Antibiotic Resistant Bacteria: Agriculture and OTC

Steve Roach, Food Safety Program Director

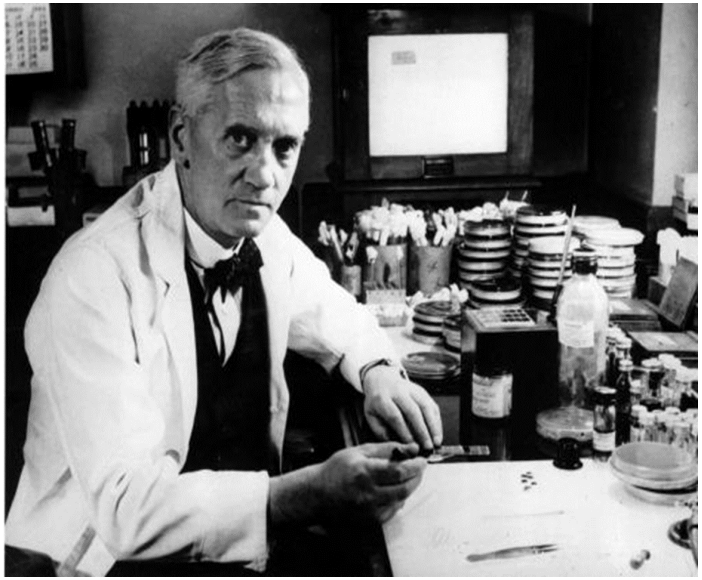
www.foodanimalconcernstrust.org

FACT
Food Animal Concerns Trust

Penicillin: The First Antibiotic

1928: Discovered by Alexander Fleming

1938: Turned into drug by Howard Florey

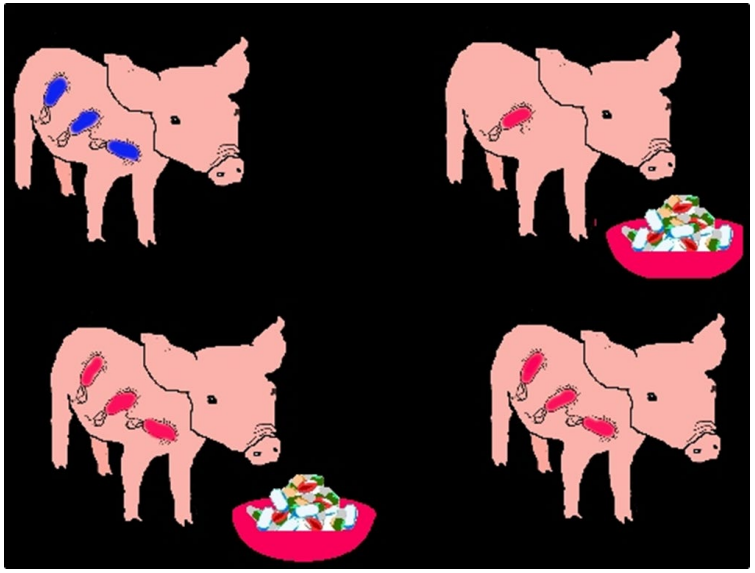


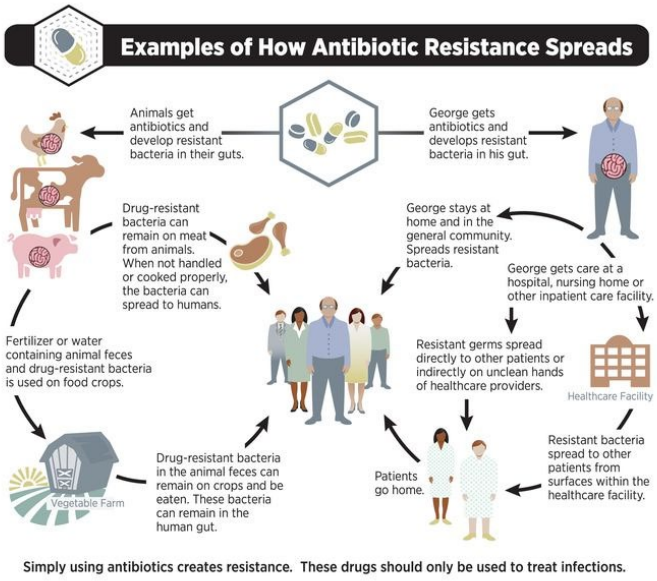
Post Antibiotic Era

A post-antibiotic era means, in effect, an end to modern medicine as we know it. Things as common as strep throat or a child's scratched knee could once again kill.

Dr Margaret Chan
Director-General
World Health Organization

Antibiotic Resistance





Antibiotic Resistance

Turkey-linked Salmonella outbreak total climbs to 164

Filed Under: **Salmonella**; **Foodborne Disease**
Lisa Schnirring | News Editor | CIDRAP News | Nov 08, 2018 Share Tweet LinkedIn Email Print & PDF

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A multidrug-resistant *Salmonella* Reading outbreak linked to raw turkey products has sickened 74 more people from 26 states, with one fatal illness reported, the first, the Centers for Disease Control and Prevention (CDC) said today.

