

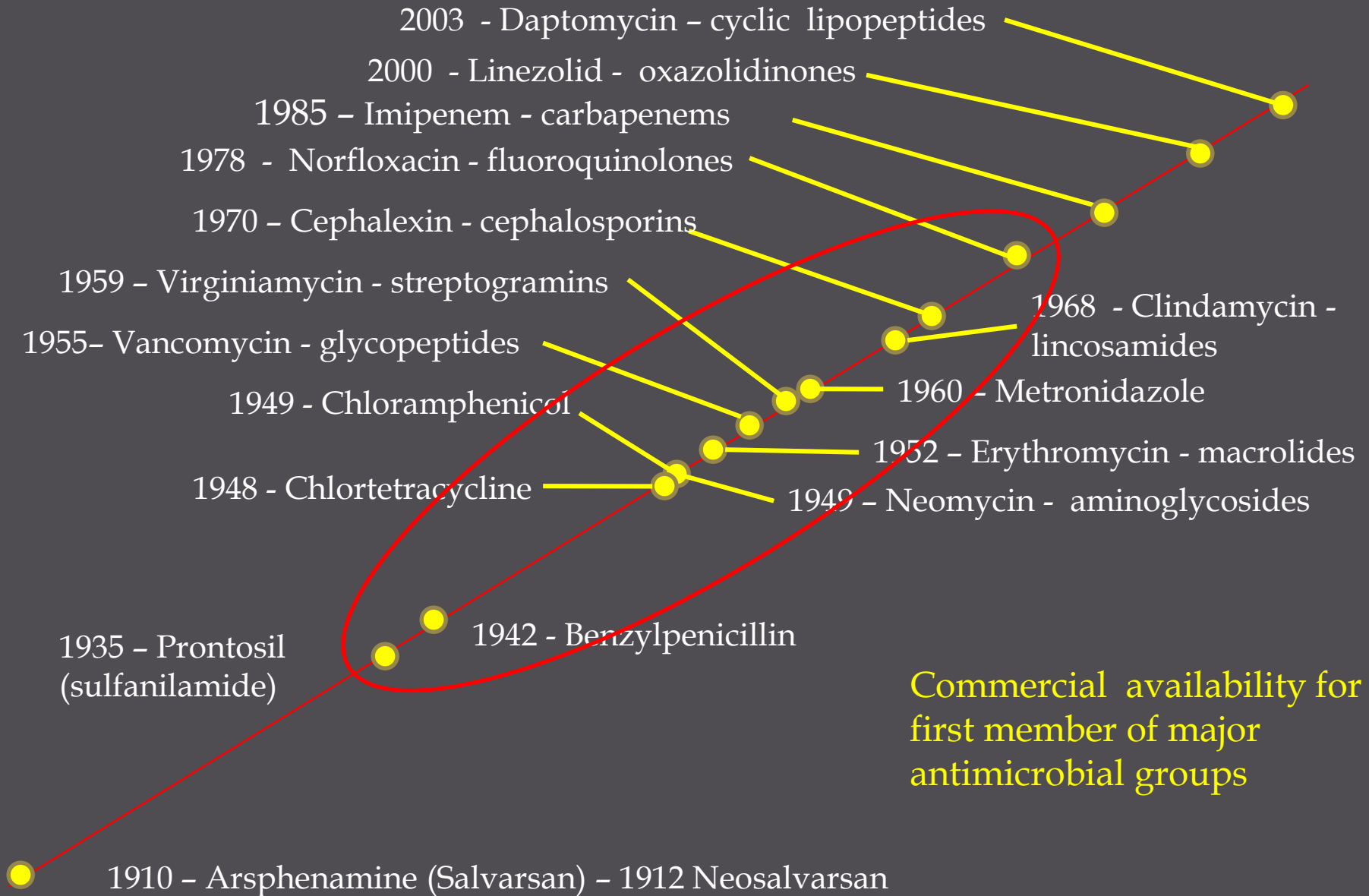
# Countdown to the New Veterinary Feed Directive

Where we are going and  
what got us here

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**HOW DID WE GET HERE?**

# Antimicrobial Timeline



Commercial availability for first member of major antimicrobial groups

# AMDUCA?

- ▣ Animal Medicinal Drug Use Clarification Act
- ▣ The same regulations as published in the Federal Register in 1996 still apply today.
  - The AMDUCA regs were utilized to limit the ability to use cephalosporins in an extralabel manner in food animals.

