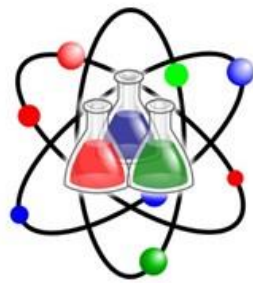


Implementation of stewardship measures for veterinary antimicrobial usage in 'various countries'



Science



Commerce

Peter Davies BVSc, PhD
College of Veterinary Medicine
University of Minnesota, USA

PERSPECTIVE

Nonmedical Uses of Antibiotics: Time to Restrict Their Use?

Richard William Meek, Hrushi Vyas, Laura Jane Violet Piddock*

- 'It is vital that the nonmedical use of antibiotics is critically examined and that **any nonessential use is halted**'

'Idealism increases
in direct proportion
to one's distance
from the problem'

John Galsworthy
Nobel Prize in Literature 1932





What really matters?

- Are animal industries doing harm, and how much?
- How are antibiotics used in food animals?
 - What is effective and what is 'necessary'?
 - What is philosophically defensible?
- How good is the evidence?
 - Harm to public health and food safety
 - Benefits to animal health and food safety
 - How best to use antibiotics in food animals
- How to do better, regardless of impact



Definitions of stewardship



IDSA: coordinated interventions designed to improve and measure the **appropriate use** of antimicrobials by promoting the selection of the optimal antimicrobial drug

- Regimen: Dose, Duration of therapy
- Route of administration

Administration

APIC: coordinated program that promotes

- **Appropriate use** of antimicrobials (including antibiotics)
- Improves patient outcomes
- Reduces microbial resistance and the spread of infections caused by MDR organisms

