor for the current GERMAP program)
APVMA	Australian Pesticides and Veterinary Medicines Authority

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Executive Summary

The Council of Chief Veterinary Officers' (CCVO) Antimicrobial Use in Animal Agriculture Committee (the Committee) struck an Antimicrobial Use (AMU) Surveillance Working group in October 2013 (the Working Group). The overarching objectives of this group were to 1) review current Canadian non-human AMU surveillance programs, 2) compare these programs to AMU surveillance programs in other countries, and 3) formulate recommendations and options for non-human AMU surveillance in Canada. The Working Group included members from the Committee as well as experts from the Public Health Agency of Canada's Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). This work began prior to the release of Canada's Antimicrobial Resistance (AMR) Federal Framework and Federal Action Plan. One of the key objectives identified in these documents was to establish and strengthen AMR and AMU surveillance systems in humans and animals in Canada. Though Canada has robust AMR/AMU surveillance programs, "there is no comprehensive and integrated national picture of AMR [and AMU] in human health and within the agri-food system in Canada." ***This report, therefore, is presented to the CCVO at a pivotal time, as Canada prepares to advance AMU surveillance.***

International comparison

Non-human AMU data are being collected nationally and across multiple countries. In Canada, national non-human AMU distribution data are provided to CIPARS by the Canadian Animal Health Institute (CAHI); CIPARS conducts on-farm AMU surveillance in broiler chickens and grower-finisher swine. The Working Group conducted an extensive review of and consolidated international program information into a list of 5 key observations and compared with the characteristics of existing Canadian non-human AMU surveillance programs (see [Table 2](#)).

Non-human AMU Surveillance – possible objectives and models

There are two broad objectives for non-human AMU surveillance programs:

- Objective 1:** To educate stakeholders about AMU by providing accurate, representative AMU data at the level that is required.
- Objective 2:** To provide data to direct future AMU through policy, regulation or other initiatives.

While both objectives require similar types of data, the latter requires the data be collected at a much more detailed level (i.e., at the level of individual veterinarians or animal owners). This work identified short, medium, long-term and ultimate outcomes of non-human AMU Surveillance (see [Table 3](#)). The level of detail in the data captured by a surveillance program will determine to what extent these outcomes can be achieved and how specific/targeted the proposed policies and programs could be. In other words, AMU data need to be measured at the level that future AMU direction is desired/required (e.g., owner/producer/farm, veterinarian, animal species/sector, or region or nation levels). Should Canada choose to enact

a strict system at the farm level or the veterinary level, then data at the individual farm or veterinarian level are required.

The review of current Canadian and international non-human AMU surveillance programs revealed that these programs are based on one or more of the following three distinct data sources/providers:

1. Pharmaceutical companies and affiliates - antimicrobial sales/distribution
2. Veterinary clinics - veterinary antimicrobial prescriptions/clinical records
3. Animal owners and producers - farm-level records

Each of these data sources has the potential to provide progressively more detailed information about AMU closer to the level of the individual animal. However, the current quality of owner-level treatment data is uncertain and AMU data from veterinarians would provide an incomplete picture due to over-the-counter (OTC) distribution and medicated feeds from feed mills manufactured as per the drug approval listed in the Compendium of Medicating Ingredients Brochures (CMIB).

Three potential AMU surveillance models are described below, each representing one of the main data sources listed above:

Model 1 (Distribution/Sales Data) uses AMU sales and/or distribution data from pharmaceutical companies. These data are centralised, may be easy to access and can provide an excellent overview of AMU distribution. They are not appropriate to enforce or monitor compliance with new AMU policies and practices at an individual owner or veterinarian level, but they can be used to assess effectiveness of new regulations/interventions at a high level.

Model 2 (Veterinary Data) makes use of AMU data collected from veterinary clinics. These data may be composed of clinic purchase data (what antimicrobials were purchased by the clinic for sale to clients), clinic sales data (what antimicrobials were sold to a client), or prescription data (what prescriptions were filled or provided to a client). Additional detail about AMU can also be accessed from the clinic records (e.g. reason for use, dose, duration of use, etc.).

Model 3 (Owner Data) is similar to Model 2 but uses data collected at the farm/owner level instead of the veterinary clinic. The data collected on farm could be composed of purchase data (what antimicrobials did the owner/producer purchase) or farm records (what antimicrobials were administered to the animals). Like the veterinary record, farm records could also provide additional AMU data about reasons for use, dose, duration, etc.

Recommendations and Conclusions

All three of the presented models can address Objective 1 (to educate stakeholders): they can provide AMU estimates by antimicrobial class or by specific antimicrobial agent over time, across regions and by different animal species and sectors. However, a combination of Model 1 (Distribution/Sales data) with Model 2 (Veterinary data) and/or Model 3 (Owner data) would be

a better AMU surveillance framework as it would provide more detailed AMU data that is closer to use at the animal level.

Both Models 2 and 3 can be used to address Objective 2: to measure compliance with new AMU policies or inform regulations to direct AMU. Model 1 is not able to provide data that could be used to measure compliance with or enforce new or proposed AMU regulations at the farm or veterinary level. Distribution data can, however, be used to evaluate effectiveness of new regulations at a regional or national level. If the purpose of the surveillance program is to enforce antimicrobial use policies and regulations, the data must be available from all veterinarians or owners, rather than a sample or subset. This would be extremely difficult to set up at this time and would require a large investment in financial and human resources. It may be desirable to first create a sentinel system, using a sample or subset of veterinarians or owners, that has the capability for expansion once the framework for data collection is established. Adequate Information Technology support and resources for data collection, management, analysis and reporting are crucial to the success of an AMU surveillance program to report valid, timely data.

Ultimately, timely decisions must be made about objectives for non-human AMU surveillance in Canada so that frameworks can be developed with these in mind. If AMU surveillance frameworks are developed specifically to address Objective 1, they may not be able to meet Objective 2 in the future unless flexible, expandable and scalable mechanisms are built into address Objective 2 at the outset.

One of the major obstacles identified by the Working Group was a lack of government policy to support and facilitate development of a more robust non-human AMU surveillance program in Canada. Beyond what is captured in this report, Federal-Provincial-Territorial discussion will be required to solidify national AMU surveillance objectives, and to define the overarching government policy position that will then require stakeholder consultation. These decisions will ultimately impact the type of non-human AMU surveillance model that is required and the level of complexity and detail that it must have.

It is apparent that this process will be lengthy and threatens to slow the development of a robust, national and representative non-human AMU surveillance program in Canada. Several components of the described models are already in use within existing CIPARS activities. Consideration should be given as to how they can be expanded and leveraged to improve AMU surveillance in Canada in the short-term. This would improve current AMU surveillance while the bigger policy pieces and consultation continue to inform the broader, more extensive non-human AMU surveillance framework for Canada.

Introduction and Scope

The Council of Chief Veterinary Officers' (CCVO) Antimicrobial Use in Animal Agriculture Committee (the Committee) struck an Antimicrobial Use (AMU) Surveillance Working group in October 2013 (the Working Group). The objectives of this group were to 1) review current Canadian non-human AMU surveillance programs, 2) compare these programs to AMU surveillance programs in other countries, and 3) formulate recommendations and options for non-human AMU surveillance in Canada. The Working Group included members from the Committee as well as experts from the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS).

When the Committee was established in 2012, one of its objectives was to answer questions about non-human AMU surveillance. This work began prior to the release of national frameworks and action plans to tackle antimicrobial resistance (AMR) in both the US¹ and Canada. In Canada, the "Antimicrobial Resistance and Use in Canada: A Federal Framework for Action"² (the Framework) and the "Federal Action Plan on Antimicrobial Resistance and Use in Canada: Building on the Federal Framework for Action"³ (the Action Plan) were released in the fall of 2014 and spring of 2015, respectively. One of the key objectives identified in these documents was to establish and strengthen AMR and AMU surveillance systems in humans and animals in Canada. Though Canada has robust AMR/AMU surveillance programs (i.e. CIPARS and the Canadian Nosocomial Infection Surveillance Program (CNISP)), it was acknowledged that **"there is no comprehensive and integrated national picture of AMR [and AMU] in human health and within the agri-food system in Canada."**³ This gap was highlighted in the Office of the Auditor General of Canada's report on AMR released in April 2015⁴. In response, the Public Health Agency of Canada (PHAC) established the Canadian Antimicrobial Resistance Surveillance System (CARSS) to strengthen coordination and integration of AMR/AMU surveillance available from CIPARS and CNISP⁵; however, CARSS remains very human-centric and relies on existing surveillance data without filling recognized gaps. The Framework and Action Plan outline the roles of several federal agencies and set milestones with timelines; timelines for completion of many activities related to AMU surveillance are set for 2016. ***This report, therefore, is presented to the CCVO at a pivotal time, as Canada prepares to advance AMU surveillance.***