In its update on the outbreak, first announced in the middle of July, the CDC said the illness total is now 164 in 35 states. States with more than 10 cases are California, Illinois, Minnesota, New York, and Texas.

So far 63 people have been hospitalized, and the fatal infection involves a person from California. Illness-onset dates range from Nov 20, 2017, to Oct 20, 2018. Patient ages range from younger than 1 year to 91, and 56% of the patients are female.

Re-estimating annual deaths due to multidrug-resistant organism infections

Jason P. Burnham MD[1], Margaret A. Olsen PhD, MPH[1] and Marin H. Kollef MD[2]
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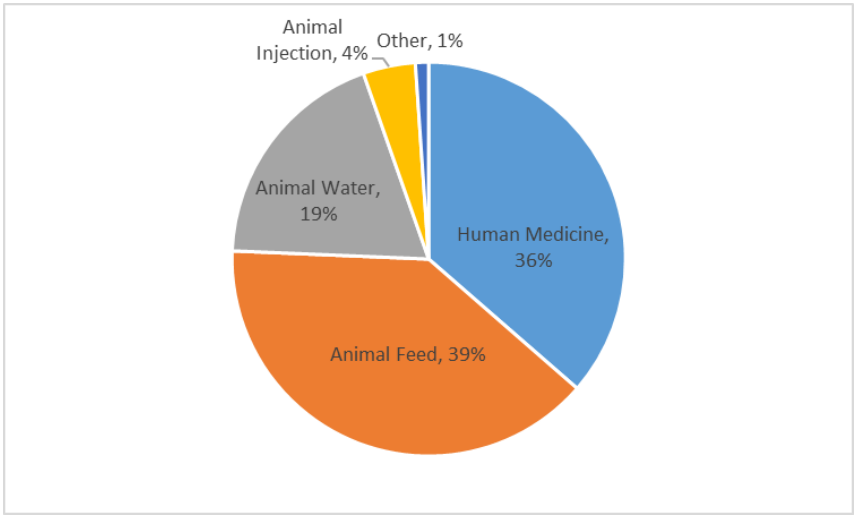
Table 1. Estimates of Number of Deaths Due to Infection and Multidrug-Resistant Organisms in the United States in 2010

Category	Deaths Due to Infection	Deaths Due to Multidrug-Resistant Organism Infection
Inpatient	245,960	70,837
Outpatient	285,680–316,690	82,276–91,207
Total	531,640–562,650	153,113–162,044

Antibiotic use in agriculture

- 2017 – 63% of sales of medically important antibiotics for food animals
- Mainly food and water
- Tetracyclines, penicillins, macrolides, and aminoglycosides most used

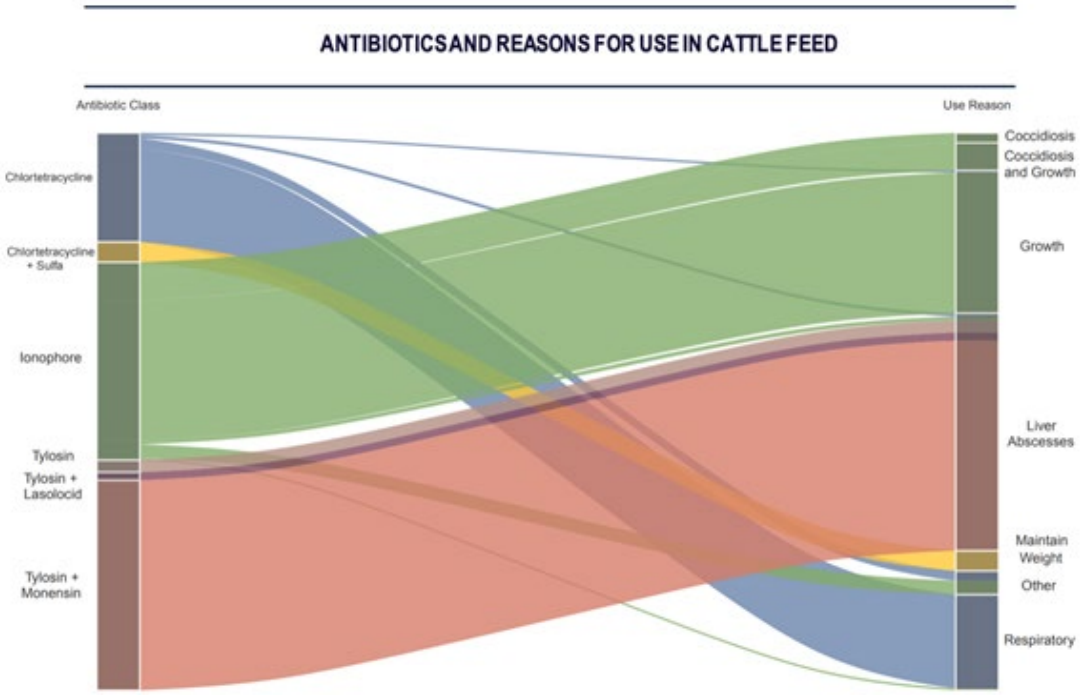
U.S. Antibiotic Sales 2017, 19.23 million pounds