Outcomes

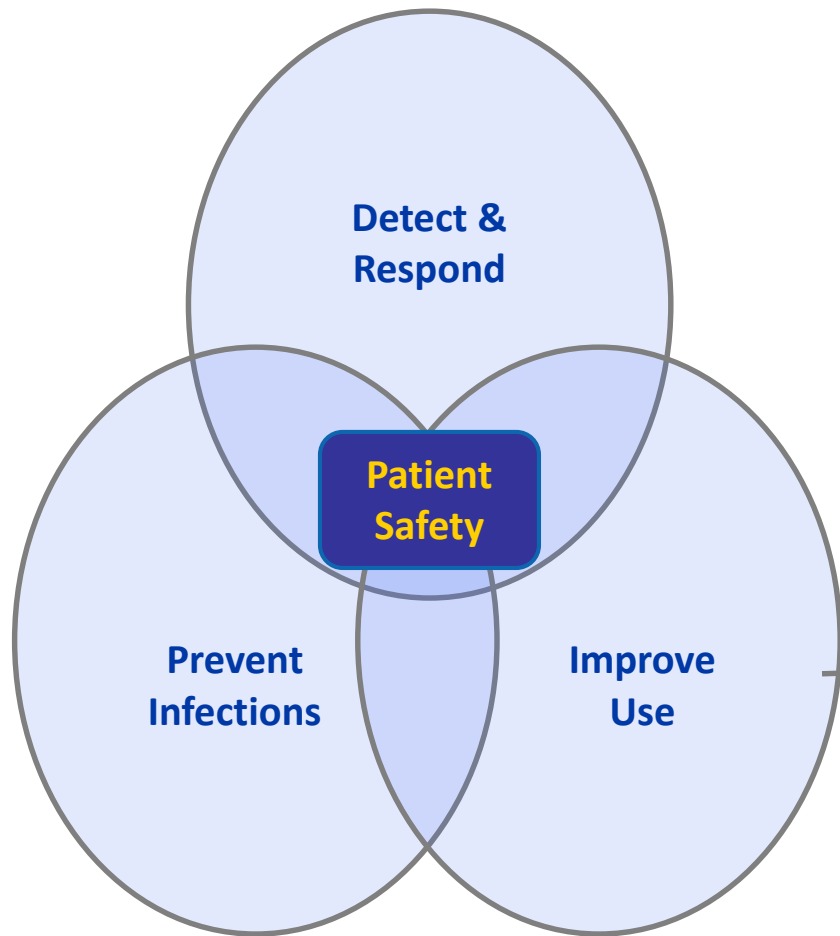
SHEA: = APIC + reduce unnecessary costs



If You Can't
Measure It,
You Can't
Improve It

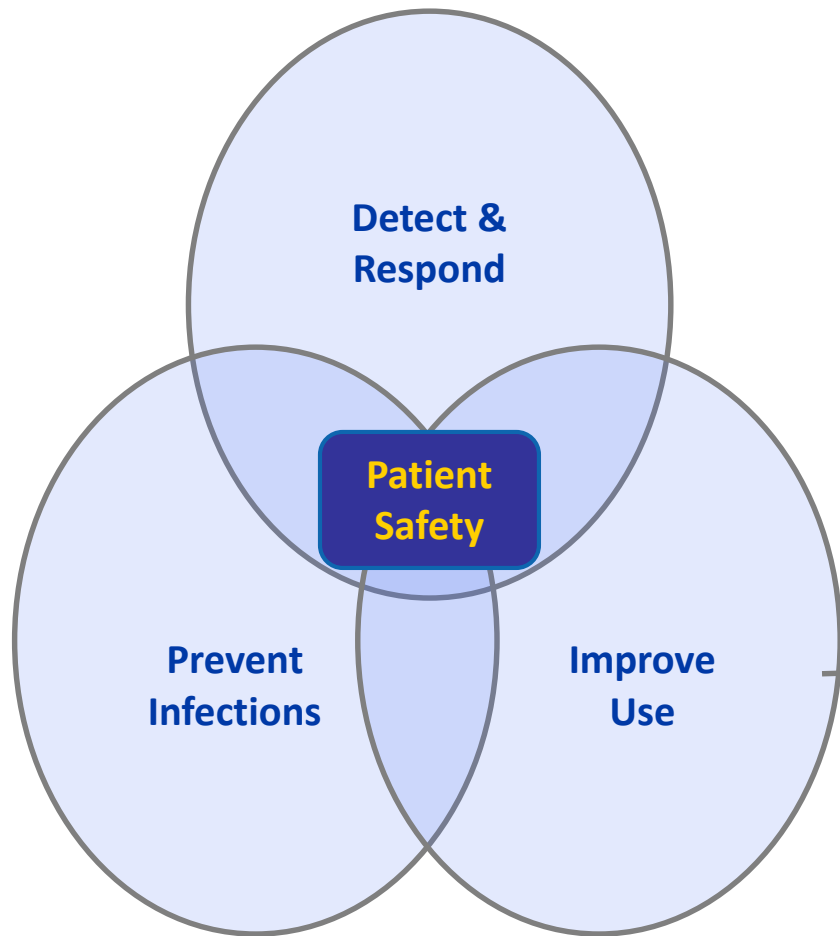
(William Thomson, Lord Kelvin)

CDC model – protecting patient safety



- Measure antibiotic use
- Assess appropriate use
- Assess impact on outcomes
- Implement antibiotic stewardship programs
- Implement strategies to improve antibiotic stewardship practices
- Develop new interventions
- Engage partners and policy makers

CDC model – protecting patient safety



- Measure antibiotic use
- Assess appropriate use
- Assess impact on outcomes
- Implement antibiotic stewardship programs
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Overview

- Information on stewardship initiatives in veterinary medicine
 - USA
 - Australia
 - Canada
- Focus on food animals
 - Regulatory and non-regulatory efforts
 - Reference to measurement of use

The scope of stewardship?



Authority and Access



Quality and Availability



Oversight



Compliance



United States

- 2015 National Action Plan
 - “One Health” approach
- 2017 regulatory changes for food animals
 - FDA GFI#213
 - Veterinary Feed Directive
- USDA survey 2017
 - pigs and cattle on feed
- ‘Surveillance’ initiatives to estimate usage



FDA guidance 213 – January 1, 2017

- Use of medically important antibiotics (MIA) for growth promotion became illegal
- All MIA use in feed/water under veterinary oversight
- 5 OTC products remain (non MIA by FDA GFI#152)
 - Ionophores
 - Bambermycins
 - Bacitracin
 - Tiamulin
 - Carbadox

