

The Pacific Northwest Economic Region Presents:

Agriculture & Cross-Border Livestock Health

Wednesday, August 18th | 10:45am-11:45am

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Regents Prof., Molecular
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Antimicrobial resistance in food animal production...missed opportunities and unintended consequences?

Douglas R. Call, Regents Professor Paul G. Allen School for Global Health Washington State University, Pullman, WA drcall@wsu.edu

Take-home messages

- ABR bacteria can persist for reasons other than selection from antibiotics
- Younger animals are a primary source of resistant bacteria

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, July 2006, p. 4583–4588 0099-2240/06/\$08.00+0 doi:10.1128/AEM.02584-05 Copyright © 2006. American Society for Microbiology. All Rights Reserved. Vol. 72, No. 7

Use of a Nonmedicated Dietary Supplement Correlates with Increased Prevalence of Streptomycin-Sulfa-Tetracycline-Resistant *Escherichia coli* on a Dairy Farm

Artashes R. Khachatryan, Thomas E. Besser, Dale D. Hancock, and Douglas R. Call Artashes R. Khachatryan, Thomas E. Besser, Dale D. Hancock, Dale D. Hancock, and Douglas R. Call

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APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Jan. 2008, p. 391–395 0099-2240/08/\$08.00+0 doi:10.1128/AEM.01534-07 Copyright © 2008, American Society for Microbiology. All Rights Reserved. Vol. 74, No. 2

The Streptomycin-Sulfadiazine-Tetracycline Antimicrobial Resistance Element of Calf-Adapted *Escherichia coli* Is Widely Distributed among Isolates from Washington State Cattle[∇]

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Journal of Applied Microbiology



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ORIGINAL ARTICLE

Microcin MccPDI reduces the prevalence of susceptible Escherichia coli in neonatal calves

L.J. Eberhart^{1,2}, J.N. Ochoa¹, T.E. Besser^{1,2} and D.R. Call^{1,2}

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APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Oct. 2011, p. 7255–7260 0099-2240/11/\$12.00 doi:10.1128/AEM.05352-11 Copyright © 2011, American Society for Microbiology. All Rights Reserved.

β-Lactams and Florfenicol Antibiotics Remain Bioactive in Soils while Ciprofloxacin, Neomycin, and Tetracycline Are Neutralized[∇]

Murugan Subbiah, Shannon M. Mitchell, Jeffrey L. Ullman, and Douglas R. Call, at Call, and Douglas R. Call, and Do

Departments of Veterinary Microbiology and Pathology¹ and Biological Systems Engineering² and Paul G. Allen School for Global Animal Health,³ Washington State University, Pullman, Washington 99164, and Department of Agricultural and Biological Engineering, University of Florida, Gainesville, Florida 32611⁴





Urine from Treated Cattle Drives Selection for Cephalosporin Resistant *Escherichia coli* in Soil

Murugan Subbiah^a, Devendra H. Shah^{1,2}, Thomas E. Besser^{1,2}, Jeffrey L. Ullman³, Douglas R. Call^{1,2}*

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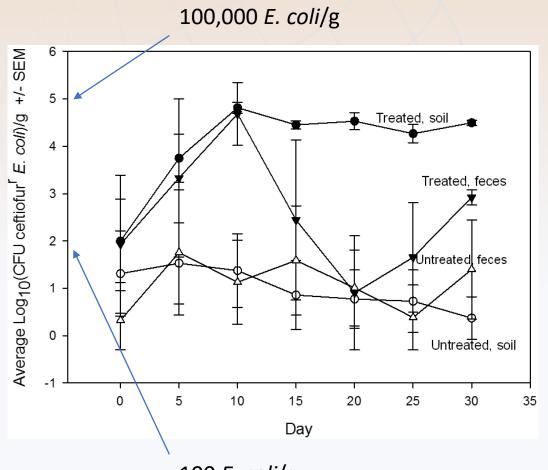
environmental microbiology



