

# ***Antimicrobial Stewardship: Health Canada's Efforts to Strengthen Canada's Regulatory Framework for Veterinary Antimicrobials***

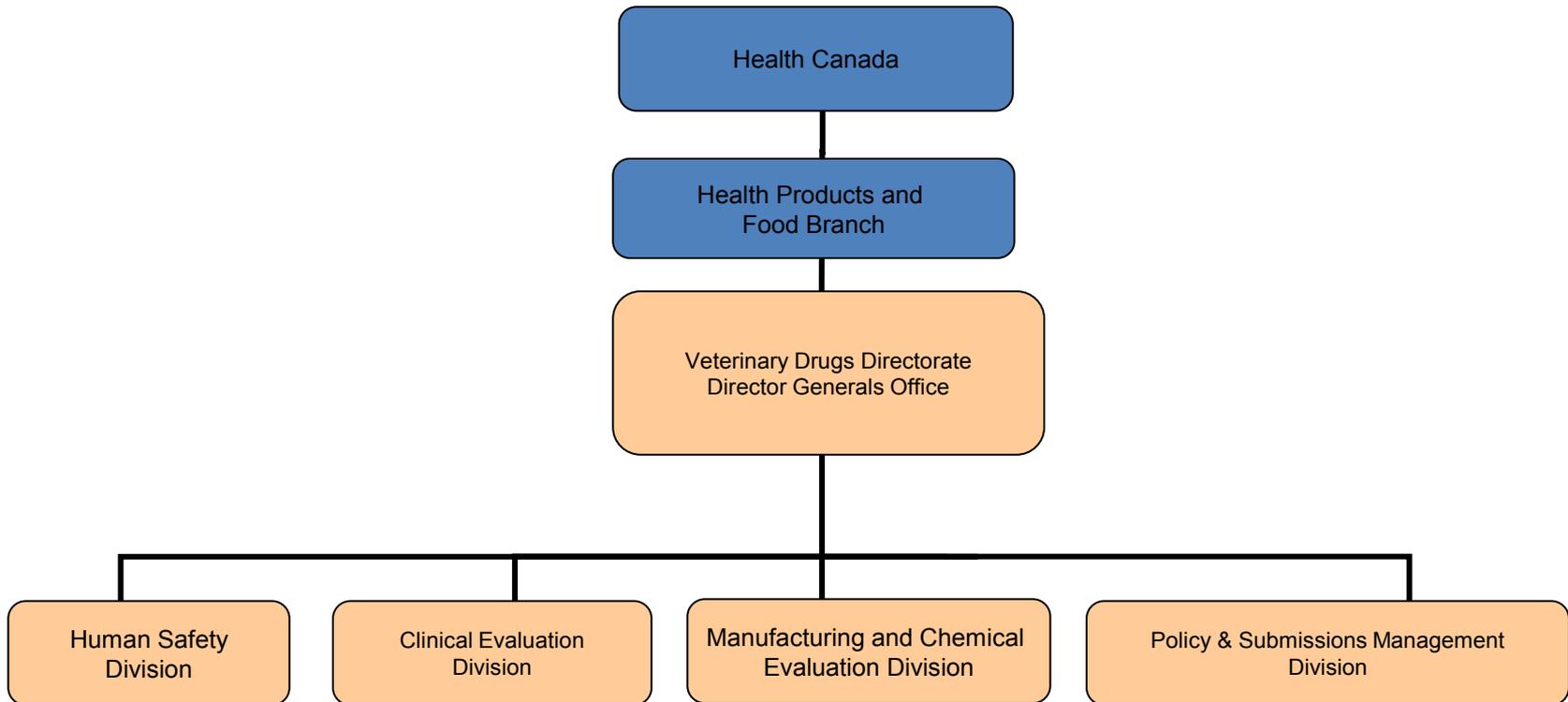
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# Outline