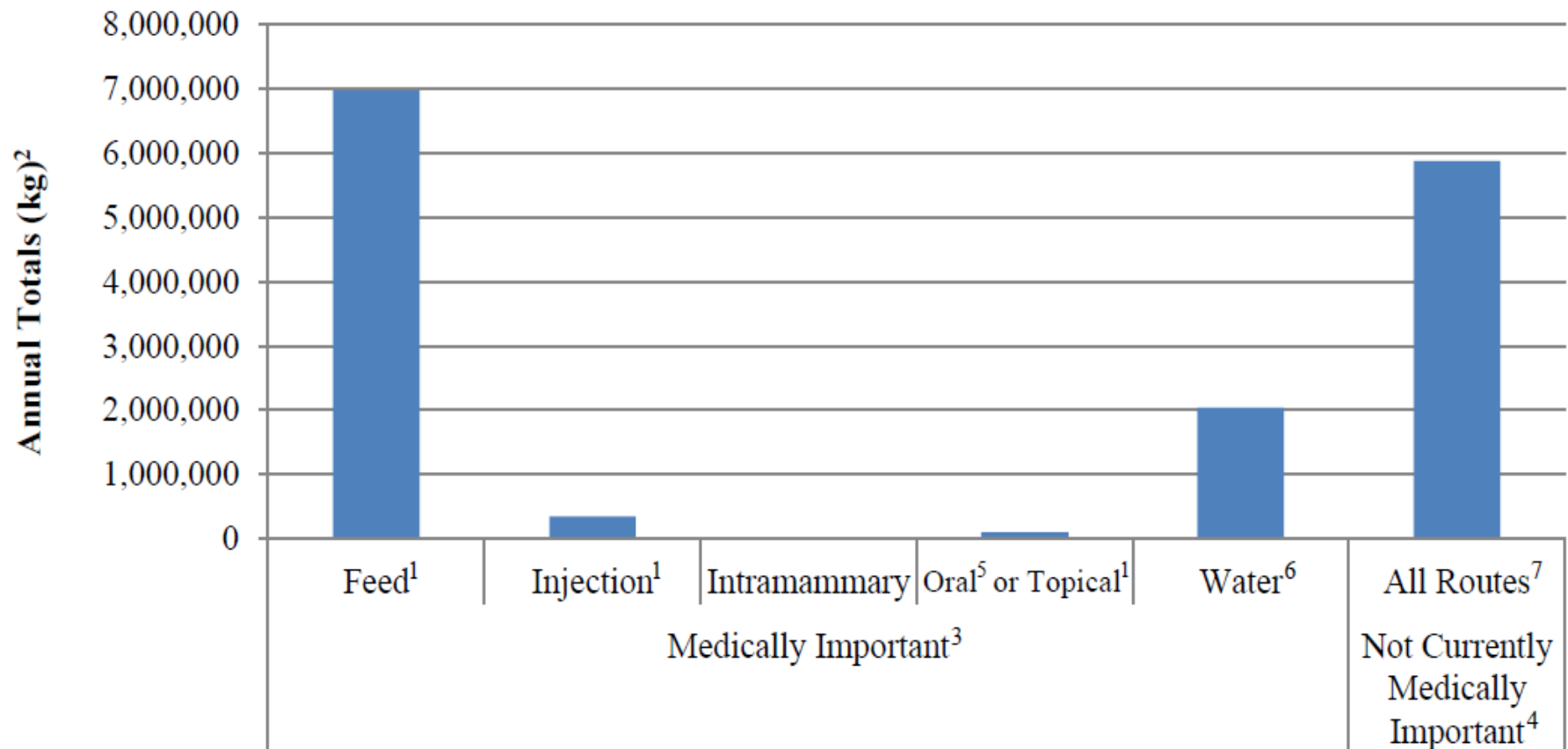


FDA guidance #213 – January, 2017

- Veterinary oversight
 - Valid `Veterinary Client Patient Relationship (VCPR)
 - Veterinary Feed Directive (VFD) for feed
 - Prescription for water medication
- All OTC products with MIA removed apart from injectables, boluses, topical products
- Education efforts to for veterinarians and producers

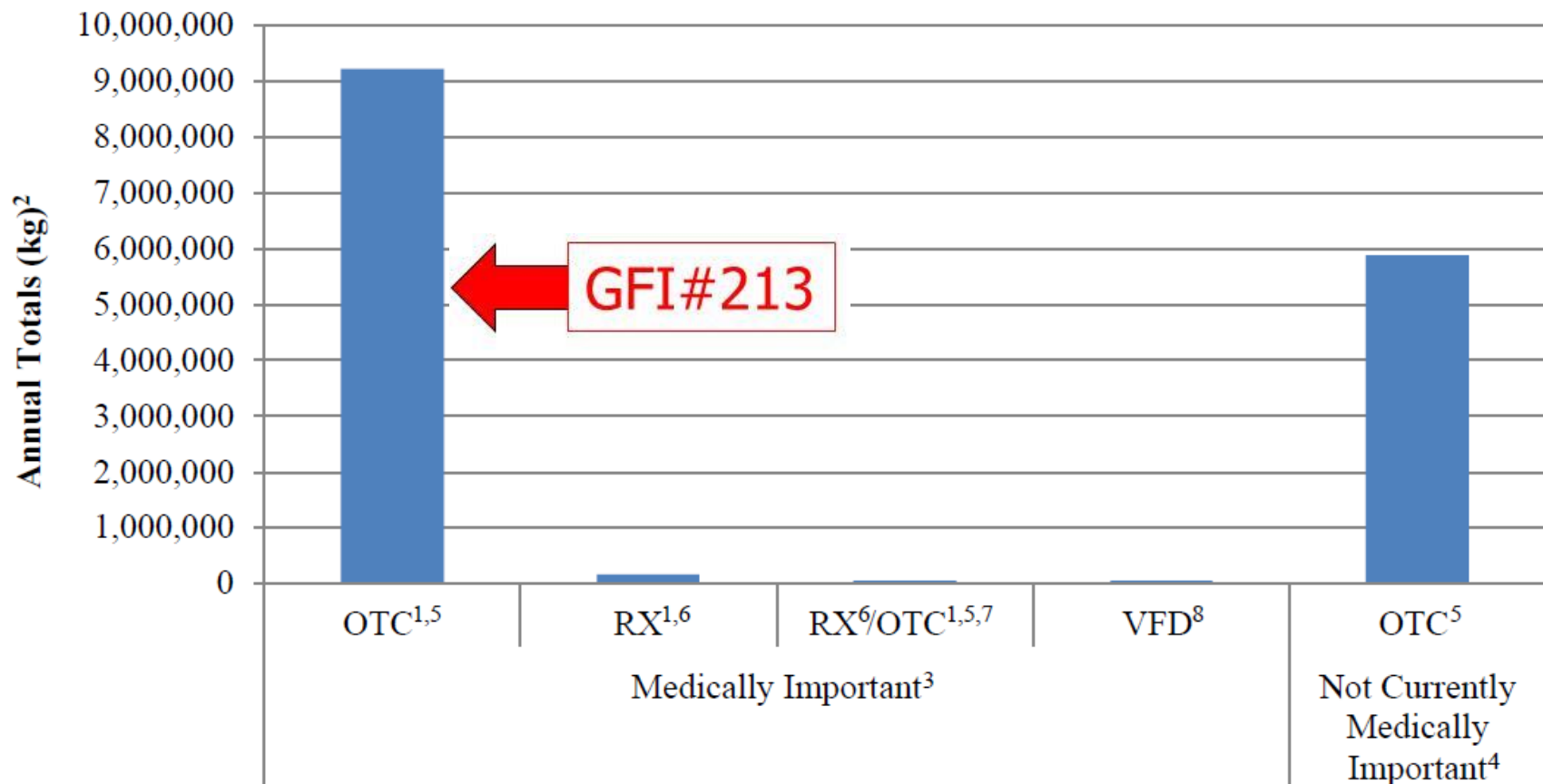
Antimicrobial drugs approved for use in food-producing animals in 2014 by medical importance and route of administration