The Working Group defined the scope of the work to be performed and received approval on the work plan from the CCVO in November 2013. The scope included surveillance of AMU in food animals, companion animals, horses, bees, aquaculture and horticulture. Recognizing that

¹ A Public Health Action Plan to Combat Antimicrobial Resistance (USFDA/CDC): <http://www.cdc.gov/drugresistance/pdf/public-health-action-plan-combat-antimicrobial-resistance.pdf>

² <http://healthycanadians.gc.ca/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/antimicrobial-framework-cadre-antimicrobiens-eng.php>

³ <http://healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/action-plan-daction-eng.php>

⁴ http://www.oag-bvg.gc.ca/internet/English/parl_oag_201504_01_e_40347.html

⁵ <http://healthycanadians.gc.ca/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/antimicrobial-surveillance-antimicrobioresistance-eng.php>

the epidemiology of bacteria and their resistance elements spans all of these sectors⁶, the Working Group included all of these components even though the primary focus of the Committee is food animals. The Working Group focused on review and comparison of existing non-human AMU surveillance programs and recommendations for future surveillance, it did not collect, analyse or report any actual AMU surveillance data.

The following provides some clarity of scope and terms used in the report:

1. “Non-human” refers to AMU in animal species/sectors other than humans.
2. “Surveillance framework” includes the programs, mechanisms, and/or tools required to collect surveillance data on AMU.
3. This report does not seek to define judicious or prudent antimicrobial use.
4. In Canada, antimicrobial sales data are not necessarily the same as distribution data. Data provided to CIPARS by the Canadian Animal Health Institute (CAHI) represent the weights of antimicrobials (kg) distributed for use in animals and includes information from 15 companies that manufacture antimicrobial products for use in animals in Canada and 5 major wholesalers/distributors. Kilograms of active antimicrobial ingredients are reported to CIPARS at the feed manufacturer/veterinary clinic/over-the-counter outlet level. Distribution values should approximate amounts sold, particularly when data from more than one year are included. However, when data from only one year are included, distribution values may vary from amounts actually used because of the time lag between distribution and actual use, as well as stockpiling of antimicrobials at various points in the distribution system. The distribution data also do not account for drug wastage due to drug expiry.
5. The discussion of non-human AMU surveillance often refers to the “owner”, “producer” or the “farm”. For the purposes of this report, these terms are used synonymously to encompass all owned domestic animals (livestock, companion animals, aquaculture and apiculture).

In this report, the Working Group compares Canadian and international non-human surveillance programs and presents possible non-human AMU surveillance models for Canada with recommendations for future surveillance based on a range of desired outcomes.

Methods and Overview of Work

The review of international programs should be considered current to April 30, 2015. However, the report includes more recent developments in Canada, but may not be inclusive of all new elements, as AMU/AMR work is accelerating in Canada.

Information pertaining to non-human AMU surveillance programs was gathered under two major sections: 1) existing Canadian non-human AMU surveillance programs; and 2) international non-human AMU surveillance programs. In addition, Canadian human AMU

⁶Epidemiology of AMR: <http://www.phac-aspc.gc.ca/cipars-picra/gfx/epi-lg-eng.png>

surveillance programs were reviewed at a high-level and compared to non-human programs to highlight any gaps in data sources, activities and collection structures that might exist in the latter. The following information was captured for all Canadian and international non-human AMU surveillance programs identified:

- surveillance program objectives
- data collected
- population of interest, outputs/reporting
- program lead (who is responsible)
- cost of surveillance program (where available)
- regulatory and non-regulatory factors that affect how the program collects data

Any country with an AMR/AMU surveillance program (with information provided in English or French) was considered for review. The list of international programs identified and included is provided in Table 1. Canadian program review included CIPARS as well as the Public Health Agency of Canada’s Human AMU surveillance.

Table 1: International AMU Surveillance Programs Identified and Reviewed

International Programs
<ul style="list-style-type: none"> • DANMAP/VetSTAT (Denmark) • ESVAC (European Union), • SWEDRES-SVARM (Sweden) • ANSES (France) • NARMS (USA) • FDA (USA) • VARSS (UK) • MARAN (Netherlands) • FINRES-Vet (Finland) • NORM-Vet (Norway) • SARIS (Scotland) • New Zealand • COIPARS (Columbia) • JVARM (Japan) • BelVet-SAC (Belgium) • AURES (Austria) • ARCH-VET (Switzerland) • German strategy and related research (precursor for the current GERMAP program) • APVMA (Australia)

In addition to review and comparison of existing Canadian programs and identification of gaps, the Working group outlined proposed rationale for conducting non-human AMU surveillance in Canada and theorized potential program objectives. Using the knowledge gained from the

international comparison and these proposed program objectives, the Working Group created 3 different models for non-human AMU surveillance options for Canada. The Working Group considered several possible “what if” scenarios when formulating recommendations for non-human AMU surveillance in Canada.

Results

Review of International Programs and comparison with Canadian Non-Human AMU Surveillance Programs

Overall, 16 national and 1 multinational surveillance programs (European Surveillance of Veterinary Antimicrobial Consumption – ESVAC) collecting non-human AMU data were identified. The details of these are included in a separate spreadsheet: “**CCVO-WG-AMU_InternationalSurveillance_v9_FINALReport_2016-03-18.xlsx**”. The details of the review of Canadian surveillance are included in a separate spreadsheet: “**CCVO-WG-AMU_CANADA_Surveillance_FINALReport_2016-03-18.xlsx**”. Within the European Union, national reports are limited or missing for Spain, Germany and Switzerland, but the sales data for those countries are included in ESVAC. The animal populations (species or commodity) included in the surveillance programs varied depending on the animal production profile of the country (i.e., companion, production/food animals, aquaculture).

The methods used to measure or report on AMU varied across the different programs and no one country reports on all of the different types of metrics used to report AMU data (see Table 2 for details on the different metrics). Most programs reported on the quantity (kg) sold and the quantity sold adjusted by animal population and weight (Population Corrected Unit (PCU)). Neither of these measures account for the concentration of the active ingredient in a given dose. Very few programs capture information needed to calculate metrics such as defined daily dose (DDD) (n=4 programs) or defined course dose (DCD) (n=1 program). Though four countries calculate DDD’s, different countries use different data sources (e.g., on-farm versus sales data), and not all countries calculate DDD’s for every animal species/sector.

At the time of review only DANMAP, through their VetStat Program, had regulatory authority to collect farm-level AMU data. ESVAC has conducted pilot projects on-farm in 10 volunteer countries and focused on farrow-to-finish swine farms by country starting in 2014, with potential expansion to poultry and cattle in coming years. Where there is no regulatory authority, programs rely on voluntary data providers to quantify farm-level AMU as well as the factors that influence AMU such as reasons for use, specific diseases treated, duration of exposure, etc. Only two programs use non-human AMU surveillance data to direct future AMU through regulation (Denmark and the Netherlands).

International program information was consolidated into a list of 5 key observations and compared with the characteristics of existing Canadian non-human AMU surveillance programs (Table 2). Further information regarding the gap analysis performed by comparing Canadian to

international AMU surveillance programs is included in the document titled, “[CCVO_AMUCommittee_Non-HumanAMUSurveillance_GapAnalysis_2016-03-18.pdf](#)”.

Table 2. Summary comparison of international and Canadian non-human AMU surveillance programs.