- Veterinary Drug Regulation in Canada
- AMR as a cross-cutting Public Health Issue
- Overview and update on Health Canada led-AMR initiatives to enhance Antimicrobial Stewardship
- Next steps

# Organizational Chart



# Federal Regulatory Authorities

- ❑ **VDD Mandate:** To protect human and animal health and the safety of Canada's food supply, the Veterinary Drugs Directorate (VDD) evaluates and monitors the safety, quality and effectiveness, sets standards, and promotes the prudent use of veterinary drugs administered to food-producing and companion animals
  
- ❑ *Food and Drugs Act and Regulations*
  - Sale and advertising of food, drugs, natural health products, and medical devices in Canada
  
- ❑ *Feeds Act & Regulations* (under the Canadian Food Inspection Agency)
  - Regulation of Drugs in Livestock Feed
  - *Compendium of Medicating Ingredients Brochures* stipulate the drugs to be included in feeds  
<http://www.inspection.gc.ca/english/anima/feebet/mib/mibe.shtml>
  
- ❑ **What we do not have authority over**
  - Practice of medicine: compounding, drug use, extra-label drug use

# VDD's Core Activities

Regulatory oversight throughout the lifecycle of veterinary drugs:

## ❑ **Drug Submissions Review:**

❑ **Pre-Market** – review of veterinary drug submissions from industry and establishment of limits for veterinary drugs in foods – safety, efficacy, quality

❑ **Post-Market** – pharmacovigilance, advice on enforcement and compliance of drugs as well as food (support role to Inspectorate & CFIA)

❑ **Priorities** – Antimicrobial Resistance, Veterinary Health Products, Drug vs Feed, Drug Compatibilities in-feed, Minor Use Minor Species, International Regulatory Collaboration

# Antimicrobial Resistance

*Antimicrobials are essential for the treatment, control and prevention of bacterial infections in humans and animals...*

- Microbes can change in ways that reduce or eliminate the effectiveness of antimicrobial action (i.e. the treatment of infections).
- **Antimicrobial resistance (AMR) = reduced or eliminated effectiveness of antimicrobials.**
- Antimicrobial drugs are used across multiple sectors which indicates complex contributing factors
  - » Health care
  - » Agriculture
  - » Environment
  - » Consumer products

*...but the inappropriate use of antimicrobials in all sectors is leading to increases in the emergence and spread of AMR*

# Why is the world worried about AMR?

- By 2050, annual deaths due to AMR could reach 10 million worldwide, overtaking deaths due to diabetes and cancer combined, and is expected to cost the global economy \$100 trillion USD<sup>1</sup>
- Every year, over 20,000 hospital patients in Canada develop infections that are resistant to antimicrobial drugs, resulting in over \$250M in direct medical costs<sup>2</sup>
- Resistance can emerge from any country and spread: travel, medical tourism, the shipment of food and animals, environmental contamination and the food chain are vehicles for the spread of AMR
  - MCR-1, a gene that increases resistance to important antibiotics, emerged in China and has since spread to countries around the world, including Canada and the United States

1. O'Neill, *Review on Antimicrobial Resistance* May, 2016

2. *CIHR Statement on World Antibiotic Awareness Week 2016*

## A global response is underway

- On September 21, 2016 the President of the United Nations General Assembly convened a High Level Meeting (HLM) of Member States on AMR
  - AMR was recognized as a challenge to health, food security, and development
  - The World Health Organization Global Action Plan on AMR (WHO GAP) was also recognized as the blueprint for action
- Global Action Plan on AMR endorsed by Member States at the World Health Assembly, including Canada (May 2015)
  - Requires countries to have national plans in place by May 2017
  - United States, United Kingdom, European Union and others have already developed and funded national AMR strategies, with leadership at the highest level
- G7 and G20 have identified AMR as a priority at the Leaders level, and by Ministers of Health, Agriculture and Science
- The Global Health Security Agenda has also identified AMR as a priority
  - Canada is one of the countries that co-leads the Action Package on AMR; will Chair in 2017
- Multi-lateral organizations and NGOs are contributing to or supporting work on AMR (e.g., World Organisation for Animal Health (OIE), Food and Agriculture Organization (FAO), Wellcome Trust, Codex Alimentarius Commission)