(<http://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM476258.pdf>)



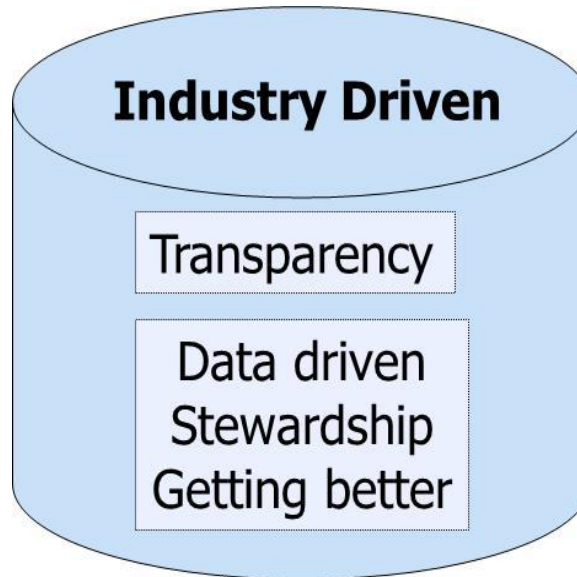
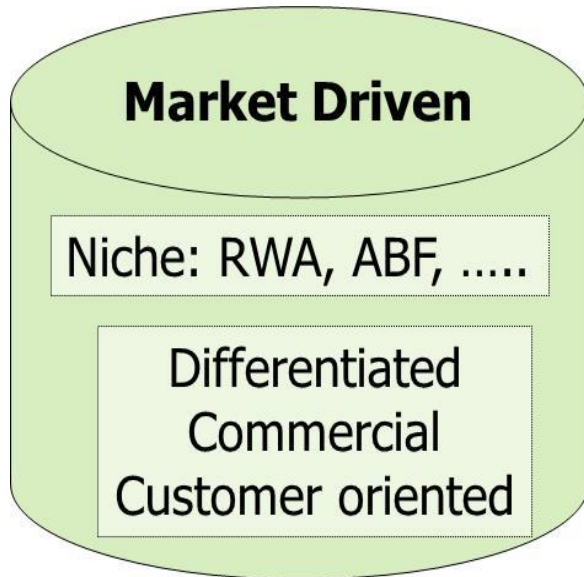
Sales of antimicrobials in food-producing animals in 2014 by medical importance and dispensing status

(<http://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM476258.pdf>)



Measurement and Stewardship

Ways forward



Compliance with the law

Residue avoidance
Guidance 213/VFD
VCPR and veterinary oversight
Extra-label drug use,



National Action Plan for Combating Antibiotic Resistant Bacteria

**Government
driven**

Availability
Oversight
Enforcement
Reduction

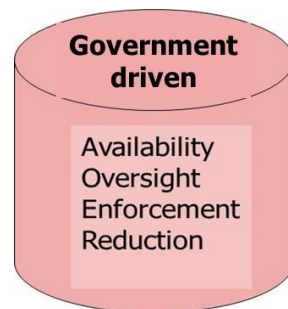
1. Slow the Development of Resistant Bacteria and Prevent the Spread of Resistant Infections
2. Strengthen National One-Health Surveillance Efforts to Combat Resistance
3. Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria
4. Accelerate Basic and Applied R&D for New Antibiotics, Other Therapeutics, and Vaccines
5. Improve International Collaboration and Capacities for Antibiotic Resistance Prevention, Surveillance, Control, and Antibiotic Research and Development