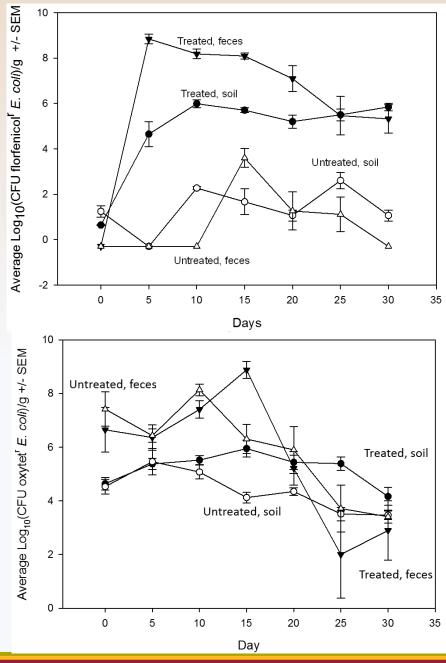
Environmental Microbiology (2016) 18(2), 557-564

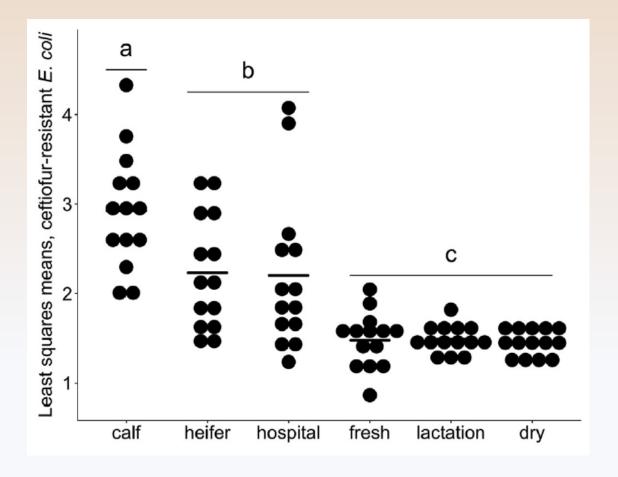
doi:10.1111/1462-2920.13097

Soil-borne reservoirs of antibiotic-resistant bacteria are established following therapeutic treatment of dairy calves



100 *E. coli/*g





Take-home messages:

- Not all antibiotics present the same magnitude of risk
- Environmental reservoirs can become established quickly and they are predictable

In feed chlortetracycline prophylaxis of beef cattle

- 300 calves arrived 9 Feb 2015; on 14 Feb, 150 calves received 5day in-feed CTC prophylaxis treatment; 150 untreated control calves.
- 25% of control calves developed illness requiring treatment with a macrolide (tildipirosin).
- Only 2 animals in CTC group required treatment
- No difference in prevalence of AMR after 27 days.
- Highest AMR shedding rate for both groups was 75 and 117 days post treatment.

Agga et al. 2016. AEM





Summary

- We will always find antimicrobial resistant bacteria on farms.
 The key is to reduce the total numbers to reduce transmission.
- Younger animals and their housing locations are "hotspots" for antimicrobial-resistant bacteria. Different strategies can be used for different age groups.
- When they work, some antibiotics will have less effect on AMR than others.
- Regulations designed to stop preventative use of antibiotics will likely have unintended consequences.

Agriculture and Crossborder Livestock Health

Richard Rusk, DVM, MD, MPH
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August 18th 2021



Presenter Disclosure

- Speaker: Dr Richard Rusk
- Relationships with commercial interests:
 - **Grants/Research Support:** PHAC grant Lyme Disease
 - Speakers Bureau/Honoraria: MCFP, University of Manitoba
 - Consulting Fees: HyLife Foods Ltd., Maple Leaf Foods.



