

**ANTIBIOTICS USED IN ANIMALS  
RAISED FOR FOOD**

**PERCEPTION VS. REALITY**

NEBRASKA MEDICAL  
ASSOCIATION  
House of Delegates

September 18, 2015  
Richard Raymond M.D.

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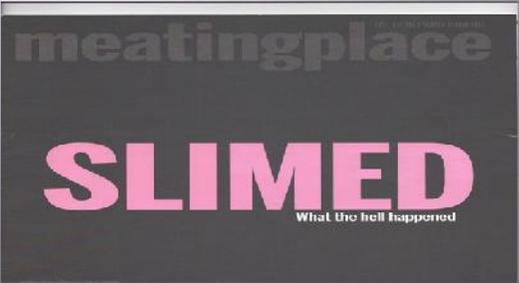
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**Power of the Media**



The image shows a newspaper clipping with the word 'meatingplace' in a grey font at the top. Below it, the word 'SLIMED' is written in large, bold, pink letters. Underneath 'SLIMED', the phrase 'What the hell happened' is written in a smaller, white font.

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**Perception vs. Reality**

- ❑ Foodborne illnesses down 26% from 2002-2011
- ❑ Foodborne outbreaks down 42% from 2002-2011
- ❑ Media hits for foodborne illnesses up 150% in same period
- ❑ Media hits for recalls of food up 250% in same period ( Peanut Corporation of America; Wright Egg Farms; Jensen Family Farms; Hallmark/Westland; Salinas Valley Spinach farm)
- ❑ WHY ????

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### PulseNet

- ❑ CDC's new effort to enhance epidemiologic efforts to find the source in 1996 following the Jack in the Box outbreak. PFGE
- ❑ The more illnesses added to a cluster, the better chance you have of finding the source, and
- ❑ Once you have a source, you have a culprit
- ❑ Eventually resulted in the realization that E coli o157:H7 was not limited to Beef, and Salmonella was not limited to Poultry.

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### Who and What to Blame?

- ❑ Consumers are growing leery of "Big Ag", CAFOs, GMOs and other technology, even though we need them all to feed a hungry world.

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### Technology is not just Beta-agonists and Antibiotics



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### Def: Low Dose vs. High Dose ABX

- ❑ A low dose may prevent or control an infection in the herd or flock
- ❑ Without a prevention or control dose, illnesses may result requiring higher doses of antibiotics for a longer time to a larger number of animals
- ❑ Is “low dose use” or “high dose use” more likely to cause resistance? **We don't know.**

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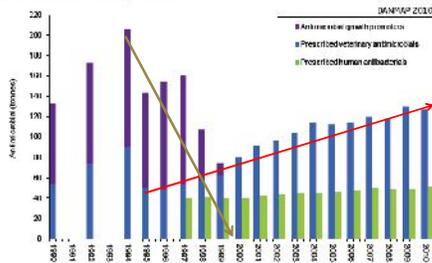
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### Denmark

Figure AP1.1. Consumption of antimicrobial agents and growth promoters in animal production and prescribed antibacterials in humans, Denmark



Source: Human therapeutics: The Danish Medicines Agency; Veterinary consumption: 1990-2010, data based on reports from the pharmaceutical industry of total annual sales; (Data: 1990-1994: Use of antibiotics in the pig production, Federation of Danish pig producers and slaughterhouses; N. S. Benn (Ed.), 1996; 2006: Danish Medicines Agency and Danish Food Directorate); 2010-2010: Data from VETSTAT.

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### Def: "Subtherapeutic dosing"

- ❑ Sometimes terms such as “sub-therapeutic” are inappropriately used by groups to describe the use of antimicrobials in animals to promote growth, prevent disease, control disease and to improve feed efficiency.
- ❑ **Perception:** The inappropriate use of “subtherapeutic” is intended to deceive and paint a bad picture of Animal Ag practices
- ❑ **Reality:** The FDA and AVMA do not use this term as it incorrectly describes an FDA approved use and approved dose for an approved indication.