National Action Plan for Combating Antibiotic Resistant Bacteria



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5. Improve International Collaboration and Capacities for Antibiotic Resistance Prevention, Surveillance, Control, and Antibiotic Research and Development



1.3 Identify and implement measures to foster stewardship of antibiotics in animals

Implementation steps include working with veterinary organizations, animal producer organizations, and other partners to:

- i. Develop, implement, and measure the effectiveness of evidence-based educational outreach to veterinarians and animal producers to advance antibiotic stewardship and judicious use of antibiotics in agricultural settings.
- ii. Foster collaborations and public-private partnerships with public health, pharmaceutical, and agricultural stakeholders to facilitate identification and implementation of interventions (e.g., good husbandry practices) to reduce the spread of antibiotic resistance.
- iii. Identify, develop, and revise key agricultural practices that allow timely and effective implementation of interventions that improve animal health and efficient production.
- iv. Develop appropriate metrics to gauge the success of stewardship efforts and guide their continued evolution and optimization.



2.4. Enhance monitoring of antibiotic-resistance patterns, as well as antibiotic sales, usage, and management practices, at multiple points in the production chain from food-animals on-farm, through processing, and retail meat

ii. Enhance collection and reporting of data regarding antibiotic drugs sold and distributed for use in food-producing animals

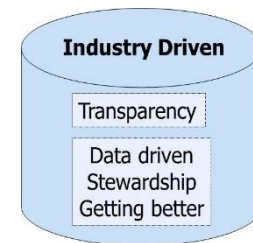
- Goal of use by species
- Implemented but problematic

iii. Implement voluntary monitoring of antibiotic use and resistance in pre-harvest settings to provide nationally-representative data while maintaining producer confidentiality

- Unfunded by congress
- Pilot projects funded by FDA

“Food Animal” activities on stewardship

- “Quality assurance” programs
 - Producer education programs focused on residue prevention and legal obligations of producers
- “Judicious use” guidelines
 - FDA
 - AVMA (companion animal)
 - Species based vet groups (swine, cattle..)
- Industry initiatives on measurement

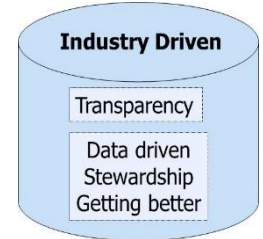
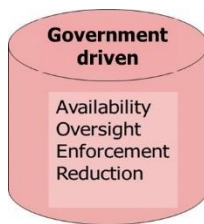


'Barnyard' meetings in 2015-2017

- Swine, beef, dairy, broilers, turkeys, layers
 - FDA, USDA participation
- Doing nothing is not an option!
- FDA funded projects for voluntary data sharing
- Major issues
 - Confidentiality, Representativeness, Buy-in
- Metrics – quantitative and qualitative

FDA RFP on ABU Surveillance in animals

- Detailed antimicrobial drug use data that accurately reflects actual on-farm use
- “Baseline” data on antimicrobial use (i.e., data prior to GFI #213)
- Pilot methodologies for collecting, summarizing, and reporting antimicrobial use data
- Foster public-private partnerships and collaboration
- Leverage existing data systems and minimize burden and disruption to animal producers
- Incorporate strategies for protecting farm/producer identity and other confidential information



FDA RFA on ABU Surveillance in animals

- Characterize the extent to which the collected data are representative of the particular relevant industry segment
- Annual summary report of the data collected, including a detailed description of the data collection methodology
- 2 projects over 5 years from September, 2016
 - Beef/Dairy (KSU, UMN)
 - Poultry/Swine (Mindwalk Consulting, LLC)
 - Interact on methodology and metrics
- Report to FDA on 2016-2017 data in late 2018



FDA RFA on ABU Surveillance in animals

- Complementary to sales data
- Quantum leap forward in quantifying use in major food animal species in the USA
 - Details vary among species
- Primary goal to support stewardship
 - Understand practices and indications to establish benchmarks and inform discussions
 - Not seen as a precursor to comprehensive monitoring

Pipestone Antibiotic Resistance Tracker

<http://www.pipestonepart.com>

Market Driven

Niche: RWA, ABF,

Differentiated
Commercial
Customer oriented



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WORKING ALONGSIDE ANIMAL CARETAKERS
TO ADVANCE ANIMAL CARE.

FEEL FREE TO ASK ANY QUESTION YOU HAVE...