# Guidance Documents

- ▣ **Guidance for Industry (GFI) 209 – April, 2012**
  - Imagining a delineation between growth promotion, prevention/control, and therapy
  - “judicious” vs. “hazard”
- ▣ Principle 1: The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health.

*“However, the Agency believes that it is not limited to making risk determinations based solely on documented scientific information, but may use other suitable information as appropriate.”*

# Who defines medically important?

- ▣ Appendix A, GFI #152
- ▣ List is determined by an expert FDA panel managed by the Center for Drug Evaluation and Research (CDER) Within the FDA
- ▣ The World Health Association also has a list of medically important antibiotics
  - Human health
  - Animal health

# WHO Prioritization...

- ▣ within the critically important designation
  - Glycopeptides
  - Fluoroquinolones
  - Cephalosporins
  - Macrolides



# Antimicrobials Not Classified as “Medically Important”

- ▣ **Ionophores:** monensin, lasalocid
- ▣ **Flavophospholipol:** bambermycins (e.g., Flavomycin®, Gainpro®)
- ▣ **Bacitracin**
- ▣ **Pleuromutilins: Tiamulin**
  - Not medically important in the U.S., but classified as highly important by WHO
- ▣ **Carbadox**

# Medically Important Antimicrobials with Feed or Water Labels

- ▣ **Aminoglycosides:** gentamicin, neomycin
- ▣ **Lincosamides:** lincomycin
- ▣ **Macrolides:** tylosin, tilmicosin (Pulmotil® currently requires a VFD in swine and cattle)
- ▣ **Penicillins (natural):** penicillin G included in combination products
- ▣ **Florfenicol:** CHPC included as highly important drug in GFI #152 appendix A, Florfenicol is considered medically important. Existing VFD status for feed in aquaculture.

# Medically Important Antimicrobials with Feed or Water Labels

- ▣ Streptogramins: virginiamycin
- ▣ Sulfonamides: Includes both potentiated (e.g., trimethoprim/sulfa) and non-potentiated sulfonamides.
- ▣ Tetracyclines: chlortetracycline, oxytetracycline, tetracycline

# Guidance 209

- ▣ Principle 2: The use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation.



# Guidance for Industry 213

- ▣ December, 2013
- ▣ This guidance document puts forth nonbinding recommendations for companies to comply with Guidance 209.
- ▣ There was a 3 month period for companies to communicate with the FDA/CVM regarding their intent to comply with the voluntary recommendations in Guidance 209.
- ▣ A 3 year period for companies to comply ends in December of 2016.

# GFI 213

- ▣ CVM updates every 6 months on progress...
  - June 30<sup>th</sup>, 2014 – all 26 sponsors committed to complying with guidance, 283 products affected,
    - ▣ 2 label changes approved, 1 pending
    - ▣ 31 labels withdrawn
  - Summary table of affected labels and status is available on the FDA website



# GFI 213

- ▣ A company may remove the label indications for growth promotion and insert label requirements for veterinary authorization without being subjected to other requirements such as updating the label in other areas (e.g., microbial safety).



# Changes in the VFD Rule

- The new VFD rule took effect on October 1, 2015
- VCPR?
- Who keeps the original?
- Category II?
- Type A, B, and C?
- When mg/lb per day and g/ton don't match up?

# Changes in the VFD Rule

- Expiration vs. duration
- Refills?
- Pulsing the same animals with repeated regimens?

# What's next?

- “The FDA believes long-term or open-ended use of medically important antibiotics is a significant **stewardship** issue.”
- “...medically important antibiotics labeled for continuous or undefined durations of use is not consistent with **judicious use** principles, as outlined in previously-released guidance documents.”