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### FDA Approved Uses of ABX in Feed Animals

- ❑ **Treatment** of infectious diseases (antibiotics only to sick animals)
- ❑ **Control** of infectious diseases (disease is present in members of the flock or herd)
- ❑ **Prevention** of infectious diseases (there is a known disease risk, such as weather, weaning, disease in neighboring herd or flock, etc.)
- ❑ **Growth promotion/Feed efficiency** (Maximize production from animals, at the least cost) Will be eliminated by January 1, 2017

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### Reality

- ❑ Human health care providers treat individuals when they are infected, and they stay home and don't spread germs.
- ❑ Veterinarians must treat herds and flocks when a few are sick to prevent the spread of germs.
- ❑ Companion animal practices are more like human medicine clinics, with many of the same pressures and motivations at work. They need to be included in the discussions, not just poultry, pork and beef.

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### Federal Government's Role in Antibiotic Use in Food Animals

- ❑ **Food and Drug Administration (FDA):**
- ❑ Regulates antimicrobial use and collects data on sales. Has authority to remove a product from use for food producing animals if a danger is felt to be present in human health, as it did in 2005 when it announced that flouoroquinolones could no longer be used in poultry and banned all off label use in food animals and in 2012 when it took similar action for some cephalosporins. Has also limited or prohibited use of Methicillin, Vancomycin, and aminoglycosides to protect human health.
- ❑ Establishes Maximum Residue Limits (MRLs) for antibiotics in meat and poultry

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### Federal Government's Role (cont.)

- ▣ **National Antimicrobial Resistance Monitoring System (NARMS)** was established by HHS, USDA and the CDC to perform research and provide information about antimicrobial resistance in humans, animals and retail meats.

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### 2015 NARMS Report on Meat and Poultry **SALMONELLA**

- ▣ "All *Salmonella* isolates were susceptible to nalidixic acid and ciprofloxacin"
- ▣ From 2002-2012 third-generation cephalosporin resistance in chicken rose from 10% to 28%
- ▣ Ampicillin resistance rose from 17% to 29% in chicken
- ▣ **Reality: "no flouroquinolone resistance in *Salmonella* from any source. This is the drug of choice for treating adults with Salmonellosis."** (FDA)

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### More NARMS report **CAMPYLOBACTER**

- ▣ Macrolide resistance in *Campylobacter* remained low at 0.5% for *C jejuni* but rose to 12% for *C. coli*. **Macrolides are the drugs of choice to treat *Campylobacter* for severe cases.**
- ▣ Tetracycline resistance was the most common at 50%. They have been used for over 50 years.
- ▣ Multi-drug resistance (MDR) increased in *Salmonella* while remaining very rare in *Campylobacter* but exposure was the same.
- ▣ **Reality: we don't know why.**

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### Multidrug Resistant *Salmonella*

- ▣ **Perception:** The NARMS report stated that MDR *Salmonella* was increasing in percentage. Those against the slaughter of animals for food acted enraged and alarmed. "We are standing on the brink of a public health disaster."
- ▣ **Reality:** The NARMS report shows that for retail chicken and ground turkey, the four most common antibiotics that *Salmonella* showed resistance to were tetracycline, streptomycin, sulfisoxazole and penicillin
- ▣ **Reality:** None of these drugs would be used to treat a *Salmonella* infection. Macrolides, Bactrim DS and quinolones are first line antibiotics for foodborne illnesses and little or no resistance in *Salmonella* was found in the NARMS study

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### FDA's Comments on the EWG's report on the 2013 NARMS report

- ▣ **Reality:** "NARMS data indicates that first-line treatments for all four bacteria that we track are still effective."
- ▣ "We believe EWG is **inaccurate and alarmist** to define bacteria resistance to one, or even a few, antimicrobials as 'superbugs' if these bacteria are treatable by other commonly used antibiotics."