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Market Driven

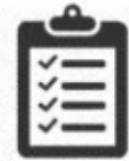
Niche: RWA, ABF,

Differentiated
Commercial
Customer oriented

DOING OUR **PART** FOR THE RESPONSIBLE USE OF ANTIBIOTICS:

- Began Jan 1, 2017
- Interactive, web-based tool to track total antibiotic use
- Demonstrates responsible use
- Works to track resistance over time
- Gives better information to:
 - Select best treatment for sick animals
 - Track use/progress overtime
 - Benchmark internally and externally
 - Safeguard antimicrobial resistance

186 producers – 3.5 million pigs



RECORD



REVIEW



RESPOND



Australia



Australian Government
Department of Agriculture
and Water Resources



- National Antimicrobial Resistance Strategy 2015-2019
- AMR Surveillance
 - Funded by DAWR
 - Generally little resistance found to the critically important antibiotics in animal samples
- Voluntarily phasing out all in feed antibiotics that are registered as growth promotants
 - Anticipating legislation
- Tighter control of prescriptions (varies by state)



AUSTRALIA

- Australian Livestock AMS Group
 - Identification of barriers that exist that impact all livestock industry efforts to progress AMS
 - Workshop on phasing out growth labelling on antimicrobials important for human health
 - Strong relationship with CVO's office
- Livestock AMS Conference November 2018



Pig Industry in Australia

- Federal Government Grant
 - ACMF, Murdoch University, University of Adelaide
 - Automate AMR testing on farm – for benchmarking
- Antimicrobial Stewardship Implementation Project
 - Steering Group
 - Producers, Vets, Nutritionists, Retailers, Poultry industry
 - Papers and case studies being developed
- Antibiotic usage calculator for use on farm (benchmark)
- Prescribing Guidelines

Australia

- No 'top down' initiative to measure use
- Larger producers goal to reduce antibiotic use
 - 'Antibiotic free' production
 - 50% reduction? (Chris Richards)
- APIQ program
 - Health and welfare
- Innovation in on-farm data collection
 - Market driven
 - i-vet

Global Technology Development

REAL TIME ANIMAL HEALTH MONITORING

iVet has been developed as an innovative management tool that assists health, welfare and food safety compliance in production animal systems.



iVet Application

INTEGRATES

- Veterinary Advice and Actions
- Wellbeing Assessments
- Scheduled Health Programs
- Recording of Treatments
- Staff Competencies
- Food Safety Compliance
- Withholding Period Management Systems

ASSISTS

- Management and Compliance of Health Programs
- Welfare Standard Monitoring
- Individual and Group Animal Care
- Tracking of All Treated Animals
- Analysis of Health Program Effectiveness



CANADA

FEDERAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE AND USE IN CANADA

BUILDING ON THE FEDERAL
FRAMEWORK FOR ACTION



Medical & Science

CIPARS

means

Canadian Integrated Program for
Antimicrobial Resistance
Surveillance

by [acronymsandslang.com](https://www.acronymsandslang.com)