PRESIDENTIAL ADVISORY COUNCIL ON  
COMBATING ANTIBIOTIC-RESISTANT BACTERIA



# Executive Order 9-18-2014

- The Executive Order directs the Secretary of HHS, in consultation with the Secretary of Agriculture, to establish a **Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria**, to be composed of leading non-governmental experts



# Executive Order 9-18-2014

- The Presidential Advisory Council will provide advice, information, and recommendations regarding programs and policies intended to:
  - preserve antibiotic effectiveness;
  - strengthen surveillance of antibiotic-resistant infections;
  - advance the development of rapid, point-of-care diagnostics for use in human healthcare and agriculture;
  - advance research on new treatments for bacterial infections;
  - **develop alternatives to the use of antibiotics for some agricultural purposes;**
  - and improve international coordination of efforts to combat antibiotic resistance.

# Executive Order 9-18-2014

*The National Strategy* provides detailed actions for five interrelated national goals to be achieved by 2020 in collaboration with partners in healthcare, public health, **veterinary medicine, agriculture, and food safety**, as well as in academic, Federal, and industrial research and development. The goals are:

1. **Slow the emergence and prevent the spread of resistant bacteria.**
2. Strengthen National efforts to identify and report cases of antibiotic resistance.

# Executive Order 9-18-2014

## *The National Strategy*

3. Advance the development and use of rapid diagnostic tests for the identification and characterization of antibiotic-resistant bacteria.

4. Accelerate basic and applied research and development for new antibiotics as well as other therapeutics and vaccines.

5. Improve international collaboration, capacities for antibiotic-resistance prevention, surveillance, control, and antibiotic research and development.



# So, where to from here

- Realities
  - I don't think sales of antimicrobials for food animals are going to change significantly due to 209 and 213
  - A usable, acceptable method of end-user antimicrobial use to evaluate actual applications of antimicrobials in food animals isn't going to be in place before December, 2016.
    - Even if it could, what was the baseline?

# So, where to from here

- Realities
  - Routine prevention and control will be the next highly scrutinized use...
    - when our only metric is reduction in use

The veterinary profession is not only going to be **responsible** for all medically-important antimicrobial uses in food animals...

we are going to be **accountable**

Sooooo, what are we  
using?

ANTIMICROBIAL DRUGS APPROVED FOR USE IN FOOD-PRODUCING ANIMALS<sup>1</sup>  
 ACTIVELY MARKETED IN 2013  
 DOMESTIC SALES AND DISTRIBUTION DATA  
 REPORTED BY MEDICAL IMPORTANCE AND DRUG CLASS

	<b>Drug Class</b>	<b>Annual Totals (kg)<sup>2</sup></b>	<b>% Subtotal</b>	<b>% Grand Total</b>
<b><u>Medically Important<sup>3</sup></u></b>	<i>Aminoglycosides</i>	270,342	3%	2%
	<i>Cephalosporins<sup>4</sup></i>	28,337	<1%	<1%
	<i>Fluoroquinolones</i>	15,099	<1%	<1%
	<i>Lincosamides<sup>4</sup></i>	236,450	3%	2%
	<i>Macrolides</i>	563,251	6%	4%
	<i>Penicillins<sup>4</sup></i>	828,721	9%	6%
	<i>Sulfas<sup>4</sup></i>	384,371	4%	3%
	<i>Tetracyclines<sup>4</sup></i>	6,514,779	71%	44%
	<i>NIR<sup>5</sup></i>	355,452	4%	2%
	<b><i>Subtotal</i></b>	<b>9,196,803</b>	<b>100%</b>	<b>62%</b>
<b><u>Not Currently Medically Important<sup>4</sup></u></b>	<i>Ionophores</i>	4,434,657	79%	30%
	<i>NIR<sup>6</sup></i>	1,157,095	21%	8%
	<b><i>Subtotal</i></b>	<b>5,591,752</b>	<b>100%</b>	<b>38%</b>
<b><i>Grand Total</i></b>		<b>14,788,555</b>		<b>100%</b>

ANTIMICROBIAL DRUGS APPROVED FOR USE IN FOOD-PRODUCING ANIMALS<sup>1</sup>  
 ACTIVELY MARKETED IN 2013  
 DOMESTIC SALES AND DISTRIBUTION DATA  
 REPORTED BY MEDICAL IMPORTANCE AND ROUTE OF ADMINISTRATION