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### FDA's GFI #213, #209 and VFD

- ▣ Specific direction for drug sponsors on how to make voluntary changes to the status of their products such as:
  1. voluntary removal of performance indications and change in marketing status
  2. Sponsor can seek new therapeutic indications at current doses
- ▣ 3. All feed additives must be prescribed by a DVM

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## The Numbers Game



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## Hyperbole leads to Deaf Ears

- ❑ “Over 80% of all antibiotics sold in the United States are given to perfectly healthy animals raised for food.” (Congresswoman Slaughter, Watchdog and advocacy groups, multiple media and bloggers.)
- ❑ “When they do use antibiotics, they do so according to label and dosing approved by the FDA and under the care of a Veterinarian” (USFRA)

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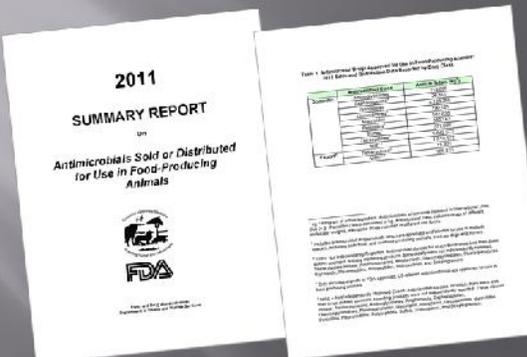
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## The Numbers Game



Antimicrobial	Quantity	Value
Amoxicillin	1,000,000,000	\$10,000,000
Penicillin	500,000,000	\$5,000,000
Clavulanic acid	100,000,000	\$1,000,000
Trimethoprim	50,000,000	\$500,000
Sulfamonomethoxime	50,000,000	\$500,000
Other	1,000,000,000	\$10,000,000

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## Antibiotic Use Numbers

- ▣ Any number cited includes companion animals and treatment of disease. (FDA footnote #2 in 2011 report, footnote #1 in 2013 report)
- ▣ Numbers are in kilograms, not doses or treatments.

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## Kilograms vs. Milligrams



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## Reality Check

- ▣ FDA 2013 report on all “antibiotics sold or distributed for use in food-producing animals”:
- ▣ Ionophores 30% (not used in human medicine at all) are antiparasitics
- ▣ Not Individually Reported (NIR) 8.0% (Almost none used in human medicine)
- ▣ Tetracyclines 44% (71% of Medically Important antibiotics used in animal ag)

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### The Reality Facts

- ❑ Of the total weight of antibiotics sold for possible use in animals, 82% of that total is either not approved for use in human medicine (the ionophores and most NIRs for example) or are rarely prescribed for use in human medicine as a poor second or third choice drug (chlor- and oxy-tetracycline for example)
- ❑ It is my firm belief that it is the 18% where there is overlap that we should focus our attention and discussions on.

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### Top Five Classes of ABX Used in Human Health

- ❑ 1. Penicillin (Augmentin) Kg share = 44.0%
  - ❑ 2. Cephalosporins (Keflex) Kg share = 15.1%
  - ❑ 3. Sulfa and TMP (Bactrim) Kg share = 14.2%
  - ❑ 4. Quinolones (Cipro) Kg share = 9.2%
  - ❑ 5. Macrolides (Z-Pak) Kg share = 5.3%
- ❑ These top five classes represent 88 % of all antibiotics sold for use in human medicine.
- ❑ Source: FDA letter to Congresswoman Slaughter

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### Reality Check

- ❑ Two of the top four classes of antibiotics of critical importance in human health are rarely sold for use in animals:
- ❑ 1. Cephalosporins: 0.2% of all sales for use in animals
- ❑ 2. Flouroquinolones: Less than 0.1% of all sales for use in animals
- ❑ These two comprise 25% of human abx

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### Other Medically Important Antibiotics used in Animals

- ☐ Aminoglycosides 3%
- ☐ Lincosamides 3%
- ☐ Macrolides 6%
- ☐ Penicillins 9%
- ☐ Sulfas 4%
- ☐ Tetracyclines 71%