(Animal Sales 2017, FDA; Human sales 2015 NRDC and CDDEP)

Cattle

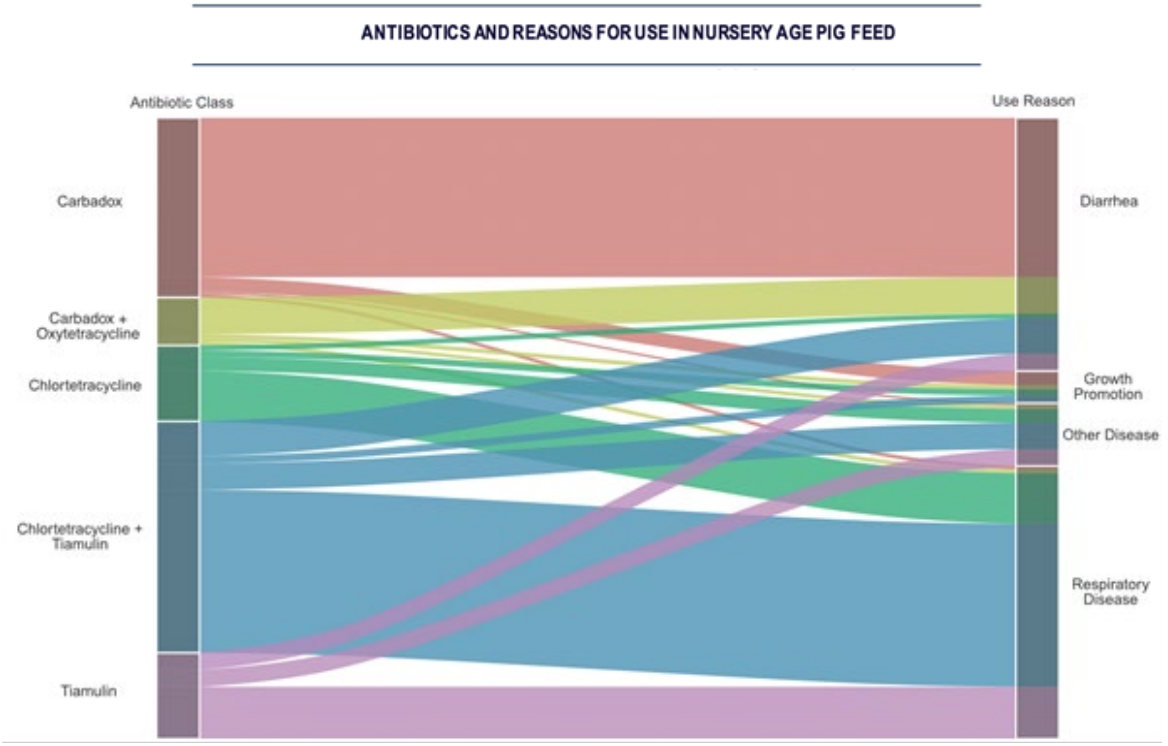
- 2017 – 42% of food animals sales
- Use significantly higher amounts per pound animal than UK, France, Netherlands, Denmark
- Chlortetracycline for respiratory disease
- Tylosin for liver abscesses
- Ionophores



(FACT from USDA Data)

Swine

- 2017 – 36% of food animals sales
- Use significantly higher amounts per pound animal than France, Netherlands, Denmark
- Chlortetracycline and tiamulin for respiratory disease
- Carbadox and tetracyclines for diarrhea



(FACT from USDA Data)

Poultry

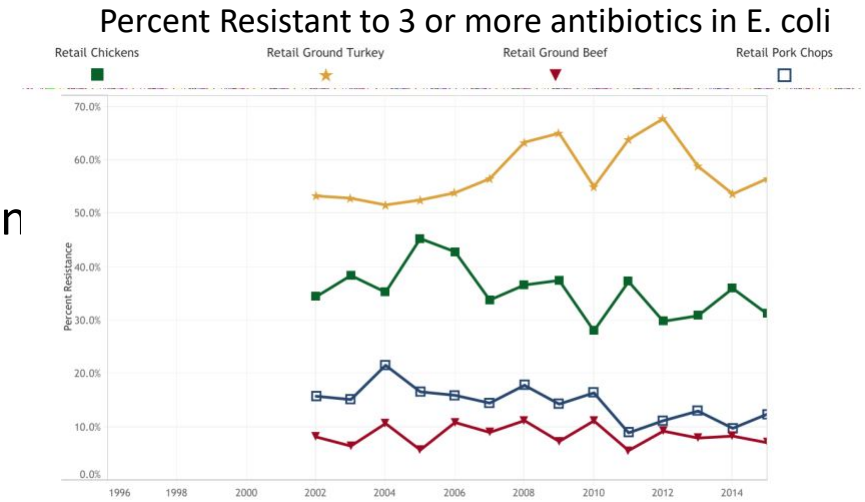
- 2017 – Chicken 5% of food animals sales, Turkey 12%
- Turkey uses significantly higher amounts per pound animal than other countries
- Chicken consumption of anitbiotics is low and has gone down recently