	Route	Annual Totals (kg) <sup>2</sup>	% Subtotal	% Grand Total
<u>Medically Important</u> <sup>3</sup>	<i>Feed</i> <sup>1</sup>	6,828,506	74%	46%
	<i>Injection</i> <sup>1</sup>	352,693	4%	2%
	<i>Intramammary</i>	9,875	<1%	<1%
	<i>Oral</i> <sup>1,5</sup>	98,854	1%	<1%
	<i>Water</i> <sup>6</sup>	1,906,875	21%	13%
	<b><i>Subtotal</i></b>	<b>9,196,803</b>	<b>100%</b>	<b>62%</b>
<u>Not Currently Medically Important</u> <sup>4</sup>	<i>All Routes</i> <sup>7</sup>	5,591,752		38%
<b><i>Grand Total</i></b>		<b>14,788,555</b>		<b>100%</b>

ANTIMICROBIAL DRUGS APPROVED FOR USE IN FOOD-PRODUCING ANIMALS<sup>1</sup>  
 ACTIVELY MARKETED 2009-2013  
 DOMESTIC SALES AND DISTRIBUTION DATA  
 REPORTED BY MEDICAL IMPORTANCE AND DRUG CLASS

	Drug Class	2009 Annual Totals (kg) <sup>2</sup>	2010 Annual Totals (kg) <sup>2</sup>	2011 Annual Totals (kg) <sup>2</sup>	2012 Annual Totals (kg) <sup>2</sup>	2013 Annual Totals (kg) <sup>2</sup>	% Change 2009 - 2013	% Change 2012 - 2013
<u>Medically Important</u> <sup>3</sup>	<i>Aminoglycosides</i>	223,117	211,790	214,895	273,536	270,342	21%	-1%
	<i>Cephalosporins</i> <sup>4</sup>	20,145	24,588	26,611	27,654	28,337	41%	2%
	<i>Lincosamides</i> <sup>4</sup>	93,330	154,653	190,101	218,140	236,450	153%	8%
	<i>Macrolides</i> <sup>4</sup>	562,062	553,229	582,836	616,274	563,251	<1%	-9%
	<i>Penicillins</i> <sup>4</sup>	691,644	884,419	885,304	965,196	828,721	20%	-14%
	<i>Sulfas</i> <sup>4</sup>	505,880	517,128	383,105	493,514	384,371	-24%	-22%
	<i>Tetracyclines</i> <sup>4</sup>	5,260,995	5,602,281	5,652,855	5,954,361	6,514,779	24%	9%
	<i>NIR</i> <sup>1,5</sup>	329,391	281,221	319,991	344,428	370,551	12%	8%
	<b>Subtotal</b>	<b>7,686,564</b>	<b>8,229,309</b>	<b>8,255,697</b>	<b>8,893,101</b>	<b>9,196,803</b>	<b>20%</b>	<b>3%</b>
<u>Not Currently Medically Important</u> <sup>4</sup>	<i>Ionophores</i>	3,739,352	3,820,004	4,122,397	4,573,795	4,434,657	19%	-3%
	<i>NIR</i> <sup>6</sup>	1,161,541	1,237,784	1,190,943	1,151,532	1,157,095	<1%	0%
		<b>Subtotal</b>	<b>4,900,893</b>	<b>5,057,788</b>	<b>5,313,340</b>	<b>5,725,327</b>	<b>5,591,752</b>	<b>14%</b>
	<b>Grand Total</b>	<b>12,587,457</b>	<b>13,287,097</b>	<b>13,569,037</b>	<b>14,618,428</b>	<b>14,788,555</b>	<b>17%</b>	<b>1%</b>

ANTIMICROBIAL DRUGS APPROVED FOR USE IN FOOD-PRODUCING ANIMALS<sup>1</sup>  
 ACTIVELY MARKETED IN 2013  
 DOMESTIC SALES AND DISTRIBUTION DATA  
 REPORTED BY MEDICAL IMPORTANCE AND DISPENSING STATUS