# Government of Canada response to AMR

- The Government of Canada is addressing AMR through a multi-sectoral “One Health” Approach:

**October 2014:** Release of *Antimicrobial Resistance and Use in Canada: A Federal Framework for Action* outlining strategic objectives in the areas of:

- **Surveillance** activities that enhance and integrate human health, animal health and agri-food surveillance systems;
- **Stewardship** activities, including increased participation in Antibiotic Awareness Week and enhanced regulatory oversight for antimicrobials;
- **Innovation** through federally supported research, international collaboration and public/private partnership

**March 2015:** Release of *Federal Action Plan on Antimicrobial Resistance and Use in Canada: Building on the Federal Framework for Action* which builds on the *Framework* strategic areas of focus by identifying concrete steps that the Government of Canada will undertake

Work underway on developing a Pan-Canadian Framework on AMR

# Draft Pan-Canadian Framework on AMR

Surveillance

Stewardship

Infection Prevention &

Research and



## Desired Outcomes

Enhanced understanding of how AMR spreads in human and animal settings

Comprehensive picture of AMR and AMU in Canada

Effectiveness of current antimicrobial drugs of importance to humans maintained

Health professionals and the public adopt appropriate antimicrobial use practices

Reduced infections in health care and the community

Better tools and approaches to detect and treat drug resistant infections in humans and animals

## Potential Actions

Support the development of a centralized, harmonized database platform to integrate human and animal health data

Identify priority organisms that contribute to AMR in animals and humans

Enhance human AMR/AMU data collection in community-based settings

Strengthen the promotion of appropriate AMU in human and animal medicine

Develop awareness, education and training to improve prescribing practices in human and veterinary settings

Strengthen regulatory oversight and framework on veterinary medicines and medicated feeds

Increase awareness and understanding of AMR, and the role that infection prevention and control play in limiting the spread of infectious agents

Improve management practices to reduce the need for antimicrobials

Increase awareness and understanding of the importance of biosecurity measures to limit the spread of infectious agents and the need for antimicrobial use

Support the development of rapid diagnostics that guide the choice of treatment and therapeutic use

Support clinical trials for drugs that are already on the market, and/or don't have other support

Explore alternative and adjuvants to antibiotics as a made in Canada approach that addresses both veterinary and human medicine

# Managing AMR in Veterinary Drugs Context

- **AMR risk from animals** is one part of a multi-faceted problem
  - In Canada, an estimated 70 % of all medically important antimicrobial drugs are sold for use in food-producing animals
  - Shared jurisdiction (F/P/T) over sale and use of veterinary medicines
  - Multiple stakeholders, including federal, P/T and municipal governments, industry and stakeholders all have a role to play to manage AMR risk

# Role of Health Canada as a Federal Regulator in Antimicrobial Stewardship:

- Ensuring safe and effective drug products are available on the market
- Proper oversight over importation and sale of safe and effective drugs
- Promoting prudent use of such products
- Work with other partners to support their stewardship activities (P/Ts, animal nutritionists, veterinarians etc.)

## Current Activities to address AMR

- We are making important Regulatory and Policy changes to strengthen prudent use of Medically important antimicrobials (MIAs) in livestock production

# Snapshot – Veterinary Drugs AMR Initiatives Underway

These regulatory and policy initiatives are interconnected and mutually supportive:

## 1) Increasing oversight on importation of veterinary drugs (Own Use Importation)

- *new regulatory proposal*

## 2) Increasing oversight on importation and quality of active pharmaceutical ingredients (APIs)

- *new regulatory proposal*

## 3) Mandatory reporting of sales volume from manufacturers and importers to support antimicrobial use surveillance

- *new regulatory proposal*

## 4) Facilitating access to low risk veterinary health products (VHPs), as additional tools for the maintenance of animal health and welfare