	Antimicrobial Usage in Broilers (g of antimicrobial per million lbs liveweight)			% Change	
Antimicrobial Class	2013	2016	2017	2013-2017	2016-2017
Aminoglycosides	42.5	17.7	10.6	-75%	-40%
Lincosamides	96.0	93.1	54.9	-43%	-41%
Macrolides	201.0	223.3	19.0	-91%	-92%
Penicillins	474.4	596.8	366.6	-23%	-39%
Sulfonamides	143.3	40.8	39.8	-72%	-2%
Tetracyclines	2,662.9	470.7	322.0	-88%	-32%

(Singer, R.S., Porter, L. Estimates of On-Farm Antimicrobial Usage in Broiler Chicken and Turkey Production in the United States, 2013 – 2017.)

Antibiotic Resistance

- NARMS data available up to 2015
- MDR *E coli* common on meat
- Resistance to last resort drugs in low numbers in food animals
  - Polymyxins (mcr-1)
  - CREs
  - Linezolid
  - Vancomycin



(Food and Drug Administration (FDA). NARMS Now)

FDA and Antibiotics

- The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

FDA and Antibiotics

- Approves drugs (animal or human) before marketing and sale
- Requires safety and efficacy studies and for food animals human food safety
- Label indicates reason and method of use
- Extra-label use in animals not allowed for feed
- Since 2003 antimicrobials for use in food animals require risk assessment

FDA and Food Animal Antibiotics

- 2003 requires risk assessment
- 2005 bans fluoroquinolone use in poultry
- 2008 Congress requires FDA to collect and report sales data
- 2012 Extra-label restriction on cephalosporins
- 2017 ban on growth promotion and requirement for veterinary oversight
- 2018 Five year Plan

FDA Releases Draft GFI to End OTC Sales of Most Animal Antibiotics

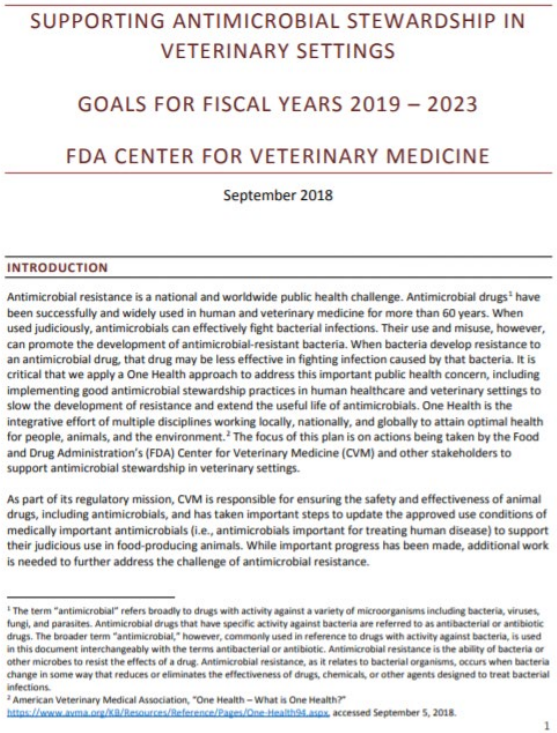
John Maday
September 23, 2019 04:43 PM

Print

The draft guidance covers dosage forms such as injectable or intra-mammary antibiotic products now available over the counter for use in beef and dairy cattle. (Geni Wren)

FDA Five Year Plan

- Move additional products to Rx
- Update list of medically important drugs
- Require drugs to have duration limits
- Improve collection of data on use and on resistant bacteria



SUPPORTING ANTIMICROBIAL STEWARDSHIP IN VETERINARY SETTINGS

GOALS FOR FISCAL YEARS 2019 – 2023

FDA CENTER FOR VETERINARY MEDICINE

September 2018

INTRODUCTION

Antimicrobial resistance is a national and worldwide public health challenge. Antimicrobial drugs[1] have been successfully and widely used in human and veterinary medicine for more than 60 years. When used judiciously, antimicrobials can effectively fight bacterial infections. Their use and misuse, however, can promote the development of antimicrobial-resistant bacteria. When bacteria develop resistance to an antimicrobial drug, that drug may be less effective in fighting infection caused by that bacteria. It is critical that we apply a One Health approach to address this important public health concern, including implementing good antimicrobial stewardship practices in human healthcare and veterinary settings to slow the development of resistance and extend the useful life of antimicrobials. One Health is the integrative effort of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals, and the environment.[2] The focus of this plan is on actions being taken by the Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) and other stakeholders to support antimicrobial stewardship in veterinary settings.

As part of its regulatory mission, CVM is responsible for ensuring the safety and effectiveness of animal drugs, including antimicrobials, and has taken important steps to update the approved use conditions of medically important antimicrobials (i.e., antimicrobials important for treating human disease) to support their judicious use in food-producing animals. While important progress has been made, additional work is needed to further address the challenge of antimicrobial resistance.