	Dispensing Status	Annual Totals (kg) <sup>2</sup>	% Subtotal	% Grand Total
<u>Medically Important</u> <sup>3</sup>	<i>OTC</i> <sup>1,5</sup>	8,968,260	98%	61%
	<i>RX</i> <sup>1,6</sup>	128,038	1%	<1%
	<i>RX</i> <sup>6</sup> / <i>OTC</i> <sup>1,5,7</sup>	54,942	<1%	<1%
	<i>VFD</i> <sup>8</sup>	45,562	<1%	<1%
	<i>Subtotal</i>	<b>9,196,803</b>	<b>100%</b>	<b>62%</b>
<u>Not Currently Medically Important</u> <sup>4</sup>	<i>OTC</i> <sup>5</sup>	5,591,752		38%
<i>Grand Total</i>		<b>14,788,555</b>		<b>100%</b>



TABLE 5. NATIONAL ESTIMATE OF TOTAL KILOGRAMS OF SWINE IN-FEED ANTIMICROBIALS FOR ALL PRODUCTION CYCLES IN A YEAR BY ANTIMICROBIAL AND REASON

	<i>Antimicrobial</i>	<i>Growth promotion</i>	<i>Prevention</i>	<i>Therapy</i>	<i>Any reason 'yearly basis'</i>
Antimicrobials or classes listed as <b>Highly Important</b> in Guidance 152 Appendix A	Chlortetracycline <sup>b</sup>			533,973	
	as Chlortetracycline alone	83,331	206,076	217,622	507,029
	as Chlortetracycline/Sulfathiazole/ Penicillin G (CSP)	942	14,673	3,784	19,398
	as Chlortetracycline/Sulfamethazine/ Penicillin G (ASP)	2,735	3,663	1,148	7,546
	Lincomycin <sup>c</sup>	356	4,246	20,844	25,446
	Neomycin				
	as Neomycin/Oxytetracycline	4,068	2,632	16,394	23,094
	Oxytetracycline <sup>b</sup>				
	as Oxytetracycline alone	2,615	31,699	97,547	131,862
	as Neomycin/Oxytetracycline	4,068	2,632	16,394	23,094
Antimicrobials or classes listed as <b>Critically Important</b> in Guidance 152	Penicillin				
	as Chlortetracycline/Sulfathiazole/ Penicillin G (CSP)	471	7,336	1,892	9,699
	as Chlortetracycline/Sulfamethazine/ Penicillin G (ASP)	1,367	1,832	574	3,773
	Virginiamycin <sup>d</sup>	26,108	54,858	493	81,459
	Tilmicosin <sup>e</sup>	1,068	46,906	22,786	70,761
	Tylosin <sup>e</sup>				
	as Tylosin alone	25,641	37,893	91,160	154,694
	as Tylosin/Sulfamethazine	7,500	149	3,460	11,109

64% of medically important use

66% of medically important P and T

<sup>a</sup>Only potentiated sulfonamides are listed in Guidance 152, Appendix A.

<sup>b</sup>The tetracycline class representative in Guidance 152, Appendix A is tetracycline.

<sup>c</sup>The lincosamide class representative listed in Guidance 152, Appendix A is clindamycin.

<sup>d</sup>The streptogramin class representative in Guidance 152, Appendix A is dalfopristin/quinupristin.

<sup>e</sup>The macrolide class representatives listed in Guidance 152, Appendix A are erythromycin, azithromycin, and clarithromycin.

Antimicrobials are grouped according to classification or lack of classification in Appendix A of FDA/CVM guidance 152.

15%      39%      46%      165,803

## Comparison of Human and Food Animal Sales in 2011

Relationship	Antimicrobial	Food Animal Sales 2011 (kg)	Human Sales 2011 (kg)
More Total Use by Humans	Cephalosporins	26,611	496,910
	Penicillins	885,304	1,460,421
	Sulfas (and TMP for humans)	383,105	481,664
	Quinolones		277,439
	Nitroimidazoles		120,976
	Carbapenems/penems		14,184
	Oxazolidinones		5,009
	Monobactams		4,771
	Lipopeptides		1,131
	Vancomycin		44,256
	Nitrofurantoin		18,348
	Rifampin		6,949
	Fosfomycin		857
	Colistin		144
	Telavancin		85
	Chloramphenicol		46
	Ketolides		62
	Polymyxin B		91
	Streptogramins		32
	Colistimethate sodium		