- *new regulatory proposal and existing policy tools*

## 5) Removing growth promotion claims from medically-important antimicrobials

- *policy under existing regulatory tools*

## 6) Increasing veterinary oversight over all MIAs (Prescription status switch)

- *policy under existing regulatory tools*

# 1) Oversight on Importation of vet drugs (OUI)

## Current Situation

- Veterinary drugs, including over the counter antimicrobials, can be imported to Canada for own use purposes with limited regulatory oversight. In this context, own use importation refers to importation by an individual for use on animal(s) under their care or guardianship, and not for further sale.

## Regulatory proposal

- Prohibits importation of unapproved drugs for own use, with an exemption for specified drug products that do not represent an unacceptable risk to food safety and public health
- Exempted product list to be *Incorporated by Reference* and established based on specified criteria established by Health Canada
- No MIAs or Pr drugs will be allowed to be imported for own use purposes for use in food-producing animals

## 2) Oversight on Importation and Quality of APIs

### Current Situation

- There is limited oversight on the importation of antimicrobials as APIs for veterinary use.
- Currently, manufacturers, importers and compounders of APIs for veterinary use are not required to have an Establishment Licence (EL) or to follow Good Manufacturing Practices (GMPs).

### Regulatory proposal

- Expand existing regulatory requirements of GMPs for APIs used in human drugs to all veterinary APIs
- Restrictions on who can import MIAs (e.g. Importation of MIA APIs by food animal producers for their direct use in food animals will not be allowed)
- Require an EL for individuals seeking to import APIs for MIA drugs

### 3) Mandatory Reporting of antimicrobial sales volume

#### Current Situation

- No Regulatory authority to collect sales volume for drugs

#### Regulatory proposal

- Require manufacturers or importers of veterinary drugs in dosage form that contain an API for medically important antimicrobial to provide on an annual basis, a report identifying for each drug the total quantity sold and an estimate of the quantity sold for each intended animal species; and
- Require persons, including pharmacists and practitioners, that import and compound and sell an API for medically important antimicrobial drugs (List A) for veterinary use to provide on an annual basis the same report

*Data gathered will support the surveillance pillar of the Federal Action Plan...*

## 4) New Pathway for Veterinary Health Products (VHPs)

### Current Situation

- No regulatory provisions for sale of low risk veterinary health products

### Regulatory proposal

- Creating a risk-based regulatory pathway to allow importation and sale of low risk veterinary health products for use in animals, including food animals
- The proposal builds on the successes and lessons learned from the “Interim Notification Pilot Program (INPP)” for companion animal drugs, and would need continued support from Producer groups and on Farm Food Safety Programs

## 5) Removal of Growth Promotion Claims

- Phase out non-prudent uses of MIAs in animals for long-term non-therapeutic purposes i.e. growth promotion and weight gain
- No growth promotion claims approved for new MIAs post-2004
- There is lack of modern data to show that these products are still effective at the approved dosage (approved several decades ago)
- Positive responses from manufacturers of all implicated products; overall support from food animal producers, veterinary professionals and other stakeholders
- About 64 products are implicated
- Minimizing impact on availability of treatment options

## 6) Increasing Veterinary Oversight of all MIAs (Pr)

- Moving all existing over the counter MIAs to the Prescription Drug List (Pr status);
- All in-feed MIAs to be included in CMIB; and require a Prescription (Pr) prior to sale for on-label products
- About 300 products implicated in all dosage forms (with about 75 in-feed MIAs)

**Update Notice to Stakeholders posted February 13, 2017:**

- <http://www.hc-sc.gc.ca/dhp-mps/vet/antimicrob/amr-notice-ram-avis-2017-eng.php>