Objectives

- Overview of Human Health Antimicrobial Stewardship (AMS) programs in Canada
- AMS Interventions in Human Health
- Influencers to progress with AMS in north America
- Re-addressing AMS After COVID

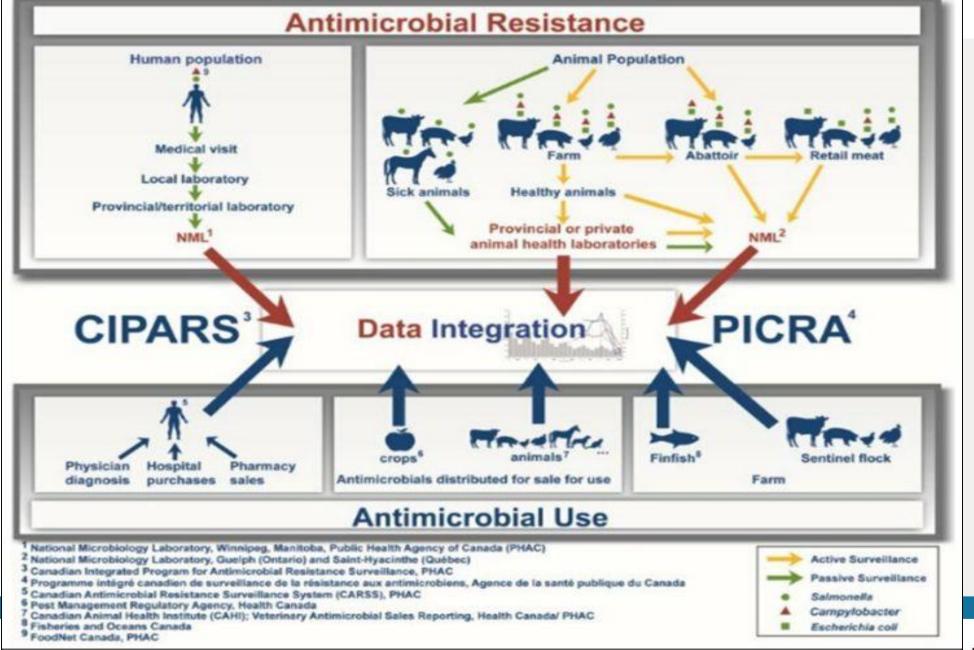


AMS Overview

- Chief Public Health Officer of Canada's 2019 Spotlight Report: "Handle with Care: Preserving Antibiotics Now and into the Future"
 - Big picture focus
- Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) Annual Reports
 - Antimicrobial Use data

https://www.canada.ca/en/public-health/corporate/publications/chief-public-health-officer-reports-state-public-health-canada/preserving-antibiotics/message.html





https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars/cipars-reports/2018-annual-report-integrated-findings.html



AMS INTERVENTIONS

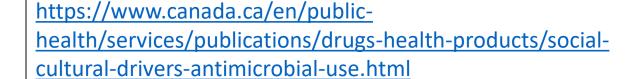
- Community-based interventions
 - Public awareness, community education and stewardship, National AMS Strategy
- Primary-care interventions
 - Educational programs, feedback to physicians, shared decision making, Electronic health records (EHR) surveillance
- Health system interventions
 - Guidelines, vaccinations, Point-of-care testing, Restricted reimbursement

https://www.canada.ca/en/public-health/services/publications/drugs-health-products/interventions-address-antimicrobial-use.html



SOCIAL DETERMINANTS of AMS

- Organization and health system-related
 - Availability and access to diagnostic tools and guidelines, peer influence, systems for self-monitoring (EHR), OTC sales, economic incentives from pharma, malpractice laws, sick leave policies, daycare policies, vaccination campaigns
- Practitioner-related
 - Knowledge, beliefs, and attitudes towards antibiotics, perceived expectations, shared decision making, patient-practitioner relationships, practice volume, medical training
- Patient-related
 - Attitudes, knowledge, or beliefs about antibiotics, illness and health behaviours, expectation of a prescription, previous experience, demographics and social determinants of health
- Sociocultural factors
 - Power distance, uncertainty avoidance, cultural perceptions, income inequality