## Comparison of Human and Food Animal Sales in 2011

Relationship	Antimicrobial	Food Animal Sales 2011 (kg)	Human Sales 2011 (kg)
More Total Use by Food Animals	Aminoglycosides	214,895	6,485
	Lincosamides	190,101	71,455
	Macrolides	582,836	164,028
	Tetracyclines	5,652,855	113,832
Not Individually Reported: Includes aminocoumarins, phenicols, diaminopurimadines, fluoroquinolones, glycolipids, streptogramins, pleuromutilins (not medically important), and polypeptides		1,510,934	

	<b>Food Animal Sales 2011 (kg)</b>	<b>Human Sales 2011 (kg)</b>
Medically Important Antimicrobial Totals (kg)	9,446,641	3,289,175
Expressed as percent of total human and food animal sales of medically important antimicrobials	74.2%	25.8%
<p>So, where does the "80% used in food animals" come from? Well, if you add the 4,122,397 kg of ionophores sales reported for 2011, then you come up with the following values. It doesn't move the value that much to take the ionophores out because they go into both the numerator and denominator.</p>		
All Antimicrobial Sales Totals	13,569,039	3,289,175
Expressed as percent of total human and food animal sales	80.5%	19.5%

	Animal #	Human #	
Humans - 2011 population as of July 1, 2011		311,591,917	Source <a href="http://www.census.gov/popest">http://www.census.gov/popest</a>
Cattle and calves (Beef and Dairy) Inventory as of January 1, 2012	90,777,000		Source: <a href="http://www.aphis.usda.gov/animal_health/nahms/downloads/Demographics2011.pdf">http://www.aphis.usda.gov/animal_health/nahms/downloads/Demographics2011.pdf</a>
Hogs - Number slaughtered in 2011	110,900,000		
Sheep and lamb inventory as of January 1, 2012	5,350,000		
Goat inventory as of January 1, 2012	2,860,000		
Broiler-type chickens hatched in 2011	9,060,000,000		
Egg-type chickens hatched in 2011	479,000,000		
Turkey poults hatched in 2011	285,000,000		
<b>Total populations</b>	<b>10,033,887,000</b>	<b>311,591,917</b>	

<b>Classification</b>	<b>Number in Inventory</b>	<b>human equivalent for the year</b>	<b>Explanation</b>
Cattle and calves (Beef and Dairy) Inventory as of January 1, 2012	90,777,000	453,885,000	Used average weight between cattle and calves of 750 lbs, or 5 people
Hogs - Number slaughtered in 2011	110,900,000	110,900,000	Used slaughter hog as equal to the weight of 2 people, with two turns per year, so number stays the same)
Sheep and lamb inventory as of January 1, 2012	5,350,000	2,675,000	Used sheep and lamb average as 0.5 people
Goat inventory as of January 1, 2012	2,860,000	1,859,000	Used goats as equal to 0.65 people
Broiler-type chickens hatched in 2011	9,060,000,000	50,333,333	Used a conversion factor of 30, 5 lb broiler chickens = weight of 150 lb human, then 6 turns per year, making 180 broilers/year equaling one person per year for weight.
Egg-type chickens hatched in 2011	479,000,000	19,160,000	For a Hen, she will live most of a year between growing and laying, so at 6 lbs, 25 hens = one human
Turkey poults hatched in 2011	285,000,000	9,500,000	150 lb human, then 3 turns/year, meaning 30 birds equals one human for a year
<b>Totals</b>	<b>10,033,887,000</b>	<b>648,312,333</b>	

# The Basics of Clinical Pharmacology (in one slide)

- Can I do some good?
- **Can I do any harm?**
- Can I get it in the animal(s)?
- What is the cost?