## 6) Increasing Veterinary Oversight over all MIAs (contd..)

### *Implicated MIAs for switch from OTC to Pr status*

- Apramycin
- Bacitracin
- Erythromycin
- Lincomycin
- Neomycin
- Penicillin G
- Spectinomycin
- Streptomycin/Dihydrostreptomycin
- Sulphonamides
- Tetracycline/Chlortetracycline/Oxytetracycline
- Tilmicosin
- Tiamulin
- Tylosin/Tylvalosin
- Virginiamycin
- Or their salts or derivatives

# Who can sell Prescription Drugs?

The responsibility for the sale, dispensing and distribution of prescription drugs is shared between federal and provincial/territorial authorities

## Federal level:

- Categories of individuals who are allowed to sell a prescription drug are specified in the *Food and Drug Regulations* including record keeping requirements

## Provincial/Territorial level:

- Provincial/Territorial rules may specify individuals who are entitled under the laws of a province/territory to dispense prescription drug and to sell it in that province

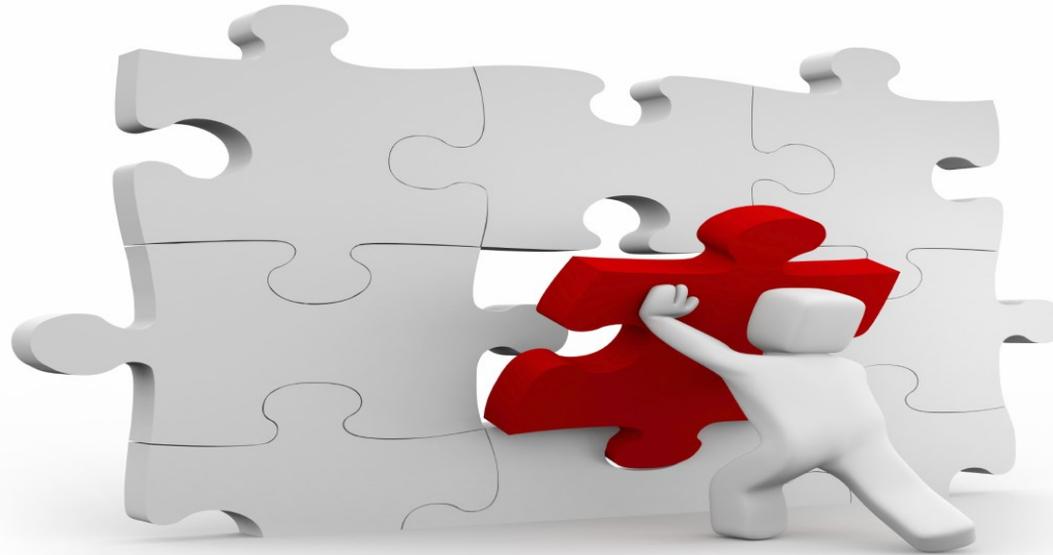
## Path Forward for In-feed Medications containing MIAs

- **A veterinary prescription will be required prior to sale when an MIA drug is mixed in a livestock feeds.**
- All the approved in-feed drugs (including OTC and Pr) to be included in the Canadian Medicating Ingredients Brochure (CMIB).
- There will be no restriction on manufacturing (floor stocking) of such MIA-medicated feeds if manufactured pursuant to Health Canada approvals (i.e. as per CMIB).
- Restrictions remain if manufacturing a medicated feed in a manner deviating from Health Canada's approvals and Veterinary prescriptions will continue to be required prior to manufacturing (i.e. no floor stocking).

## Update & Next Steps

- Formal 75 day Canada Gazette, Part I consultation – July 2 to September 14, 2016
- Anticipating Canada Gazette, Part II publication of final regulations in 2017
- Work underway on implementation details and guidance documents, incorporating feedback received
- Implementation considerations for the proposed regulations as well as the policy initiatives

**VDD's AMR initiatives roll up to just one piece of this complex puzzle... Need Continued Collaboration and Support from key Stakeholders like you!**



YOUR HEALTH AND SAFETY... OUR PRIORITY.