Non-human AMU surveillance programs outside of Canada	Canadian non-human AMU surveillance programs
<p>AMU sales, distribution or similar data are being collected at the national level, and in one case, across multiple countries (ESVAC); on-farm AMU data collection exists in various forms in some countries.</p>	<p>National distribution data are provided to CIPARS by CAHI; CIPARS conducts on-farm AMU surveillance for broiler chickens and grower-finisher pigs using surveys of sentinel farms in the major pork and chicken-producing provinces.</p>
<p>There are 4 major metrics for measuring/reporting AMU data:</p> <ul style="list-style-type: none"> • Quantity (kg) of antimicrobials sold • Quantity (kg) standardized by the population and weight of animals (kg/population corrected unit (PCU)) • Defined Daily Dose – Animal (DDDA) • Defined Course Dose – Animal (DCDA) 	<p>CAHI data enable Canada to report on:</p> <ul style="list-style-type: none"> • Quantity (kg) of antimicrobials distributed for sale • Quantity (kg) standardized by the population and weight of animals (kg/PCU) <p>CIPARS farm data enable Canada to report on:</p> <ul style="list-style-type: none"> • Defined Daily Dose – Animal (DDDA) • Defined Course Dose – Animal (DCDA)
<p>Most countries that conduct AMU surveillance have the regulatory authority to collect antimicrobial sales data.</p>	<p>In Canada, there is no regulatory authority to collect antimicrobial sales or use data; these data are currently provided voluntarily.</p>
<p>At the time of review, the only country with regulatory authority to collect farm-level AMU data is Denmark.</p>	<p>In Canada, there is no regulatory authority to collect farm-level AMU data; these data are provided voluntarily by participating sentinel farms.</p>
<p>The main objectives of most AMU surveillance programs are to monitor AMU trends over time and between animal species and to have data that are comparable with other countries.</p>	<p>The CAHI data enable Canada to monitor trends over time and to compare AMU with other countries; AMU comparisons between animal species are not currently possible with the CAHI data. The current CIPARS farm program monitors trends over time in pigs and broiler poultry and enables comparisons between these species.</p>
<p>Only a few countries use the AMU data collected for regulatory purposes (e.g. Denmark and Netherlands) to reduce use (at the producer or national level, respectively).</p>	<p>Canada does not use available AMU data to direct AMU in the form of policy or regulation. Specific industry sectors have used AMU and AMR data to enact their own policies to improve stewardship.</p>

Rationale for Conducting Non-human AMU Surveillance

In designing any surveillance program, the tendency is to immediately focus on “what data are needed and methods for their collection”. However, the work of this group highlighted a need to first define why non-human AMU surveillance is important and what the data will be used for.

The rationale for conducting non-human AMU surveillance can be clarified by first asking two questions:

- 1) Why should we collect non-human AMU data?
- 2) How will non-human AMU data be used?

In considering these questions, the working group identified potential short, medium and long-term outcomes resulting from non-human AMU surveillance (Table 3).

Table 3: Desired outcomes from non-human AMU surveillance.

Ultimate outcome	Reduced health burden posed by AMR infections in people and animals		
	↑		↑
Long term outcomes	Ability to assess whether or not AMU practices are judicious or not		Improved understanding of how non-human AMU contributes to AMR in humans and non-humans
	↑	↑	
Medium term outcomes	Better informed stakeholders	Increased ability to make evidence-based decisions about non-human AMU policies and practices	
	↑	↑	↑
Short term outcomes	Improved understanding of non-human AMU in Canada (drivers of use, trends, etc.)		
	Ability to assess compliance with new or proposed AMU stewardship policies/regulations		

Short term outcomes:

Access to regularly collected non-human AMU data will enable provincial and federal agencies to better understand AMU in Canada. The surveillance data will provide answers to the following types of questions:

- How does non-human AMU in Canada compare to other countries? How does non-human AMU in one province/region compare to another?
- How does non-human AMU compare to AMU in humans?
- Is non-human AMU increasing or decreasing? How does this relate to animal (or other) populations and other factors such as disease trends, outbreaks and other management factors?
- How does non-human AMU compare between animal species/sectors? E.g., Is AMU in broiler chickens different from beef cattle?

Ongoing collection and access to these data will also permit regulators and others to assess the efficacy of new AMU stewardship regulations, policies or programs. Evaluation of the effectiveness of new interventions at a broad scale is the first step towards assessing compliance of veterinarians, producers/owners and others with the new recommendations or requirements.

Medium term outcomes:

Assessment of non-human AMU surveillance data and the associated improvement in understanding of non-human AMU in Canada will enable responsible agencies, departments and antimicrobial user groups to target areas (food animal commodities, types of use, etc.) where AMU could be reduced and to direct future AMU policies and practices or strengthen existing ones. Because of the ongoing data collection, these interventions and policy recommendations would be evidence-based. Different types of policy direction are possible and may range from passive mechanisms (e.g., prudent use guidelines) to more active mechanisms that involve/require regulation and enforcement.

Improved understanding of non-human AMU will also support information and knowledge exchange with stakeholders including: producers/owners, veterinarians, policy-makers, regulators, scientists, surveillance program managers, industry stakeholders, trading partners, human and public health professionals and the public. Different types of information will be of interest to different stakeholders. For example:

- I. Analysis and interpretation of non-human AMU trends pre and post-intervention will permit assessment of intervention effectiveness.
- II. Assessment of non-human AMU data should direct future research needs and surveillance data can be used directly in research and risk assessments.
- III. Characterizing non-human AMU trends and comparison between commodities, regions or other, will support debate and dialogue about whether or not use is judicious (see below for more detail).

Long term outcomes:

As our understanding about non-human AMU grows with the sharing of better information, and as programs and policies are implemented, we will begin to be able to evaluate whether or not non-human AMU is judicious. However, through its work, the Committee recognized that it is difficult to develop a clear, manageable definition of judicious use that applies to all situations

and stakeholders as perspectives and priorities often vary, and in some cases compete with one another.

Elements of judicious use include:

- Using the appropriate antimicrobial for the targeted bacteria
- Using an antimicrobial for an appropriate reason (e.g. to treat or prevent a bacterial infection)
- Using an antimicrobial at an appropriate dose, duration and route (linked with reason for use)
- Using an antimicrobial in the appropriate population of animals (e.g. mass treatment vs. individual animal).
- Using an antimicrobial as directed by a veterinarian or other professional/recognized authority.

To determine how non-human AMU influences AMR in humans and non-humans, AMU and AMR data from many different sources must be integrated. Analysis of surveillance data often identifies trends and potential relationships between AMU and AMR, leading to further research questions about causal links, and provides data for quantitative AMR risk assessment. It can also suggest possible links between AMU and AMR that warrant further investigation and possible response to AMU practices.

Ultimate outcome:

Together, the ability to evaluate whether or not AMU is judicious and development of a better understanding of how non-human AMU affects AMR should enable reduction in the health burden posed by AMR in Canada and around the world and progress towards preserving antimicrobials as a precious health resource for the future.

Non-human AMU Surveillance Objectives

There are many possible objectives of non-human AMU surveillance that were considered in this work that ultimately could be categorized into two broad objectives:

- Objective 1:** To educate stakeholders about AMU by providing accurate, representative AMU data at the level that is required.
- Objective 2:** To provide data to direct future AMU through policy, regulation or other initiatives.

Objective 1: To educate stakeholders about AMU by providing accurate, representative AMU data at the level that is required.

- a. Educating stakeholders can take many different forms, such as comparing trends, informing policy decisions, and assessing the effectiveness of interventions to improve stewardship.

- b. Stakeholders include: owners/producers, veterinarians, policy-makers, regulators, scientists, surveillance program managers, industry stakeholders, human and public health professionals and the public.

Objective 2: To provide data to direct future AMU through policy, regulation or other initiatives.

- a. AMU must be measured at the level at which direction is desired (e.g., owner/producer, veterinarian, animal species/sector, or regional or national levels).
- b. Direction may be passive:
 - i. Prudent use guidelines (e.g., Canadian Veterinary Medical Association Antimicrobial SmartVet App⁷).
- c. Direction may be through active mechanisms that involve regulation.
 - i. Government regulation requiring the support of legislation.
 - ii. Other regulatory options that may not require formal legislation (e.g., led by veterinary professional regulatory bodies, industry groups, etc.).

These two broad objectives warrant careful consideration prior to selection of a specific non-human AMU surveillance model. The level of detail in the data captured by a surveillance program will determine to what extent the short, medium and long term outcomes can be achieved and how specific/targeted the proposed policies and programs could be. The desired level of detail needed for analysis and reporting will dictate the surveillance model that is required. At the minimum, any non-human AMU surveillance program should be able to achieve Objective 1. The outputs of surveillance programs designed to address Objective 1 potentially include:

1. Qualitative and quantitative estimates of non-human AMU by sector.
2. Temporal and spatial trend analyses of these estimates at the provincial and national-level.
3. Data for international comparisons.
4. Characterization of how antimicrobials are used (route of administration, duration, etc.).
5. Characterization of AMU at the active ingredient and class level.
6. Characterization of AMU by reasons for use.
7. Describe quantitative AMU on a population basis.
8. Characterization of AMU in terms of over-the-counter (OTC), Compendium of Medicating Ingredients Brochures (CMIB), veterinary prescription or other veterinary supervision.
9. Characterization of AMU as compounded products or imported products.
10. Characterization of AMU in terms of label vs. extra-label use.