# RESISTANCE CHALLENGES IN HUMAN MEDICINE



Antibiotic-Resistant Microorganism	Infections Included	Infections not Included	Estimated Annual Number of Cases	Estimated Annual Number of Deaths
Carbapenem Resistant Enterobacteriaceae (CRE)	HAIs caused by <i>Klebsiella</i> and <i>E. coli</i> with onset in hospitalized patients	1, 2, 3	9,300	610
Drug-resistant <i>Neisseria gonorrhoeae</i> (any drug)	All infections		246,000	<5
Multidrug-resistant <i>Acinetobacter</i> (three or more drug classes)	HAIs with onset in hospitalized patients	1,2	7,300	500
Drug-resistant <i>Campylobacter</i> (azithromycin or ciprofloxacin)	All infections		310,000	28
Drug-resistant <i>Candida</i> (fluconazole)	HAIs with onset in hospitalized patients	1,2	3,400	220
Extended-spectrum $\beta$ -Lactamase producing Enterobacteriaceae (ESBLs)	HAIs caused by <i>Klebsiella</i> and <i>E. coli</i> with onset in hospitalized patients	1,2,3	26,000	1700
Vancomycin-resistant <i>Enterococcus</i> (VRE)	HAIs with onset in hospitalized patients	1,2	20,000	1300
Multidrug-resistant <i>Pseudomonas aeruginosa</i> (three or more drug classes)	HAIs with onset in hospitalized patients	1,2	6,700	440
Drug-resistant non-typhoidal <i>Salmonella</i> (ceftriaxone, ciprofloxacin <sup>7</sup> , or 5 or more drug classes)	All infections		100,000	40

Antibiotic-Resistant Microorganism	Infections Included	Infections not Included	Estimated Annual Number of Cases	Estimated Annual Number of Deaths
Drug-resistant <i>Salmonella</i> Typhi (Ciprofloxacin <sup>7</sup> )	All infections		3,800	<5
Drug-resistant <i>Shigella</i> (Azithromycin or ciprofloxacin)	All infections		27,000	<5
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	Invasive infections	4	80,000	11000
<i>Streptococcus pneumoniae</i> (full resistance to clinically relevant drugs)	All infections		1,200,000	7000
Drug-resistant tuberculosis (any clinically relevant drug)	All infections		1,042	50
Vancomycin-resistant <i>Staphylococcus aureus</i> (VRSA)	All infections		<5	<5
Erythromycin-resistant Group A <i>Streptococcus</i>	Invasive infections	5	1,300	160
Erythromycin-resistant Group B <i>Streptococcus</i>	Invasive infections	6	7,600	440
<b>Summary Totals for Antibiotic-Resistant Infections</b>			<b>2,049,442</b>	<b>23,488</b>
<i>Clostridium difficile</i> Infections	Healthcare-associated infections in acute care hospitals or in patients requiring hospitalization		250,000	14,000

- |   |
|---|
| 1. Infections occurring outside of acute-care hospitals (e.g., nursing homes)   |
| 2. Infections acquired in acute care hospitals but not diagnosed until after discharge                                      |
| 3. Infections caused by Enterobacteriaceae other than <i>Klebsiella</i> and <i>E. coli</i> (e.g., <i>Enterobacter</i> spp.) |
| 4. Both healthcare and community-associated non-invasive infections such as wound and skin and soft tissue infections       |
| 5. Non-invasive infections including common upper-respiratory infections like strep throat                                  |
| 6. Non-invasive infections and asymptomatic intrapartum colonization requiring prophylaxis                                  |
| <sup>7</sup> Resistance or partial resistance   |

# Resistance in food animals?

- Bovine respiratory disease
  - *Mannheimia haemolytica*
  - *Pasteurella multocida*
- Swine
  - *Streptococcus suis*
  - *Escherichia coli*

**Table 5:** Minimal inhibitory concentration (MIC) summary values and frequency distributions for seven antimicrobial agents tested against *Streptococcus suis* from swine submitted to Pfizer Animal Health by veterinary diagnostic laboratories located in the United States and Canada from 2001 to 2010\*