[1] The term "antimicrobial" refers broadly to drugs with activity against a variety of microorganisms including bacteria, viruses, fungi, and parasites. Antimicrobial drugs that have specific activity against bacteria are referred to as antibacterial or antibiotic drugs. The broader term "antimicrobial," however, commonly used in reference to drugs with activity against bacteria, is used in this document interchangeably with the terms antibacterial or antibiotic. Antimicrobial resistance is the ability of bacteria or other microbes to resist the effects of a drug. Antimicrobial resistance, as it relates to bacterial organisms, occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to treat bacterial infections.

[2] American Veterinary Medical Association, "One Health – What is One Health?" https://www.avma.org/KB/Resources/Reference/Pages/One-Health%E2%84%A2.aspx, accessed September 5, 2018.

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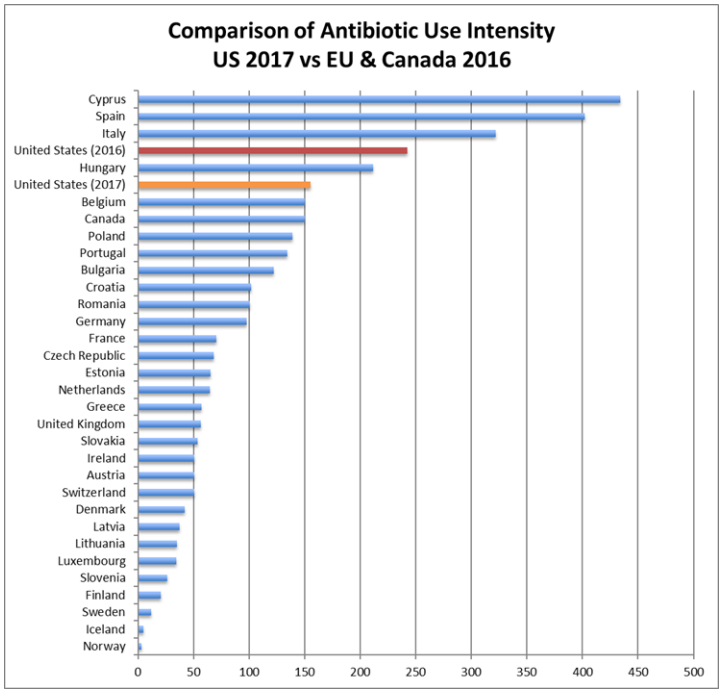
Shortcomings of FDA's plan



Farm antibiotics: Does new FDA policy go far enough?

Filed Under: **Antimicrobial Stewardship**

Chris Dall | News Reporter | CIDRAP News | Jan 23, 2017

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On Jan 3, the US Food and Drug Administration (FDA) announced the full implementation of Guidance for Industry (GFI) #213, a moment that the agency calls a "significant milestone" in national efforts to reduce the use of medically important antibiotics in food-producing animals. But questions remain about how much of an impact the policy will have.

USDA

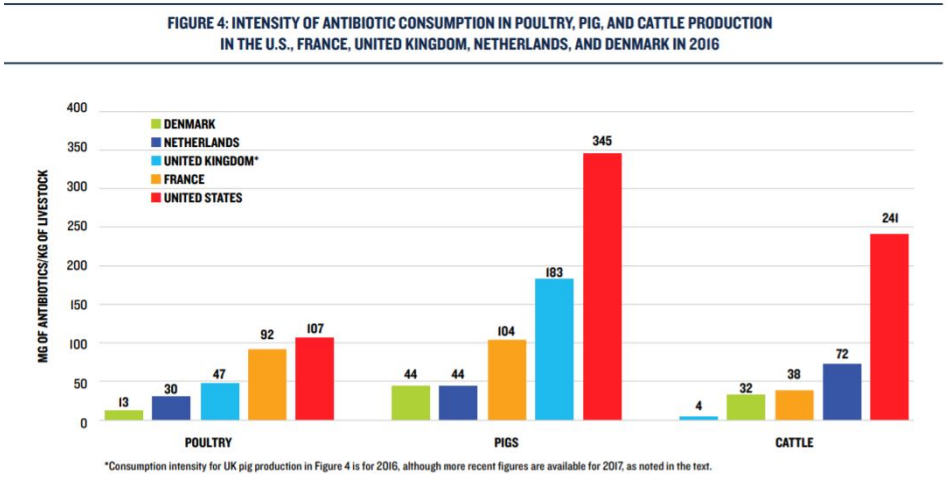
While the policy has its critics, the changes are the most significant moves made by the agency regarding

WHO recommendations

- Reduce overall use of medically important antibiotics in food animals
- Eliminate the use of medically important antibiotics for growth promotion
- Eliminate the use of medically important for disease prevention
- Use critically important antibiotics only in individual antibiotic treatment
- Do not use highest priority drugs (polymyxins, cephalosporins, fluoroquinolones, glycopeptides, and macrolides) in food animals