⁷ Canadian Veterinary Medical Association. <http://www.canadianveterinarians.net/news-events/news/antimicrobial-smartvet-app>

While both objectives require similar types of data, Objective 2 requires the data be collected at a much smaller or more finite scale (i.e., at the level of individual veterinarians or animal owners vs. at the national manufacturer level). The ability to direct AMU through enforcement of regulations, policies and/or interventions would require commitment in terms of policy changes, political will, program resources and possibly legislative/regulatory changes for non-human AMU data reporting. Should Canada choose to enact a strict system at the farm level (similar to the Netherlands or the yellow card system in Denmark) or the veterinary level, then data at the individual farm or veterinarian level are required. It is unknown whether or not AMR in food products will become a trade issue and impact market access in the future. If this were to happen, non-human AMU surveillance data could be used to direct AMU policies relative to these limitations and could also be used to assess compliance with new regulations; the level of data needed for this purpose would be greater (e.g. collected at a much smaller scale).

The program design will be directed by the specific outcomes that are desired from a surveillance program and at what level. The data required to support and enforce AMU policies and practices that aim to reduce AMU and/or improve antimicrobial stewardship will be dictated by the specifics of how AMU is to be directed. This could be at a national, regional or individual-level for all or some classes of antimicrobials or specific to antimicrobial drugs and species in which they are used. This direction may be in the form of legislation/regulation over how antimicrobials are used. All of these considerations will impact the surveillance model, data, AMU metrics, and ultimately resources required to develop a non-human AMU surveillance program that will meet the desired objective(s).

Non-human AMU Surveillance Models

The review of current Canadian and international non-human AMU surveillance programs revealed that these programs are based on one or more of the following three distinct data sources:

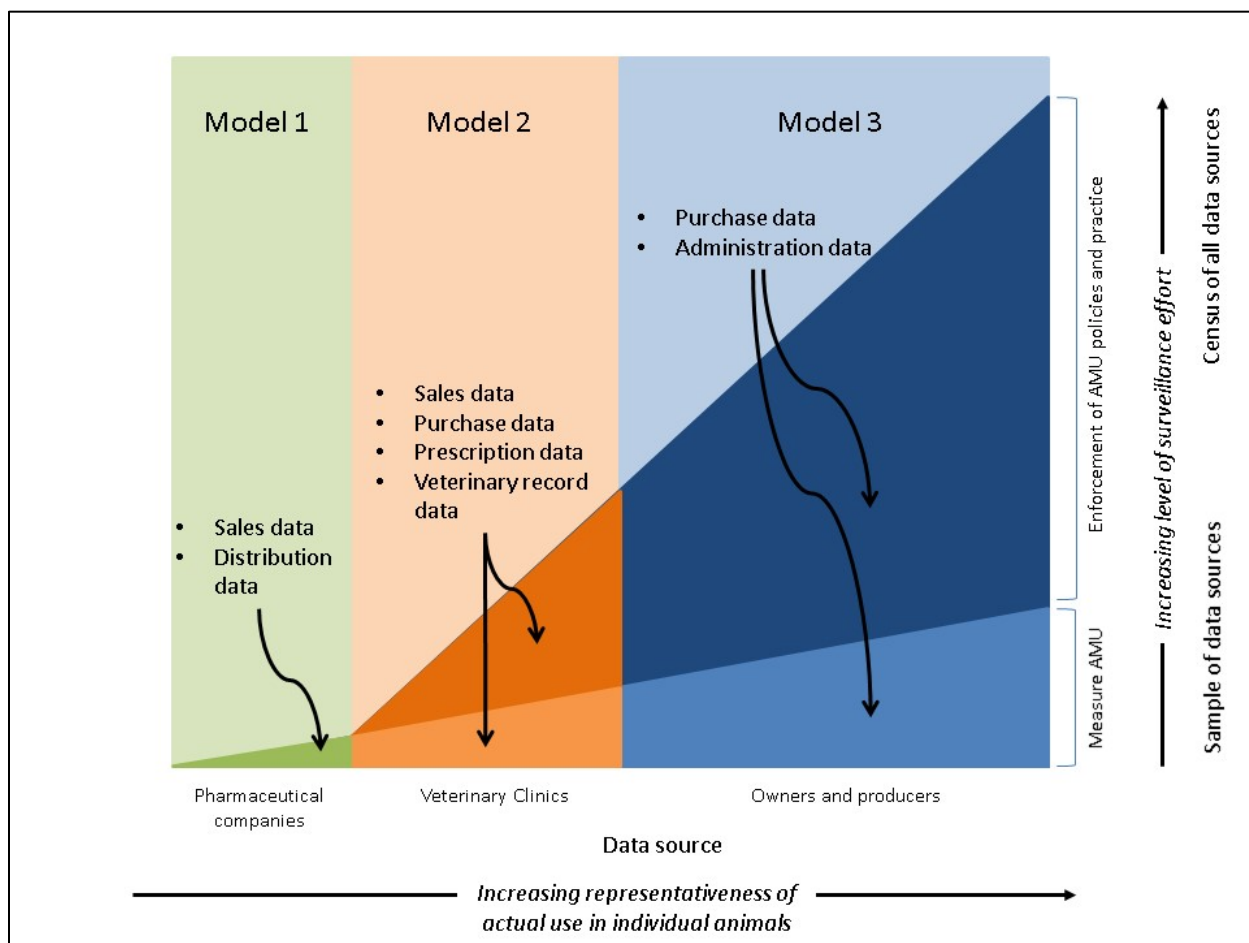
1. Pharmaceutical companies and affiliates - antimicrobial sales/distribution data
2. Veterinary clinics - veterinary antimicrobial prescriptions/clinical records
3. Animal owners and producers - farm-level records

Each of these data sources has the potential to provide progressively more detailed information about AMU as each is closer to administration at the level of the individual animal. Conversely, each becomes more resource-intensive to implement as the level of detail increases. Non-human AMU is most often administered at the farm or by an animal owner. Consequently, the surveillance system that collects data at the farm (aka “owner”) level has the potential to yield the most detailed information about AMU (which animals were treated, for what purpose, etc.). As surveillance moves further away from the owner, the level of detail in the data decreases. Veterinary records may provide less detailed data than owner/farm-level data, and antimicrobial sales or distribution data generate the least detailed measures. However, this assumes that record keeping at the veterinary and owner levels are equal in terms of accuracy, precision and coverage, which is likely not true. Another consideration is that national

distribution/sales data may have more complete coverage at a population-level than current veterinary data (due to OTC sales from other outlets or feed mixing under the CMIB) and owner/farm-level data (due to incomplete or inaccurate records).

Below, we summarize 3 models, each representing one of the main data sources listed above. An overview of the 3 different models is also provided in Figure 1. Following the summary, each model and associated options are discussed in detail.

Figure 1: Schematic diagram summarizing three potential non-human AMU surveillance models for Canada.



Model 1 (Distribution/Sales Data) uses AMU distribution and/or sales data from pharmaceutical companies. These data are centralised, may be easy to access and can provide an excellent overview of AMU distribution. They are not appropriate to enforce or monitor compliance with new AMU policies and practices at an individual veterinarian or owner level, but they can be used to assess effectiveness of new regulations/interventions at a high level.

Model 2 (Veterinary Data) makes use of AMU data collected from veterinary clinics. These data may be composed of clinic purchase data (what antimicrobials were purchased by the clinic for sale to clients), clinic sales data (what antimicrobials were sold to a client), or prescription data (what prescriptions were filled or provided to a client). Additional detail about AMU can also be accessed from the clinic records (e.g. reason for use, dose, duration of use, etc.).

Model 3 (Owner Data) is similar to Model 2 but uses data collected at the farm/owner level instead of the veterinary clinic. The data collected on farm could be composed of purchase data (what antimicrobials did the owner/producer purchase) or farm records (what antimicrobials were administered to the animals). Like the veterinary record, farm records could also provide additional AMU data about reasons for use, dose, duration, etc.

It is important to consider that the scope of all 3 of these models can be expanded or narrowed to meet the surveillance objectives by changing the:

- Data collection frequency (episodic/periodic, continuous, annual).
- Sample size (census vs. a representative sample of sales, veterinarians, or owners/producers).
- Animal species/non-human sectors (all vs. targeted).
- Antimicrobials (all vs. targeted drugs/classes/categories of importance to human medicine).

The level of surveillance effort (personnel and financial resources) increases as the level of detail, precision and accuracy in the data increases. Surveillance effort further increases if all data providers are sampled as opposed to a subset of owners. Whether or not a representative sample is adequate to meet the surveillance objectives depends on whether the surveillance program needs to meet Objective 1 alone, or Objectives 1 and 2.