Year	n	MIC <sub>50</sub> (µg/mL)	MIC <sub>90</sub> (µg/mL)	%S	Ceftiofur MIC frequency distribution (% of isolates)†‡										
					0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	> 16
2001	167	≤ 0.03	0.06	99.4	85.0	9.6	2.4	0.6	0.6	0.6	0.6	0.6	0	0	0
2002	183	≤ 0.03	0.06	100	86.9	6.6	3.8	2.7	0	0	0	0	0	0	0
2003	192	≤ 0.03	0.06	100	84.9	6.8	4.2	2.6	1.0	0	0.5	0	0	0	0
2004	231	≤ 0.03	0.12	100	81.8	7.8	7.4	0.4	1.3	0.4	0.9	0	0	0	0
2005	312	≤ 0.03	0.06	99.7	83.7	7.1	4.2	2.9	1.3	0.3	0.3	0.3	0	0	0
2006	335	≤ 0.03	≤ 0.03	100	91.9	3.0	3.3	0.6	0.6	0	0.6	0	0	0	0
2007	380	0.06	1	98.1	8.7	49.7	16.6	6.3	5.0	8.2	3.7	1.6	0.3	0	0
2008	304	0.06	1	96.7	3.3	49.0	19.1	9.2	5.9	6.6	3.6	2.0	1.0	0.3	0
2009	259	0.06	1	95.7	9.3	42.5	22.4	6.6	7.3	5.8	1.9	2.7	0.8	0.8	0
2010	254	0.06	1	98.0	8.7	48.4	18.9	4.7	5.9	5.1	6.3	0	1.2	0.4	0.4
Year	n	MIC <sub>50</sub> (µg/mL)	MIC <sub>90</sub> (µg/mL)	%S	Penicillin MIC frequency distribution (% of isolates)†‡										
					0.12	0.25	0.5	1	2	4	8	16	32	64	> 64
2001	167	≤ 0.12	0.25	NA	86.8	3.6	3.0	2.4	1.8	1.2	0	0.6	0.6	0	0
2002	183	≤ 0.12	0.25	NA	88.5	1.6	3.8	0.5	2.2	1.6	1.6	0	0	0	0
2003	192	≤ 0.12	0.5	NA	83.9	3.1	4.2	2.1	3.1	1.6	0.5	0.5	0	0.5	0.5
2004	231	≤ 0.12	0.5	NA	83.5	3.5	5.6	3.0	0.4	2.2	0.9	0.4	0.4	0	0
2005	312	≤ 0.12	0.5	NA	83.7	4.5	3.2	4.2	1.9	1.0	1.3	0.3	0	0	0
2006	335	≤ 0.12	0.25	NA	88.1	4.2	2.1	2.7	1.8	0.9	0.3	0	0	0	0
2007	380	≤ 0.12	1	NA	81.8	3.4	3.4	4.5	5.0	1.3	0.5	0	0	0	0
2008	304	≤ 0.12	1	NA	72.4	8.2	7.2	4.9	3.9	2.0	1.3	0	0	0	0
2009	259	≤ 0.12	1	NA	80.7	4.2	3.9	5.4	4.6	0.8	0.4	0	0	0	0
2010	254	≤ 0.12	1	NA	83.9	2.4	3.5	3.5	4.3	1.2	1.2	0	0	0	0

# Antimicrobial Stewardship

- ▣ Antimicrobial stewardship refers to **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, and route of administration.**
- ▣ Antimicrobial stewards seek to achieve **optimal clinical outcomes** related to antimicrobial use, **minimize toxicity** and other adverse events, **reduce the costs** of health care for infections, and **limit the selection for antimicrobial resistant strains.**

# What is **A VCPR?** ?

Is there a non-antibiotic alternative which will appropriately prevent, control, or treat this disease challenge?

*While asking...*

*If not...*

Assuring use of the antibiotic as shown to be safe and effective

*While...*

Selection of an antibiotic which has been demonstrated to be safe and effective for this purpose

# Things that are broken

- Our understanding of the relationship of magnitude and duration of exposure with relation to resistance development, and...
- our understanding of the balance between duration of therapy and treatment success/relapse rates.



# So where to from here

- Veterinarians will have control of all uses of antimicrobials in animals.
- Emphasize veterinary education on optimal use of these resources.
- Duration of therapy research is an absolute requirement
- Continue the emphasis on prevention of infectious disease