AMR Priorities

Methicillin-resistant
Staphylococcus
aureus infections

INCREASED BY

60%

since 2012



MORE THAN

50%

of all gonorrhoea infections are

RESISTANT

to at least one antibiotic



C. difficile infections

stable stable

since 2015



5X INCREASE

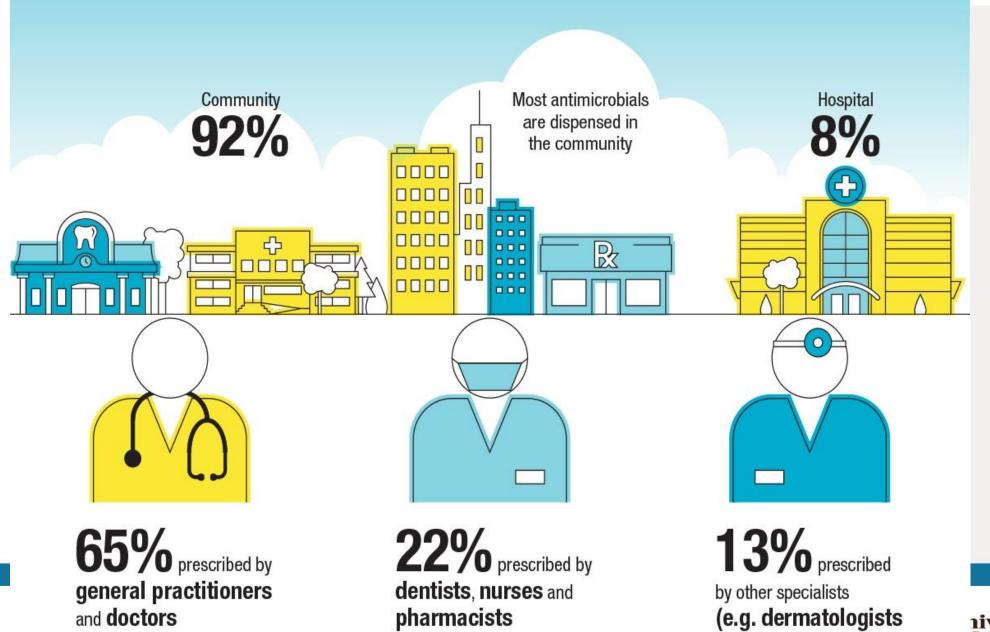
in people carrying the

BACTERIA RESISTANT

to carbapenems which are amongst the most powerful antibiotics that exist



niversity Manitoba



niversity Ianitoba

and pediatricians)

AMS Progress Concerns

- COVID 19 pandemic
- Influence of Covid on AMS
 - Diverted funding
 - Diverted personnel
 - Diverted research focus
 - Lower risk tolerance by clinicians in community who then increase the use of antibiotics
- Less educational and promotional information available



Re-addressing AMS After COVID

- Require a mosaic of actions
- Division of actions into "segments"
 - Primary care, acute care, ICU, long-term care, transplant patients, infectious diseases
- Focus on actions that impact and resonate the most for the physicians in that segment
- Use a broader team to create a safety net for the clinicians check lab results and medical orders



CONCLUSION

- Addressing AMS and AMR is a WICKED problem
- Human Health and Animal Health have overlaps but also very different issues to address and focus on
- COVID 19 pandemic has had a negative effect on progress
- Sub-divide efforts into specific sections moving forward



QUESTIONS







Intersection of Trade and Antimicrobial Resistance and Use Policies

Rachel Cumberbatch, DVM
Animal Health Institute
PNWER 30th Annual Summit 2021

Animal Health Institute (AHI): Who are we?