Set targets for use reductions

- Reductions are possible
- Exact target is not a scientific question
- Can look at what other countries have done
- US 2017 numbers still high
  - Cattle 152 mg/PCU
  - Swine 220 mg/PCU
  - Turkey 427 mg/PCU
  - Chicken 29 mg/PCU



(FACT and NRDC)

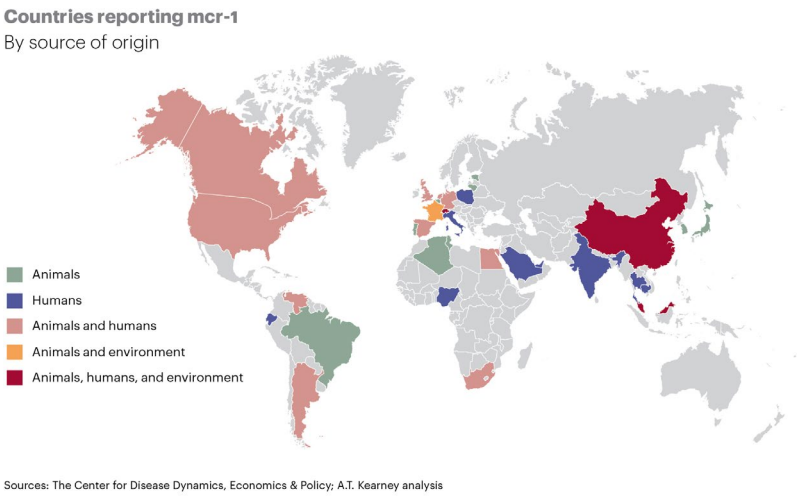
Eliminate routine use

- Prevent disease through management not antibiotics
- FDA define treatment, prevention, and control
- Eliminate use in animals that are not sick, injured, or undergoing surgery
- Set duration limits under 21 days

(Baseline Farm, Ann Arbor)

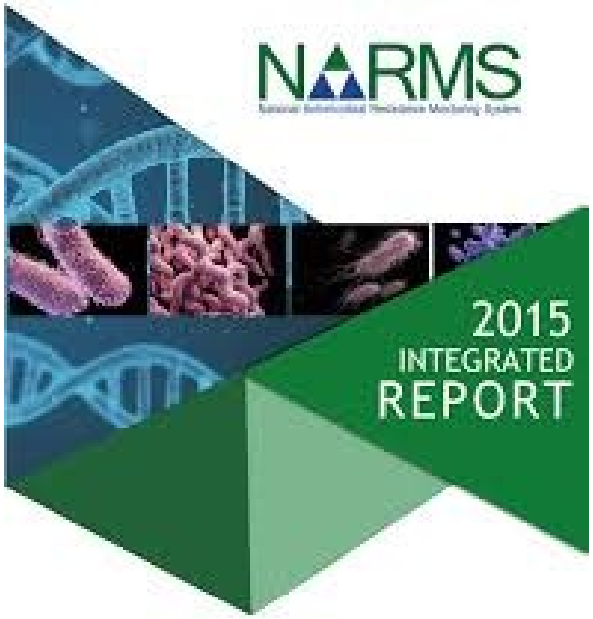
Address most important antibiotics

- Develop management for WHO reserve class drugs (WHO Essential Medicines 2018)
- Prohibit use of OTC polymyxins for humans and all use in animals
- Update FDA's ranking of drugs considered medically important for human medicine (GFI#152 Appendix A)
- Restrict use of most important drugs to disease treatment
- Additional guidance for fluoroquinolones and cephalosporins



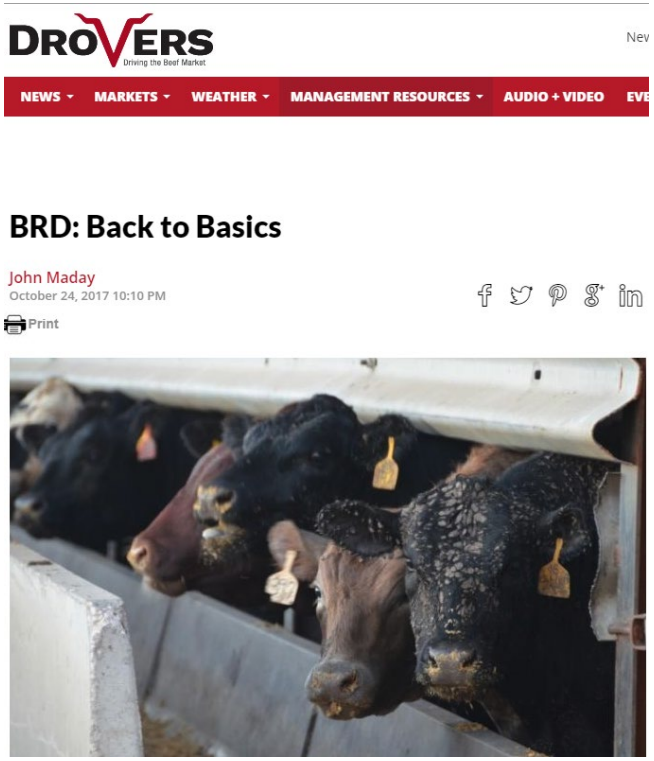
Improve surveillance and reporting

- Need system to collect antibiotic use data on annual basis
- Annual reporting of antibiotic sales
  - Adjust for animal biomass
  - Include plant/crop use
- Annual reporting of NARMS data within one year of data collection
- CDC should update estimates of resistant infections and death at least every three years.