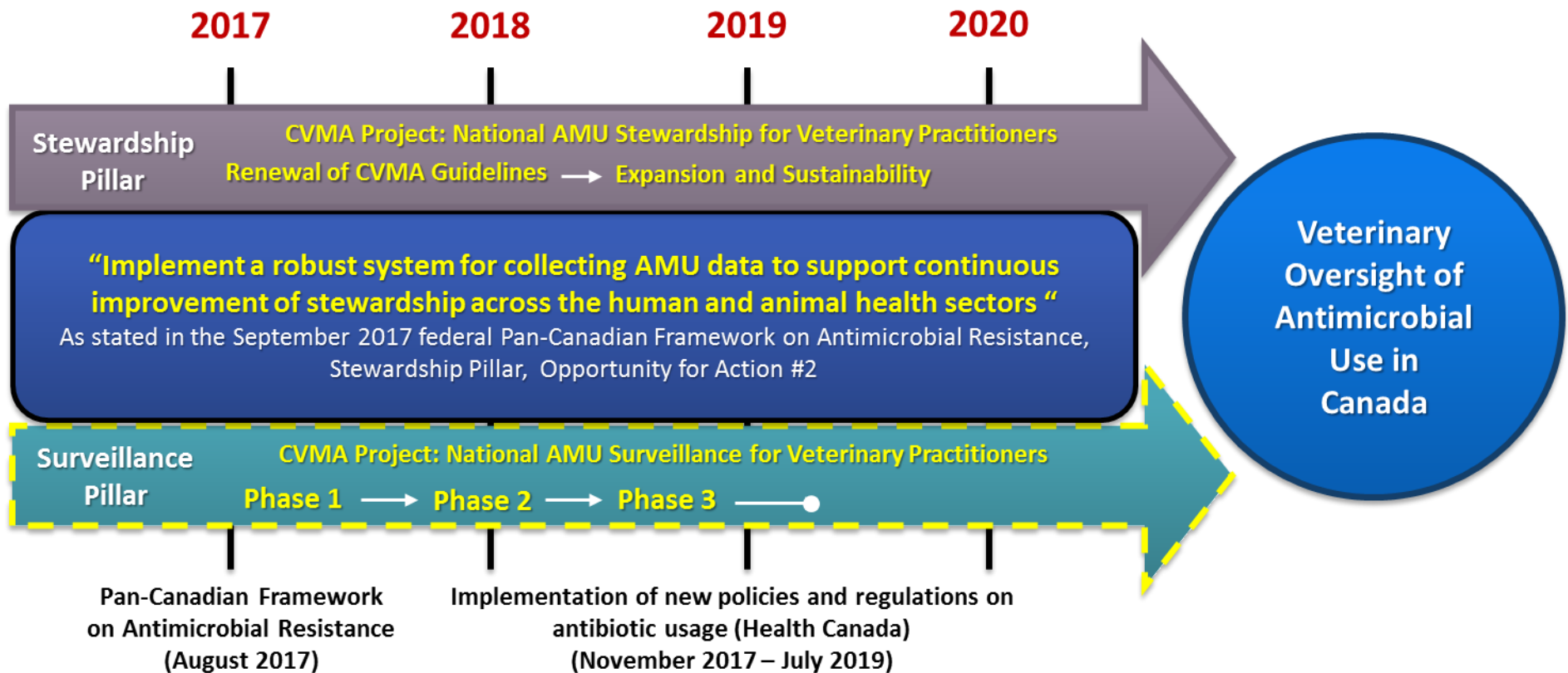
CANADA – Regulatory changes

- Removal of growth promotion claims for MIAs
- Prescription status for all MIAs (December 2018)
 - Feed, water and injectable
- Closing “Own Use Importation” and “Active Pharmaceutical Ingredient” loopholes
 - Facilitated inappropriate access of MIAs
- Mandatory reporting of antimicrobial sales volumes by species (January 2018)

Guided Evolution of Veterinary Oversight

(courtesy of Dr. John Prescott)

Guided Evolution of Veterinary Oversight of Antimicrobial Use in Canada





CANADA – stewardship initiatives

- CAN-RESIST (<https://canresist.com>)
 - Cross-sectoral: human and animal
 - In formative stages - educational
- 'Animal AMS Canada' (Weese, Prescott,..)
 - Early stages
 - Coordinate stewardship activities/communications across academic, producer, industry (pharma and ag) and government groups
- Revised CMVA prudent use guidelines (spring 2018)



Summary

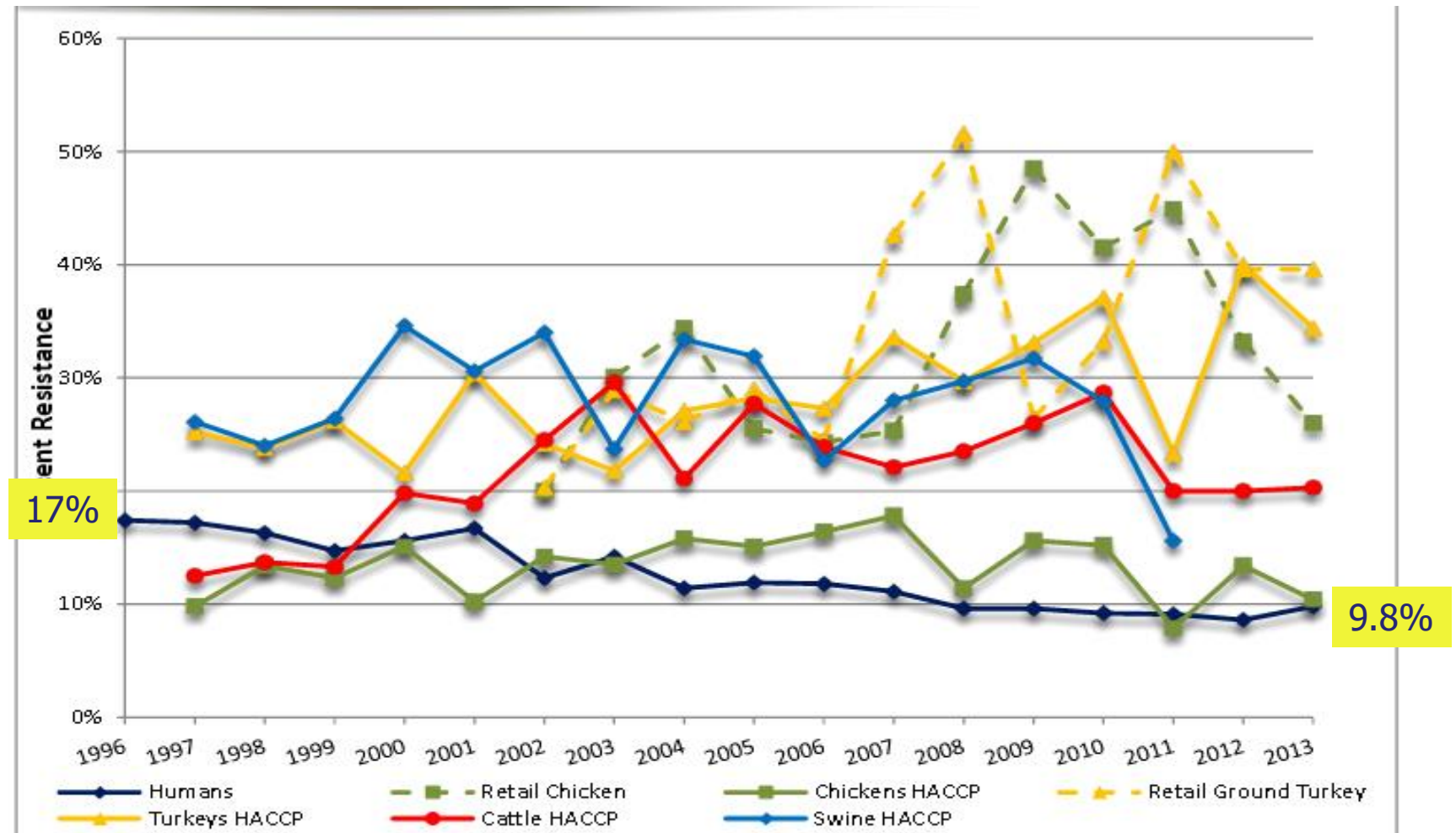
- Large countries – jurisdictional and logistic issues
- Regulatory changes advancing regarding growth promotion and veterinary oversight
- Acknowledgement of need to measure use
 - Logistics and mechanisms vary
 - Goal to support stewardship not mandate reduction
- Industry initiatives driven by market and political pressures
- Goal to reduce 'inappropriate' use