ECO









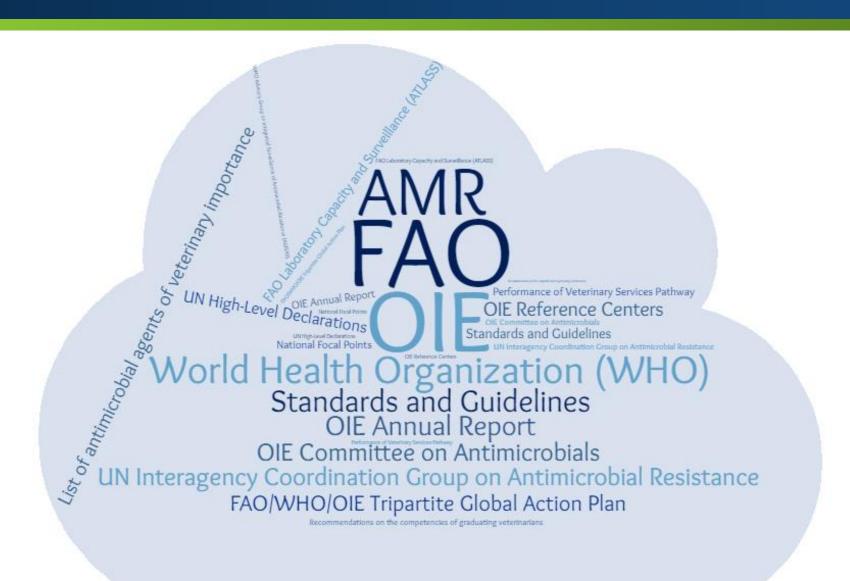
MERCK



The animal health industry is heavily regulated.

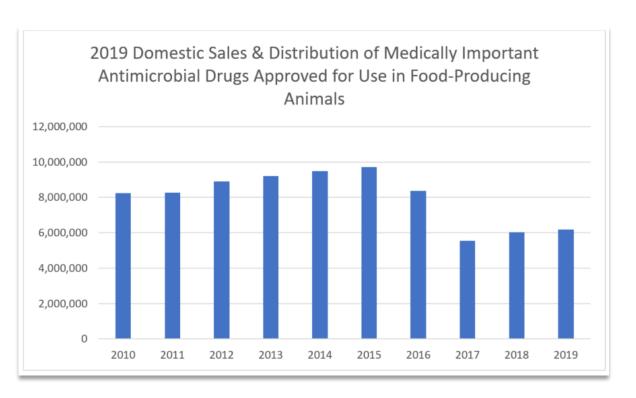


Flurry of International Activity Related to AMR



Significant Domestic Progress on AMR

- Medically Important Antimicrobials Under Veterinary Oversight
- Elimination of Growth Promotion Indications
- National Surveillance through NARMS
- FDA Antimicrobial Sales Reporting
- National Action Plan
- AVMA Judicious Use Principles
- Species Specific Guidelines



Codex Task Force on AMR

- OIE & Codex are Referenced Standards at the World Trade Organization
- Influence direction of development funding
- Serve as starting point for domestic policies



- Terms of Reference:
 - Revise the Code of Practice to Minimize and Contain Antimicrobial Resistance to address the entire food chain, in line with the mandate of Codex.
 - Consider the development of Guidance on Integrated Surveillance of Antimicrobial Resistance

Article 118

Article 118, a section in the EU vet medicines legislation, prohibits the use of certain antimicrobials in food animal production exported to the EU. The EU legislation would effectively impose EU hazard-based antibiotic use measures on meat, milk, egg, and fish producers in countries that export to the EU, including the United States. Policy is set to take force January 2022.



Reasons for Concern:

- Reduce food/meal/milk/fish/egg exports to the EU
- Threaten animal health and animal welfare by limiting animal disease control options and increased cost to third countries
- Hinder access to medicine by preventing veterinarians using products approved by the FDA
- Sets a negative precedence
- Not WTO Compliant and under WTO rules unnecessary

AMR-specific provisions in trade agreements are unnecessary and inappropriate



Any country that identifies a legitimate AMR-related food safety risk already has the right under the WTO *Agreement on the Application of Sanitary and Phytosanitary Measures* to restrict imports from the country or the operator that is the source of that risk.

Summary

- Animal medicines are heavily regulated. Veterinarians are central to judicious use programs that slow the development and spread of AMR bacteria.
- There is significant activity underway domestically and internationally.
- Activity internationally affects domestic policy. Therefore, engagement is important.
- EU legislation to take effect in Jan 2022 aims to dictate antimicrobial use in third countries.
- AMR-specific provisions in trade agreements are unnecessary and inappropriate.

Ultimately the goal is to maintain or return an animal to health.