Adequate assessment of and planning for the required information technology (IT) support for data collection, management, analysis and reporting is crucial to the success of an AMU surveillance program. It is a major consideration that is often underestimated and even left out of long-term surveillance plans. Having a clear IT support plan and dedicated resources will help to ensure timely reporting of valid data, which is critical to the sustainability of any surveillance system.

Model 1 – Non-Human AMU Surveillance Based on Antimicrobial Distribution/Sales Data

Model 1. Summary

Model 1, Core Distribution/Sales model, is presented with 2 options, each providing additional levels of data detail (Table 4). This model is the minimum level required if the main objective of surveillance is to measure AMU in Canada at the national animal species/sector-level (i.e., to have sector-level estimates of AMU, but not individual-level data). Adding Option 1 (Spatial Trends) will allow for better understanding of use practices between regions and enable AMU teaching and training opportunities to be tailored to the unique factors influencing AMU within the different regions. Option 2 (Reason for Use data) attempts to determine a reason for use of each drug by including information from each drug label. Currently, AMU distribution data from CAHI are provided voluntarily and without cost to CIPARS. CAHI currently has a cost to an outside entity to collect/collate these data. In order to measure overall AMU, compare Canadian AMU with other countries and assess AMU trends over time, the sales/distribution data should be collected at least annually.

Table 4. Model 1 – Non-human antimicrobial sales/distribution data surveillance

Model classification	Outputs (Prioritized)	Data required	Methods of Data Collection	Minimum Data Collection Frequency
<i>Core Distribution/Sales Model</i>	1. Estimates of non-human AMU by commodity/sector	Sales data by commodity	1. CAHI and/or individual pharmaceutical companies 2. Distributors and/or feed companies	Annually
	2. Temporal trends in estimates of non-human AMU	Sales data by year		
	3. Characterize AMU by antimicrobial class	Sales data by AM class		
	4. Population-based quantitative AMU estimates	National population data at the animal species/sector level		
<i>Option 1: Spatial data</i>	5. Spatial trends in estimates of non-human AMU	Sales data by province (regional) Provincial population data at the animal species/sector level		Annually
<i>Option 2: Reason for Use data</i>	6. Trends in estimates of non-human AMU by reasons for use	Reason for use (treatment, prevention, growth promotion) based on drug labels	1. Compendium of Veterinary Products 2. CMIB	Annually

Model 1. Current situation in Canada

- Reporting of AMU distribution data by CAHI is voluntary and the decision to share these data with CIPARS is made annually by the CAHI board. Since 2014, CAHI has complied with requests to provide more detailed data: data are now provided according to province and by food versus companion animal classification.
- CIPARS currently reports on CAHI antimicrobial distribution data. These data do not include antimicrobials sold by human pharmacies for companion animal use.
- Starting in 2014, CIPARS receives horticulture antimicrobial sales data from Health Canada's Pest Management Regulatory Agency (PMRA). The PMRA collects annual Canadian sales data from all pesticide manufacturers.
- Current reporting of antimicrobial distribution data in Canada does not account for imported drugs under Own Use Importation (OUI) and Active Pharmaceutical Ingredients (API) provisions. Health Canada's announcement to change the legislation around these practices will help to remedy this. It may also improve the ability to collect data from Canadian Border Services Agency (CBSA) about the volume of antimicrobials imported for OUI/API. The latest information from CAHI is that the lost opportunity value due to OUI and API was estimated to be 13% of total animal health product sales; it is unknown what this estimate would be for antimicrobials alone (*Dr. Carolee Carson, PHAC, personal communication*).
- CIPARS currently reports CAHI antimicrobial distribution data according to the "3 company rule"⁸. This rule was established to comply with the European and US anti-competition regulations and limits the reporting of an individual drug if doing so would allow identification of the manufacturer of the drug. In some cases, this prevents the reporting of Canadian antimicrobial distribution data at a useful level. For example, ceftiofur is lumped into a larger beta-lactam category. Given the importance of ceftriaxone (human equivalent to ceftiofur) to human medicine and the level of ceftiofur-resistance in *Salmonella* Heidelberg and *E. coli* from agricultural sources, there is strong interest to know how much of this particular antimicrobial is distributed annually for use in animals.
- Current antimicrobial distribution data are provided to CIPARS by province and companion versus food animal (including horses) classification. More specific data for sales by animal species/sector and by region (Option 1) would allow for a richer interpretation of the data to understand the selection pressures affecting AMU within different animal species/sectors across the country.
- Calculating standardized animal exposure estimates using sales/distribution data (PCU's) is done by including animal population data from national census information and other sources when national census data are lacking. There is a paucity of accessible animal census data at the provincial level and therefore developing valid, standardized provincial estimates for all animal species/sectors is not possible at this time.

⁸ Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), 2013 Annual Report, Chapter 1, Design & Methods, p. 32-35. http://publications.gc.ca/collections/collection_2015/aspc-phac/HP2-4-2013-1-eng.pdf

- Using drug labels to assign reasons for use (Option 2) will not always provide a mutually exclusive primary reason. Many antimicrobials (especially in-feed drugs) have multiple label claims for treatment, prevention and growth promotion purposes.

Model 1. Findings, Considerations and Possible Solutions

- There are varying levels of uncertainty in the current AMU distribution data available in Canada; however, this uncertainty should not present a barrier to the collection of these data or to the discussions on the provision and access to more detailed antimicrobial distribution/sales data in Canada.
- To improve the utility of the distribution/sales data currently provided to CIPARS by CAHI, the following will be required:
 - Industry and regulatory changes to ensure ongoing access to antimicrobial sales data by animal species/sector and to provide specific data classified by active antimicrobial ingredient/commercial product and class. Creating a regulatory requirement to report, or solidifying longer standing data sharing agreements, would allow for more certainty that the data will be shared each year. In preparing this type of agreement, there would also be an opportunity to negotiate the terms of how and what data will be collected and shared (e.g., data reporting levels such as province and animal species/sector) and possibly even drug class or individual drug-level reporting).
 - Discussion with CBSA about current and future data collection relative to proposed changes in OUI/API legislation.
 - Continued efforts to improve animal population estimates to standardize AMU sales/distribution estimates (e.g., collaboration and research with industry, improved census data, traceability of animals and medicated feeds).
- Option 1 is important to allow for regional assessment and comparison of trends in AMU and AMR. The Core Distribution/Sales Model can only provide data to understand AMU and assess compliance with regulations at a national level (provincial-level by animal species/sector are not currently available beyond companion vs. food animal division).
- Addition of Option 1 would provide more province-specific data to better understand AMU practices that might be unique to a region; decisions about non-human AMU practices could then be region specific. Option 1 would be an expansion/refinement of current data provided to CIPARS and would result in better understanding of how different AMU imparts selection pressure for AMR at the regional-level; however, refinement of population-based data to standardize AMU by region will be required.
- Option 2 provides a starting point for addressing important questions related to reasons for use, but it will not add greatly to either objective due to the lack of specificity of reasons for use afforded by drug labels and the possibility of extra-label use.

Model 1. Key findings

Model 1 - AMU Surveillance Based on Antimicrobial Distribution/Sales Data:

- Core Distribution/Sales Model (antimicrobial distribution/sales data by animal species/sector standardized by population estimates) provides the minimum data needed to measure non-human AMU over time and between animal species/sectors at a national level.
 - Including Option 1 (regional data) is highly recommended to provide provincial-level data and estimates of use and would allow for more targeted education.
- Option 2 (reason for use based on drug label data) would **not** provide much enhancement of the Core Model due to lack of specificity of drug labels for use.
- Enhancing currently available antimicrobial drug sales reporting data by providing more detail about drug class and animal species/sector would improve Canada's ability to make informed decisions about AMU, better understand how AMU influences AMR and to begin assessing whether or not AMU is judicious. This will likely require a regulatory change to allow this level of reporting.

Model 2 – Comprehensive Veterinary Non-Human AMU Surveillance Data

Model 2. Summary

Model 2, the Veterinary Practice model, has the ability to provide more detailed data about AMU than Model 1 because data are collected closer to individual animal use. The data captured by Model 2, drawn from prescriptions and sales records, are collected closer to the point in time and space where the antimicrobial was administered and therefore offer more representative estimates of non-human AMU in individual animals based on what antimicrobials are dispensed/prescribed by veterinarians. This would provide the ability to estimate AMU for groups of animals. Model 2 would not capture data on OTC antimicrobials purchased by the farmer through outlets or dispensed via a feed mill as per the CMIB, imported as APIs for compounding into feed or imported by the owner under OUI since there currently no existing mechanism or authority for collecting these data in Canada.