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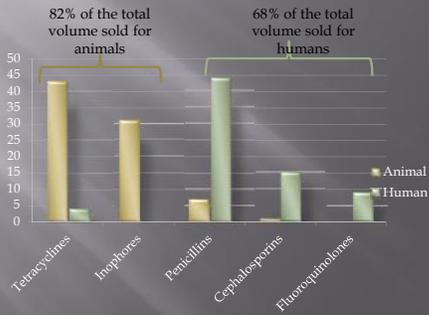
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### Animal vs. Human Use Little Overlap




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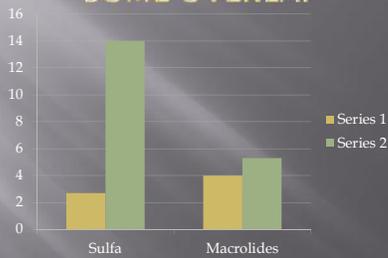
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### ANIMAL VS. HUMAN USE SOME OVERLAP



Yellow – animal sales  
Green – human sales

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### FDA ABX Sales Reports in 2013 VS. 2012

- ❑ Over all sales up 1 % and the sky is falling, BUT
- ❑ Macrolides     Down 9%
- ❑ Penicillin     Down 14%
- ❑ Sulfa           Down 22%
- ❑ Tetracyclines Up 9%
- ❑ Ionophores    Up 10% from 2009-2013 (never used in human health)

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### So Why the Change in Perception That ABX use in Animals is Bad?

- ❑ Antibiotic resistant bacteria are increasing and are deadly: FACT
- ❑ Chipotle and Chik-Fil-A's announcements (What do they know that I don't?)
- ❑ McDonald's and Costco's recent announcements of going to meat and/or poultry that will be raised without antibiotics used in human medicine (not trying to explain ionophores is smart business)
- ❑ Perdue's recent move to antibiotic free

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### More fuel to the fire

- ❑ Largest city school boards' announcement of going to antibiotic free chicken, even if the product is not available and at what cost?
- ❑ City councils of large metropolitan areas passing resolutions in favor of antibiotic free animal husbandry (are they truly reflecting their constituent's thoughts and protecting them, or putting meat and poultry prices out of their budget ranges?)

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### Definition: Superbugs

- Any bacteria with resistance to multiple antibiotics leaving limited or no options to treat, such as:
- Methicillin Resistant *Staphylococcal aureus* (MRSA) [Not just Meth, but all B-lactams]
- Extremely Drug Resistant *Tuberculosis mycobacterium* (EDRTB)
- Vancomycin Resistant *Enterococcus* (VRE) [20% of nosocomial infections]
- Vancomycin Resistant *Staph aureus* (VRSA)
- Clostridium difficile*
- Pseudomonas aeruginosa*
- Carbapenem Resistant *Enterobacteriaceae* (CRE)

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### Superbugs

- Most are health care acquired infections following a surgical procedure.
- Vancomycin Resistant *Staphylococcal aureus* (VRSA) is one of the newest, and the resistance is not because of **overuse or misuse in animal or human health that many suggest are the primary reasons for antibiotic resistance.**
- Reality:** Vancomycin is only used for life threatening infections and always under the direct guidance of a health care professional yet Staph has once again found a way to protect itself.

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### Superbugs

- Reality:** According to the Infectious Disease Society of America, the prior list of superbugs had no food-borne or animal connections.
- Others, like Multi-Drug Resistant (MDR) Salmonella, may have connections with food consumption and antibiotic use in animals but these are not necessarily superbugs.
- Perception:** the Foster Farms related outbreak was more serious because of antibiotic resistant Salmonella.
- Reality:** The drugs of choice to treat Salmonellosis remained effective.

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### New Reports on Antibiotic Resistance in September 2013



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### UK Five Year Antimicrobial Resistance Strategy Sept. 2013

- ❑ [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/244058/20130902\\_UK\\_AMR\\_strategy.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_AMR_strategy.pdf)
- ❑ Page 8 Introduction
- ❑ "Increasing scientific evidence suggests that the clinical issues with antimicrobial resistance that we face in human medicine are primarily the result of antibiotic use in people, rather than the use of antibiotics in animals."