- There are currently no approved alternatives to antibiotics for the treatment of bacterial infections in animals.
- Removing traditional antibiotics prematurely can have negative consequences.
 - A <u>2018 study</u> found that 65% of veterinarians, producers and other animal health stakeholders felt that rearing animals in a 'Raised Without Antibiotics' system slightly or significantly worsens animal health and welfare.

How does AHI view AMR?

- Managing AMR and preserving the effectiveness of antibiotics is a core goal.
- Industry is an important collaborator in the fight to reduce the development and spread of AMR.
- The goal is to reduce the need for traditional antibiotics while protecting the health and welfare of our animal patients.

EU Article 118



- EU Veterinary Medicinal Products Legislation EU 2019/6 adopted Dec 2019
- · Prohibits growth and prevention indications. Severely limits control indications.
- Applies requirements to imported animal origin products. [see next slide]

Article 118

Animals or products of animal origin imported into the Union

- Article 107(2) shall apply, mutatis mutandis, to operators in third countries and those operators shall
 not use the designated antimicrobials referred to in Article 37(5), insofar as relevant in respect of animals
 or products of animal origin exported from such third countries to the Union.
- The Commission shall adopt delegated acts in accordance with Article 147 in order to supplement this
 Article by providing the necessary detailed rules on the application of paragraph 1 of this Article.

1

EU Article 118



Scope:

Article 118: Articles 107 and 37(5) to apply.

- Article 37(5): "those operators shall not use the designated antimicrobials referred to in Article 37(5);" This includes "antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans;"
- Article 107 (2): "Antimicrobial medicinal products shall not be used in animals for the purpose of promoting growth nor to increase yield."

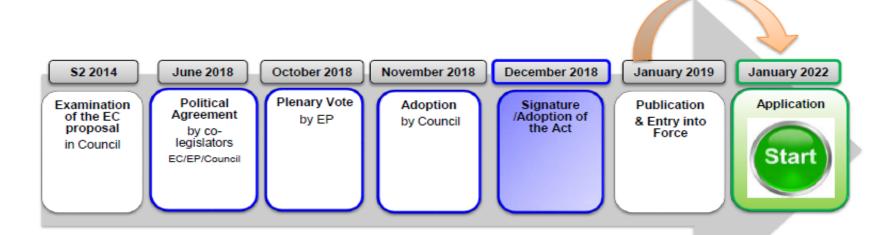
Timeline for Article 118 Implementation

Regulation (EU) 2019/6 on VMPs: Legislative Train Schedule

on the way to application...

ADDITIONAL LEGISLATION

to allow for appropriate application of the Regulation: Some 25 Delegated & Implementing Acts to draft, half of which by January 2022



Relevant WTO Rules: Agreement on the Application of Sanitary and Phytosanitary Measures

Article 4

Equivalence

1. Members shall accept the sanitary or phytosanitary measures of other Members as equivalent, even if these measures differ from their own or from those used by other Members trading in the same product, if the exporting Member objectively demonstrates to the importing Member that its measures achieve the importing Member's appropriate level of sanitary or phytosanitary protection. For this purpose, reasonable access shall be given, upon request, to the importing Member for inspection, testing and other relevant procedures.

Relevant WTO Rules: SPS Agreement

- Articles 2.2 and 5.1 require Members to base measures on scientific principles, sufficient scientific evidence and a risk assessment
- Articles 2.2 and 5.6 require Members to ensure that measures are no more trade restrictive that necessary to protect health

Relevant WTO Rules: SPS Agreement

- Article 3 requires Members to base measures on international standards unless they can justify scientifically a stricter standard
 - World Organization for Animal Health (OIE)
 - OIE Terrestrial Animal Health Code
 - OIE Aquatic Animal Health Code
 - OIE List of Antimicrobial Agents of Veterinary Importance
 - Resolution No. 36 Combating Antimicrobial Resistance through a One Health Approach: Actions and OIE Strategy
 - Codex Alimentarius
 - Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance
 - Code of Practice to Minimize and Contain Antimicrobial Resistance