Model 2 is presented with an option providing additional data detail via information gleaned from owner/patient records, survey administration or clinician diaries (Table 5). The basic veterinary practice model makes use of information captured on prescriptions and OTC clinic sales records of non-prescription drugs distributed by veterinarians. These data provide information about what antimicrobials were sold, the intended dose and frequency of administration, duration of use and by what route the drugs are meant to be administered. The location of the clinic and when the prescription was written would also be accessible information. Inclusion of data in the veterinary record (Option 1) would provide important additional information as to why the antimicrobial was prescribed (reasons for use).

In order to measure overall AMU, compare Canadian AMU with other countries and assess AMU trends over time, the veterinary practice data should be collected at least annually. If the purpose of the surveillance program is to enforce antimicrobial use policies and regulations, the data must be available from all veterinarians, rather than a subset of volunteer veterinarians.

Table 5. Model 2 – Veterinary Practice Non-Human AMU Surveillance

Model Classification	Outputs (Prioritized)	Data required	Methods of Data Collection	Data Collection Frequency
Veterinary Practice Model	1. Complete antimicrobial prescribing/dispensing data, including prescription and non-prescription antimicrobials	Prescription data: 1. Dose, frequency, duration and route of administration Animal data: 2. Species, identity +/- number of animals	1. Actual prescriptions 2. Sales records (OTC and prescription)	Annual, episodic or continuous
	2. Trends in AMU	3. Spatial data (province/region) 4. Time		
Option 1: Veterinary Record (Includes on-label and extra-label use)	3. Quantitative estimates of non-human AMU by PRIMARY reason for use*	Veterinary-record data: Treatment, prevention or growth promotion by species and/or production class	Options: 1. Clinician diary 2. Veterinary survey 3. Data pulled from clinical records	Annual, episodic or continuous
	4. Quantitative estimates of non-human AMU by SECONDARY reasons for use*	Veterinary-record data: Animal species/ sector; specific disease syndromes, bacterial species and/or production class		

* **Primary** reason of use refers to treatment, disease prevention or growth promotion. **Secondary** reasons for use refers to the specific disease/bacterial species.

Model 2. Current situation in Canada

- Veterinary practice AMU data are recorded at every clinic in Canada in the form of patient records. However, the level of detail and how the data are captured and stored varies between clinics, making data extraction and reporting easier for some clinics than others. There is currently no regulatory requirement for veterinarians to report any AMU data for surveillance purposes and there is no mechanism to extract AMU from veterinary practices.
- Owners can currently access antimicrobials without the oversight of a veterinarian through OTC distribution from non-veterinary outlets, dispensing by feed mills under the CMIB, owner OUI, and feed API importation and compounding allow producers to access some in-feed antimicrobials without the oversight of a veterinarian. Veterinary AMU data would be missing these components.
- Relying solely on veterinary data from Model 2 will currently under estimate non-human AMU relative to antimicrobials that are actually administered by producers/owners or additional antimicrobials that are sourced through non-veterinary sources.
- Some agricultural sectors do not frequently use the services of a private veterinarian, if at all (e.g., small ruminant producers, backyard poultry producers, hobby farms, bee keepers, remote communities, etc.). For these, veterinary clinic data would be sparse and would underestimate AMU in these species/locations.
- For some sectors (e.g., apiculture, horticulture), there are no veterinary-level data and regulatory responsibility is unclear.
- The potential data sources listed under Option 1 (clinician diaries, veterinary survey, and clinical records) are diverse and complex.
 - Physician diaries have been used in human medicine to provide a measure of a practitioner's prescribing habits; these typically are collected from a small sample of doctors and for short, recurring periods of time.
 - Veterinary surveys likewise would only represent general prescribing practices at a point in time and are resource-intensive to develop, administer and manage.
 - Research projects have been conducted to develop computing tools to extract AMU data from electronic medical records⁹. These are restricted to electronic records (excluding paper-based records) and are still in the research and feasibility stages of development.
- Many veterinary practices that are employed by a specific sector (e.g. swine and feedlot cattle) keep electronic AMU records, but may be unwilling to voluntarily share these data. They may be considered proprietary and have a perceived monetary value, making them cost-prohibitive to obtain unless there is a regulatory requirement to provide them.

⁹ Anholt RM, Berezowski J, Ribble CS, Russell ML, Stephen C. Using informatics and the electronic medical record to describe antimicrobial use in the clinical management of diarrhea cases at 12 companion animal practices. *PLoS One*. 2014 Jul 24;9(7):e103190. doi: 10.1371/journal.pone.0103190. eCollection 2014. PubMed PMID: 25057893; PubMed Central PMCID: PMC4109994.

Model 2. Findings, Considerations and Possible solutions

- A veterinary practice model for non-human AMU surveillance will be best achieved by developing a framework to collect both the core veterinary practice prescription and sales data along with the veterinary record data (Option 1).
 - Regulatory authority may be required to access and use these data.
 - The level of authority needed may be at the level of the provincial governments or provincial veterinary regulatory bodies (e.g., written into practice standards). Provincial governments must work closely with their veterinary regulatory bodies to determine the best path forward and with each other to ensure a consistent approach across the country. This is necessary to achieve a robust national AMU surveillance framework with the capacity for regional analysis and results.
 - When accessing and using these data, client confidentiality must be maintained.
 - Considerable work is required to create a framework to extract veterinary practice AMU data in an efficient, standardized format to allow for useful interpretation. Adding Option 1 would increase the complexity of data collection.
 - It would be most efficient to design a data collection platform that supports collection of both pieces at the outset. The specific method(s) of data collection that is selected (clinician diaries, survey or actual veterinary records) will drive development of the tool. Veterinary records would provide the most information, but designing that particular collection tool may be the most difficult relative to other collection options.
 - The regulatory pieces required to collect the AMU data could also include the pieces to direct veterinary AMU in whatever form is required (Objective 2).
- Consideration must be given as to whether or not a survey of a representative sample of veterinarians by practice type and regions is adequate to meet the surveillance objectives:
 - If the purpose is to measure non-human AMU, then a representative sample would be adequate.
 - If the purpose is to enforce new AMU regulations, policies or practices at the veterinarian or farm level, then all veterinary clinics must participate.
 - Ultimately, this will be dictated by the level at which direction is required (e.g., individual veterinarian vs. regional or national direction).
- There are important, proposed regulatory changes for non-human AMU in Canada that will impact these decisions. These include changes for API importation and a requirement for veterinary oversight for all medically important antimicrobials (Class I, II and III antimicrobials) that will be included in the CMIB. This will bring all of these antimicrobials under veterinary oversight, thereby improving data availability and creating an opportunity for collection of veterinary AMU data.
- We have not presented an option in Model 2 to collect veterinary drug importation data (for APIs). Consequently, Model 2 partially ignores (or at least does not identify) imported

antimicrobials and so does not allow for delineation of antimicrobials purchased domestically versus imported compounds/drugs. This work recognised options to fill this gap:

1. Under new, proposed legislation, Health Canada will require importers (e.g. feed mills, compounding pharmacies) to have Establishment Licenses to import APIs, providing an opportunity to collect these data. Data sources for API importation include Establishment Licensees, the Canadian Border Services Agency (CBSA), Emergency Drug Release information and veterinary records.
2. Other options to collect API data include veterinary declarations or new regulatory requirements to keep and disclose veterinary records (veterinary clinics, feed mills, pharmacies, etc.)

Model 2. Key Findings

Model 2 – Comprehensive Veterinary non-human AMU surveillance:

- The Veterinary Practice Model plus the Veterinary Record Option will ultimately provide more representative data to better measure non-human AMU over time by animal species/sector compared to the antimicrobial sales/distribution data provided by Model 1.
- Collection of these data from a representative sample of veterinary clinics from across Canada would provide robust data about AMU including what drug, how much, for how long, and by which route of administration. Data for reason of use (what animal species was prescribed the antimicrobial and why) would also be available.
 - This model would provide excellent estimates of trends over time that could be used to target education. It would provide critical data needed to assess whether or not AMU is judicious and to inform future regulation at the national, provincial, or veterinary regulatory body-levels.
- Collection of veterinary practice data from all clinics across Canada would provide representative and specific data that could be used to target individual veterinarian education, to establish thresholds for judicious use and to enforce new and existing use regulations and/or policies.
- If these data are to be used to direct veterinary AMU, the collection tool must be designed to accommodate this.
- Broad stakeholder consultation will be required before Model 2 can be implemented.
- Considerable work is required to create a framework to extract veterinary record data in an efficient, standardized format to allow for useful interpretation for a national surveillance program. The resources needed to support Model 2 will be substantially more than needed for Model 1 and will depend on the number of clinics participating.