Research changes in management not additives

- Research should focus on how to promote management that relies on less antibiotics
- Almost 50% reduction in sales between 2015 and 2017 – what worked?
- Consumers demanding meat from animals raised with responsible antibiotic use

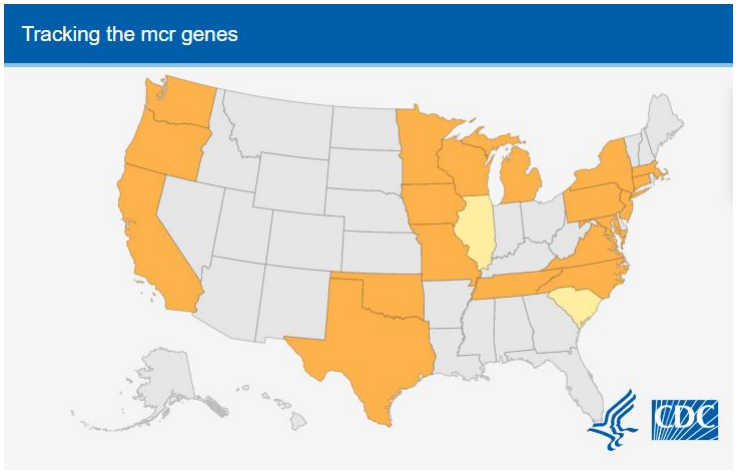


OTC in humans

- FDA moving all medically important food animal antibiotics to prescription only
- Polymyxins are drugs of last resort that save lives when no other drugs work
- Polymyxins are also available over the counter in grocery stores as part of topical ointments
- FDA allows marketing under 1987 regulation

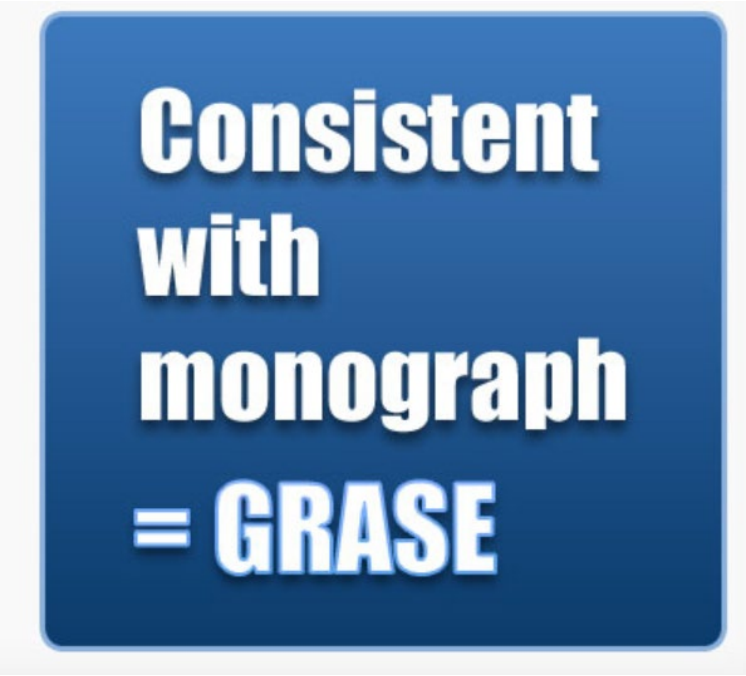
Polymyxins

- WHO – “reserve group antibiotics” should only be used in specific settings where other antibiotics would not work.
- Transmittable polymyxin resistance (mcr genes) found in China in 2015
- Linked to livestock use of antibiotics
- CDC- polymyxin resistance one of two most serious resistance concerns



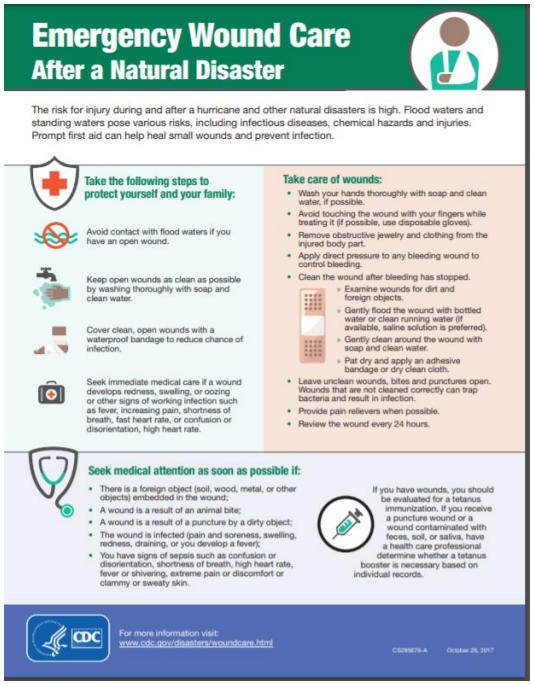
Polymyxins

- Can be marketed under 1987 OTC regulation
- Polymyxin resistance not concern when monograph published
- Efficacy of individual ingredients not compared
- Most skin infection outside spectrum