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### US Centers for Disease Control Report on Antibiotic Resistance

- ❑ From the CDC's September, 2013, press release accompanying the over 100 page report:
- ❑ "The use of antibiotics is the single most important factor leading to antibiotic resistance around the world. Antibiotics are among the most commonly prescribed drugs used in human medicine. However, up to half of the antibiotic use in humans.... is unnecessary or inappropriate."
- ❑ 3-4 pages on use of antibiotics in animals
- ❑ [www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf](http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf)

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### New Reports Since 2013

- ▣ President’s Council of Advisors on Science and Technology (PCAST) September 2014
- ▣ National Action Plan for Combating Antibiotic-Resistant Bacteria March 2015
- ▣ National Institute for Animal Agriculture’s White Papers following their third and fourth conferences on antibiotic use in animals and its interface with human medicine in November of 2013 and 2014

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### National Action Plan

- ▣ 1. Slow the emergence of resistant bacteria and prevent the spread of resistant infections
- ▣ 2. Strengthen the national “One-Health” surveillance efforts
- ▣ 3. Advance the development and use of rapid and innovative diagnostic tests
- ▣ 4. Accelerate basic and applied research and development
- ▣ 5. Improve international collaboration and capacities.

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### Reality: This is a Global Issue



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### World Health Organization

- ❑ First ever report on antimicrobial resistance released April, 2014
- ❑ 232 pages, just 4 on antibiotic use in animal agriculture
- ❑ “The magnitude of transmission from animal reservoirs to humans remains unknown.”
- ❑ “More data are needed to identify priority areas for intervention.”
- ❑ Comparison of data exists only for some EU countries, Canada and the U.S.

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### More Recent Publications

- ❑ Princeton Study July 2014  
Antibiotic use in human health, world wide, up 36% from 2000-2010  
BRICS countries account for 76% of the increase
- ❑ Princeton Report on *Global Trends in antimicrobial use in Food Animals*  
Antibiotic consumption by animals “will rise by 67% by 2030 and nearly double in Brazil, Russia, India, China and South Africa” (They also used the 80% in animals raised for food number)

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### Is Antibiotic Use in Animals Bad?

- ❑ “**Debate over the amounts sold or used is diversionary**: it is not the main issue in the public health debate about antibiotic resistance”  
(Ron Phillips, Animal Health Institute)
- ❑ The issue shouldn't be the amount or frequency of antimicrobials used. The real issue: **IS THERE A SIGNIFICANT IMPACT ON HUMAN HEALTH?**

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### This should not be another Pink Slime fiasco

- ❑ **Perception:** The Animal Agriculture industry is being painted as irresponsible and inappropriate users of massive amounts of antibiotics in healthy animals, when in fact:
- ❑ **Reality: The current uses and doses of antibiotics in animals have been approved by the FDA as appropriate.**

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### Labeling of Meat and Poultry

- ❑ 1. Raised Without Antibiotics ( Better be true)
- ❑ 2. Raised Without Antibiotics Except Ionophores
- ❑ 3. Antibiotic Free
- ❑ 4. No Antibiotics: Never Ever ( Not Really )
- ❑ 5. Organic
- ❑ 6. All Natural
- ❑ **How about raised without antibiotics used in human medicine?**

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### Developing New Policies

- ❑ What people think they want is producing change
- ❑ Large retailers and restaurants are responding to what people think they want, and can afford
- ❑ When my surgeon operates on me, I want him or her to have a very clear diagnosis based on facts before the incision is made
- ❑ We don't have a very clear understanding of how resistance to antibiotics develops, or what the interface between human, animal and environmental health even is.

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## CLOSING THOUGHT

- Statement from Ron DeHaven, DVM and Executive Vice President and CEO of the American Veterinary Medical Association:
- **“When policy regarding the judicious and safe use of antibiotics in food producing animals is being debated and formulated, it should be based on biological science, not political science.”**

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## ? Questions ?



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