Model 3 – Comprehensive Producer/Owner-Level Non-human AMU Surveillance Data

Model 3. Overview

Model 3, Owner Record model, has the ability to provide more detailed data about AMU than Models 1 or 2, as the data collection is closest temporally to the actual use in animals. This model would provide the minimum data required to understand AMU on farm/by animal owner and how it varies over time and across regions. The level of detail available would depend on which data are used and how they are collected (e.g., owner treatment records compared to surveys). Regardless of the data collection method used, Model 3 would capture data that could address the following questions: what drug was used, where, when, how (route of administration), why (reason for use) and in which animals (what species, which individual/group and how many of a given sector).

Like Models 1 and 2, Model 3 is also presented with options, each providing additional data detail (Table 6). The Owner Record model with Option 1 (Detailed Owner Records) relies heavily on the owner keeping detailed treatment records. In the current environment, the owner-level data would encompass prescription, OTC and CMIB antimicrobials. Adding Option 2 (Owner Importation) would also capture data about antimicrobials used under OUI or API importation.

Table 6. Model 3 – Producer/Owner-level non-human AMU surveillance

Model Classification	Outputs (Prioritized)	Data required	Methods of Data Collection	Data Collection Frequency
Owner Record Model	1. Complete administration data	Owner/Farm-level treatment records: 1. Dose, frequency, duration and route of administration 2. Species, identity +/- number of animals	1. Owner/Farm records including: a. purchase data b. administration data	Annual Episodic Continuous
	2. Trends in AMU	3. Spatial data (province/region) 4. Time		
Option 1: Detailed Owner Records	1. Quantitative estimates of non-human AMU by PRIMARY reasons for use	Owner/Farm-level treatment records: 5. Treatment, prevention or growth promotion	Options: 1. detailed owner records 2. owner diary 3. owner survey 4. feed purchase receipts 6. farm treatment protocols	
	2. Quantitative estimates of non-human AMU by SECONDARY reasons for use	Owner/Farm-level treatment records: 6. Animal species/sector specific disease syndromes by species and/or production class		
Option 2: Owner Importation*	5. Imported DIN (OUI) or non-DIN (API) used directly, for compounding or on-farm feed mixing	Potential data availability: 1. CBSA 2. Owner records 3. Feed mill records	Potential data availability: 1. owner declaration 2. regulatory requirement to keep and disclose records (farms, pharmacies, feed mills)	

* Proposed changes to Federal OUI/API regulations will eliminate this data source.

Model 3. Current situation in Canada

- Some of the elements included in Model 3 are already captured by current CIPARS on-farm surveillance activities (surveys of general use and feed inclusion rates in grow-finish swine and broiler chickens). However, the data captured by CIPARS farm-level surveys do not provide complete treatment information (e.g., use information for each instance of antimicrobial administration).
- It is recognized that Model 3 is predicated on detailed treatment records being available from animal owners and that these likely do not currently exist uniformly across or within animal species/sectors.
- For most sectors, there are currently no regulatory requirements for owners to keep treatment records or report this information. The only exceptions to this include:
 - Poultry (requirement under Flock Sheets¹⁰).
 - Aquaculture (these data are required to obtain a provincial or federal net pen license¹¹).
- The availability of data from non-livestock sectors such as companion animals, apiculture and horticulture are not certain. AMU data for companion animals may be more easily obtained through Model 2 as pet owners are unlikely to keep detailed records.
- The level of owner/farm record keeping will vary by sector and by individual owner. Some intensive livestock operations may keep detailed, electronic treatment records. Other operations and sectors may not.
 - One exception to this may be treatment record requirements within on farm food safety programs for some of the livestock commodities. However, CIPARS has some experience in reviewing these records and suggest they are currently not reliable sources of owner-level AMU data for livestock commodities (*Dr. Dave Leger, PHAC, personal communication*).
- It may be more feasible to measure how many animals were treated with/exposed to an antimicrobial using Model 3 than Model 2 as the animal owner will have better estimates of animal numbers.
- Option 2 may not completely include AMU under OUI/API as this relies on producer declaration. Further, the ability to differentiate prescription AMU from OUI or API will be limited by the quality of producer records and their willingness to declare this reason for use. Producers may not report OTC, CMIB, OUI and/or API.

¹⁰ Canadian Food Inspection Agency. Chapter 19 – Poultry Inspection Programs. 19.3 Ante Mortem Inspection/Examination. 19.3.4. Flock Sheets: Producers/Processors Information Exchange. <http://www.inspection.gc.ca/food/meat-and-poultry-products/manual-of-procedures/chapter-19/eng/1360962146879/1360962607138?chap=3>

¹¹ Fisheries Act. Aquaculture Activities Regulations. <http://gazette.gc.ca/rp-pr/p2/2015/2015-07-15/html/sor-dors177-eng.php>

Model 3. Findings, Considerations and Possible solutions

- Model 3 will be best achieved by developing a framework to collect AMU data using the Owner Record model with Option 1 (detailed owner records). If implemented together, some of the AMU data from Model 2 and Model 3 would overlap.
- If Option 1 is included for Model 3, additional information could be captured about who directs AMU: the producer (OTC), the feed supplier (CMIB), or the veterinarian.
- If proposed federal regulations for OUI/API come into effect, there would be little advantage in adding the Owner Importation option. The only information gained with this option would be data about imported Category IV antimicrobials (not medically important).
- Implementing the base Owner Record model may be the most achievable in the short term, given CIPARS current experience with farm-level surveys. Similar to CIPARS, a surveillance framework could be created sector-by-sector as resources become available. It is not realistic to expect to cover everything from farmed livestock commodities to companion animals, aquaculture, apiculture and horticulture in one step. Once data collection templates and systems to capture and store the data are developed, these may be replicated across some or all sectors as resources become available.
 - Improvements to the current CIPARS data collection tools are needed to improve data detail, standardization and efficiency.
 - Quality of producer/owner treatment records will likely need to be addressed.
 - The collection tool may look different depending on the commodity in question.
- It is possible that a combination of Model 2 and Model 3 will provide the most representative AMU data at the individual animal level. For example, using Model 2 to collect AMU data for companion animals may be more realistic and feasible than Model 3, whereas the opposite may be true for some livestock commodities. It is also likely that better owner/farmer-level data would be collected if their veterinarian was involved in the data collection process (e.g., survey). A sector-specific approach is likely required.
- Consideration must be given to whether or not a survey of a representative sample of owners and region is adequate to meet the surveillance objectives. This will depend on the surveillance objectives:
 - If the purpose is to monitor general trends in non-human AMU then a representative sample is adequate.
 - If the purpose is to enforce new AMU regulations, policies and practices at the farm/owner level, then all owners would need to participate (as is the case in Denmark).
 - Ultimately, this will also be dictated by the level at which direction is required (e.g., individual owner vs. regional or national direction).
 - It is not certain whether voluntary collection of owner/farm-level data is adequate or if regulatory authority is required to make AMU reporting mandatory. If there is a desire to use owner/farm-level data to direct AMU by regulation, then there would likely need to be a regulatory requirement for record keeping and reporting of AMU data.

- Collection at the individual owner level would provide additional depth of information while still allowing for data aggregation to the regional and national levels; however, this imparts a much larger cost than Model 1 or Model 2 to develop and maintain the data collection system and to analyze and communicate the results.
- The decision to use owner-level AMU surveillance data to direct future AMU will require consultation and input from a wide array of stakeholders.
- Another opportunity afforded by on-farm AMU data collection is the ability to link these data (temporally and spatially) with AMR data coming from samples collected at the same farm visit.

Model 3. Key Findings

Model 3 – Comprehensive Producer/Owner-level non-human AMU surveillance:

- The Owner Record Model plus the Detailed Owner Record Option will provide the most representative non-human AMU data over time by animal species/sector compared to Models 1 and 2.
- Collection of AMU data from a representative sample of farms/owners from across Canada would provide robust data about AMU including what drug, how much, for how long, and by which route of administration. Data for reason of use (what animal species was the antimicrobial given to, how many had the drug administered and why) would also be available.
 - This model would provide excellent estimates of trends over time that could be used to target owner education. It would provide critical data needed to assess whether or not AMU is judicious and to inform future regulation at the national, provincial, veterinary regulatory body or sector levels.
- Collection of owner record data from all farms across Canada would provide specific data that could be used to target individual owner education, to establish thresholds for judicious use and to enforce new and existing use regulations and/or policies.
- If these data are to be used to direct owner AMU, the collection tool must be designed to accommodate this.
- Broad stakeholder consultation will be required before Model 3 can be implemented. Considerable work is required to create a framework to extract owner/farm record data in an efficient, standardized format to allow for useful interpretation for a national surveillance program. The resources needed to support Model 3 will be greater than needed for Model 2 because there are many more owners/producers than veterinarians in Canada.
- There is little advantage to adding Option 2 (Owner Importation) if the Federal regulatory proposals to restrict OUI/API for medically important antimicrobials come into effect.
- The owner-level model could build on current surveillance by CIPARS and be implemented in a sector-by-sector manner as resources become available. It is possible that building Model 3 for some sectors (e.g., livestock commodities) while building Model 2 for others (e.g., companion animals) may be most practical.
- Record keeping by most animal owners will need to improve to maximize the quality of owner-level AMU data in all sectors.
- On-farm AMU data collection provides the ability to link these data (temporally and spatially) with AMR data coming from samples collected at the same farm visit.