Polymyxins

- CDC does not recommend use even for emergency wound treatment by professionals
- Topicals have been shown to select for resistance
- Use can also disrupt normal protective skin flora
- Potential cross resistance with bacitracin



Emergency Wound Care
After a Natural Disaster

The risk for injury during and after a hurricane and other natural disasters is high. Flood waters and standing waters pose various risks, including infectious diseases, chemical hazards and injuries. Prompt first aid can help heal small wounds and prevent infection.

Take the following steps to protect yourself and your family:

Avoid contact with flood waters if you have an open wound.

Keep open wounds as clean as possible by washing thoroughly with soap and clean water.

Cover clean, open wounds with a waterproof bandage to reduce chance of infection.

Seek immediate medical care if a wound develops redness, swelling, or oozing or other signs of working infection such as fever, increasing pain, shortness of breath, fast heart rate, or confusion or disorientation, high heart rate.

Take care of wounds:

- Wash your hands thoroughly with soap and clean water, if possible.
- Avoid touching the wound with your fingers while treating it (if possible, use disposable gloves).
- Remove obstructive jewelry and clothing from the injured body part.
- Apply direct pressure to any bleeding wound to control bleeding.
- Clean the wound after bleeding has stopped.
  - Examine wounds for dirt and foreign objects.
  - Gently flood the wound with bottled water or clean running water (if available, saline solution is preferred).
  - Gently clean around the wound with soap and clean water.
  - Pat dry and apply an adhesive bandage or dry clean cloth.
- Leave unclean wounds, bites and punctures open. Wounds that are not cleaned correctly can trap bacteria and result in infection.
- Provide pain relievers when possible.
- Review the wound every 24 hours.

Seek medical attention as soon as possible if:

- There is a foreign object (soil, wood, metal, or other objects) embedded in the wound;
- A wound is a result of an animal bite;
- A wound is a result of a puncture by a dirty object;
- The wound is infected (pain and soreness, swelling, redness, draining, or you develop a fever);
- You have signs of sepsis such as confusion or disorientation, shortness of breath, high heart rate, fever or shivering, extreme pain or discomfort or clammy or sweaty skin.

If you have wounds, you should be evaluated for a tetanus immunization. If you receive a puncture wound or a wound contaminated with feces, soil, or saliva, have a health care professional determine whether a tetanus booster is necessary based on individual records.

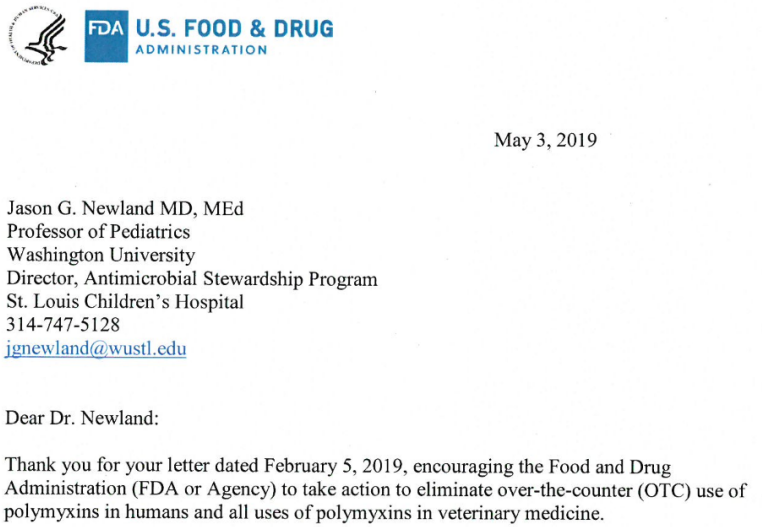
CDC

For more information visit:
www.cdc.gov/disasters/woundcare.html

CS285675-A October 26, 2017

Polymyxins

- February 2019, 155 Health Professionals asked FDA to remove OTC status of polymyxins
- May 2019, responded stating would not take action without formal petition
- Potential for consumer campaign



FDA U.S. FOOD & DRUG ADMINISTRATION

May 3, 2019

Jason G. Newland MD, MEd
Professor of Pediatrics
Washington University
Director, Antimicrobial Stewardship Program
St. Louis Children's Hospital
314-747-5128
jgnewland@wustl.edu

Dear Dr. Newland:

Thank you for your letter dated February 5, 2019, encouraging the Food and Drug Administration (FDA or Agency) to take action to eliminate over-the-counter (OTC) use of polymyxins in humans and all uses of polymyxins in veterinary medicine.

Thank You

Photos courtesy of Five Sprouts Family Farm, Willow Way Farm, and Shannon Brook Farm.