Surveillance \neq Stewardship

- Reduction in antibiotic use is an intervention, not an outcome
- Assessing appropriate use?
 - Definition?
 - Who is qualified to decide?
 - What are the criteria?
- Outcomes
 - Real or projected benefits to human health
 - Demonstrable?

% of NT *Salmonella* resistant to ≥ 3 classes (NARMS 2013)



Assessing Appropriateness of Antimicrobial Therapy: In the Eye of the Interpreter

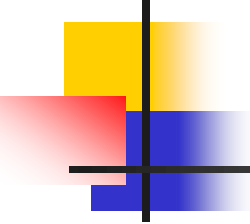
Daryl D. DePestel,¹ Edward H. Eiland III,^{2,a} Katherine Lusardi,³ Christopher J. Destache,⁴ Renée-Claude Mercier,⁵ Patrick M. McDanel,^{1,6,b} Kenneth C. Lamp,¹ Thomas J. Chung,¹ and Elizabeth D. Hermsen^{1,7}

¹Global Medical Affairs, Cubist Pharmaceuticals, Lexington, Massachusetts; ²Department of Pharmacy, Huntsville Hospital, Alabama; ³Department of Pharmacy, University of Arkansas for Medical Sciences Medical Center, Little Rock; ⁴Creighton University School of Pharmacy and Health Professions, Omaha, Nebraska; ⁵College of Pharmacy, University of New Mexico, Albuquerque; ⁶Department of Pharmacy Practice, Massachusetts College of Pharmacy and Health Sciences, Worcester/Manchester; and ⁷Department of Pharmacy Practice, College of Pharmacy, University of Nebraska Medical Center, Omaha

To address the increase of drug-resistant bacteria and widespread inappropriate use of antimicrobials, many healthcare institutions have implemented antimicrobial stewardship programs to promote appropriate use of antimicrobials and optimize patient outcomes. However, a consensus definition of appropriate use is lacking. We conducted a multicenter observational study to compare 4 definitions of appropriateness—a study site-specific definition, use supported by susceptibility data, use supported by electronic drug information resources (Clinical Pharmacology/Micromedex), or study site principal investigator (PI) opinion—among patients receiving 1 or more of 13 identified antimicrobials. Data were collected for 262 patients. Overall, appropriateness with the 4 definitions ranged from 79% based on PI opinion to 94% based on susceptibility data. No single definition resulted in consistently high appropriate use for all target antimicrobials. For individual antimicrobials, the definitions with the highest rate of appropriate use were Clinical Pharmacology/Micromedex support (6 of 7 antimicrobials) and susceptibility data (5 of 7 antimicrobials). For specific indications, support from susceptibility data resulted in the highest rate of appropriate use (4 of 7 indications). Overall comparisons showed that appropriateness assessed by PI opinion differed significantly compared with other definitions when stratified by either target antimicrobial or indication. The significant variability in the rate of appropriate use highlights the difficulty in developing a standardized definition that can be used to benchmark judicious antimicrobial use.

Antimicrobial stewardship and appropriate antibiotic use

(De Pestel et al., 2014)

- 
- Standardized definitions of appropriate/inappropriate use are lacking, as are metrics and drivers of use
 - Variety of criteria for appropriate use
 - Selection of an antimicrobial that has *in vitro* activity against the isolated pathogen
 - Consistent with current practice guidelines or accepted norms
 - In agreement with institutional protocols
 - Expert opinion
 - Lack of agreement highlights difficulty in defining a standard definition for appropriate use.

Models of antimicrobial pressure on intestinal bacteria of the treated host populations

V. V. VOLKOVA^{1*}, C. L. CAZER² AND Y. T. GRÖHN²

- “The examples highlight the extent of current ignorance and need for empirical data on the variables influencing the selective pressures imposed by antimicrobial treatments on the host’s intestinal bacteria”

The antibiotic steward