Composite Findings:

Objective 1: To educate stakeholders about AMU by providing accurate, representative AMU data at the level that is required

All three models described in this report can address Objective 1 (to educate stakeholders): they can provide use estimates by antimicrobial class or by specific antimicrobial agent over time, across regions and by different animal species and sectors.

Model 1 (Distribution/Sales Data) with Option 1 (spatial data) is ideally suited to providing these data annually at a relatively low cost. Currently, the data provided to CIPARS from CAHI is not detailed enough to be able to separate out individual antimicrobials and even some important antimicrobial classes. The data provided are not animal species/sector-specific beyond companion and food animals. If these comparisons and level of detail are desired then either additional data need to be collected and provided by CAHI or other model options should be considered. It is likely that a regulatory requirement to report sales data, changes to the 3 company competition reporting rules and closure of OUI and API importation loop holes will be needed before these additional distribution data elements can be provided.

The distribution data currently available in Canada can be used to make regional comparisons, to assess temporal trends, to compare human and non-human AMU and to compare non-human AMU in Canada with other countries. Relying on distribution data, it will be very difficult to provide antimicrobial-bacterial species-animal species/sector-specific direction about AMU to truly improve antimicrobial stewardship. Distribution/sales data also may not be an entirely accurate measure of AMU, since it only measures how much product is sold rather than how much is actually used.

Model 2 (Veterinary Prescription Data) with Option 1 (veterinary records) can provide much more detailed AMU data for surveillance. Like Model 1, the AMU data from Model 2 can be compared over time and across regions but the data from Model 2 can also allow AMU to be compared between veterinarians and veterinary practices. Further, the data captured by Model 2 could provide complete prescription data including dose, frequency and duration of use in addition to route of administration, better estimates of the number of animals exposed to the antimicrobial and more complete information about reasons for use. Data from Model 2 would be more representative of true non-human AMU than Model 1 because the data are collected closer to where the antimicrobials are actually used and would also provide more accurate information about what species of animal actually received the antimicrobial. However, under the current distribution system, OTC and feed mill CMIB AMU data will not be captured by a veterinary model. Increased veterinary oversight under the proposed federal regulatory changes would provide more complete AMU data.

The increased quality and accuracy of the data provided by Model 2 would be reflected in the higher costs and human resources needed to implement this surveillance model.

Model 3 (Owner Data) with Option 1 (detailed owner records) would provide very similar data to Model 2. However the data captured would be more representative of AMU at the level of individual animals than either Models 1 or 2. It would capture more complete information about which animals and how many were exposed to the antimicrobial than for Model 2. As would be the case for Model 2, the increased detail of the data provided by Model 3 would be reflected in the higher costs and human resources needed to implement this surveillance model.

One advantage of Model 3 over Model 2 is that the CIPARS farm surveillance component has already developed a framework in swine and poultry that captures AMU data at this level. However, this framework is based on providing general AMU data from a sample of farms based on an annual survey, rather than a census or using treatment records to capture actual use. Further, the level of record keeping at the owner-level may be an initial barrier to collecting owner-level treatment record data at this refined level. Accessing veterinary record data may be more feasible in the short-term.

Objective 2: To provide data to direct future AMU through policy, regulation or other initiatives

Model 1 is not able to provide data that could be used to measure compliance with or enforce new or proposed AMU regulations at the farm or veterinary level. Distribution data can, however, be used to evaluate effectiveness of new regulations at a regional or national level.

Both Models 2 and 3 can be used to measure compliance with new AMU regulations. Data collected from a sample of (not all) veterinary clinics or owners is better suited to measuring change in AMU practices in specific animal species/sectors and for specific drugs than the distribution data (Model 1). A sample of clinics or owners, however, is not adequate to enforce change in AMU. If this is a desired outcome for surveillance, then all veterinary clinics or all owners, would need to report AMU. This would be extremely difficult to set up for veterinary clinics or owners at this time and would require a large investment in financial and human resources. However, it would be possible to scale up a sentinel system once the framework for data collection is established. It would also likely require a regulatory requirement for AMU reporting. Selection of Model 2 or 3 would depend on the level at which regulation, policy or interventions were to be applied. It is likely that a blended model (veterinary surveillance for some sectors, owner surveillance for others) might be the best fit based on the present level of record keeping and desire to target direction of AMU.

Limitations

There are several limitations and challenges that need to be recognised in recommending and implementing a new non-human AMU surveillance model for Canada including:

- Implementing all aspects of Models 1, 2 and 3 would require vast resources, borne by different stakeholders. In a resource-limited environment, the selection of a final surveillance model (scale and scope) will be dictated by the surveillance objectives and the available resources.
- It is very likely that not all animal species/sectors can be incorporated into an AMU surveillance program at one time. It is much more realistic to build the framework to gradually include animal species/sectors in a step-wise fashion.
- Lack of a specific framework for veterinary or producer/owner AMU data is a large hurdle that must be addressed. Developing a framework that can provide adequate AMU databases, compiling data from disparate sources and addressing data standardization are only a few of the large issues that must be addressed.
- The consideration of surveillance objectives to determine whether or not regulatory changes are required to implement any of these models is an important step. If the data desired are detailed and comprehensive, serious consideration must be given to the regulatory requirements that must be put in place to guarantee reporting of non-human AMU.
- Distribution of antimicrobials through feed mills and distribution centers (such as the Western Drug Distribution Center) was not considered as a potential data source for non-human AMU surveillance in these three models. Current proposed changes in federal regulations may include AMU data from these parts of the drug distribution system.

Recommendations

Ultimately, timely decisions must be made about objectives for non-human AMU surveillance in Canada so that frameworks can be developed with these in mind. If AMU surveillance frameworks are developed specifically to address Objective 1 without consideration for Objective 2, they may not be able to meet this objective in the future. Unless flexible, expandable and scalable mechanisms are built into the framework at the outset, addressing Objective 2 in the future may not be possible without redesigning the entire system.

To meet current needs, additional data elements need to be incorporated into the distribution data: of primary importance is data by antimicrobial drug and class and separated by animal species (beyond the production and companion animal break down that is currently provided). The distribution data should continue to be provided annually. Incorporating data from a sample of veterinary clinics (Model 2) or animal owners (Model 3) would provide additional, more detailed and representative data about AMU on farm including: dose, frequency of administration, duration and route of administration, and what animal species. Including the

respective Option 1 for either model would provide data for how many animals were exposed and why the antimicrobial was used. Incorporating and using data from multiple sources also provides additional ability to validate the data coming in; similar trends in both data sources strengthens confidence in the AMU estimates. Adequate IT support and resources for data collection, management, analysis and reporting are crucial to the success of an AMU surveillance program to report valid, timely data.

Conclusions

It is well recognized that non-human AMU surveillance in Canada needs to be improved. In this report we outline 3 different methods for collecting non-human AMU data – each with specific pros and cons. We recommended a combination approach with Model 1 (distribution/sales data) and consideration of Model 2 (veterinary data) or Model 3 (owner record data). The decision of Model 2 and/or 3 and their options will be dictated by the surveillance objectives.

One of the major obstacles identified by the Working Group was a lack of government policy to support and facilitate development of a more robust non-human AMU surveillance program in Canada. Beyond what is captured in this report, Federal-Provincial-Territorial discussion will be required to solidify national AMU surveillance objectives, and to define the overarching government policy position that will then require stakeholder consultation. These decisions will ultimately impact the type of non-human AMU surveillance model that is required and the level of complexity and detail that it must have.

It is apparent that this process will be lengthy and threatens to slow the development of a robust, national and representative non-human AMU surveillance program in Canada. Several components of the described models are already in use within existing CIPARS activities. Consideration should be given as to how they can be expanded and leveraged to improve AMU surveillance in Canada in the short-term. This would improve current AMU surveillance while the bigger policy pieces and consultation continue to inform the broader, more extensive non-human AMU surveillance framework for Canada.