# Antimicrobial Restrictions

## Swine Industry Perspective

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# Legislation vs. Regulation

- Legislation – law created by Congress
- Regulation – mechanism developed by government agency to implement the law

# Legislation

- Federal Food, Drug, and Cosmetic Act
  - 1938
  - Authorizes FDA to oversee the safety of food, drugs and cosmetics
- Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA)
  - Allows vets to prescribe extra-label uses

# Proposed legislation

- Preservation of Antibiotics for Medical Treatment Act (PAMTA – HR 965)
  - Introduced in March, 2011 by Rep. Louise Slaughter – reintroduction of HR 1549
  - Referred to:
    - House Committee on Energy and Commerce
    - House Committee on Rules (Slaughter is ranking member)
  - Has not been referred out of committee

# PAMTA

The purpose of this Act is to preserve the effectiveness of medically important antibiotics used in the treatment of human and animal diseases by reviewing the safety of certain antibiotics for nontherapeutic purposes in food-producing animals.

# Critical Antimicrobial Animal Drug

The term ‘critical antimicrobial animal drug’ means a drug that--

- ‘(1) is intended for use in food-producing animals; and
- ‘(2) is composed wholly or partly of--
  - ‘(A) any kind of penicillin, tetracycline, macrolide, lincosamide, streptogramin, aminoglycoside, or sulfonamide; or
  - ‘(B) any other drug or derivative of a drug that is used in humans or intended for use in humans to treat or prevent disease or infection caused by microorganisms.

# Antimicrobial use estimates

FOODBORNE PATHOGENS AND DISEASE
Volume 9, Number 3, 2012

DOI: 10.1089/fpd.2011.0983

## Use Estimates of In-Feed Antimicrobials in Swine Production in the United States

Michael D. Apley, Eric J. Bush, Robert B. Morrison, Randall S. Singer, and Harry Snelson

Abstract

When considering the development of antimicrobial resistance in food animals, comparing gross use estimates of different antimicrobials is of little value due to differences in potencies, duration of activity, relative effect on target and commensal bacteria, and mechanisms of resistance. However, it may be valuable to understand quantities of different antimicrobials used in different ages of swine and for what applications. Therefore, the objective of this project was to construct an estimate of antimicrobial use through the feed in swine production in the United States. Estimates were based on data from the National Animal Health Monitoring System (NAHMS) Swine 2006 Study and from a 2009 survey of swine-exclusive practitioners. Inputs consisted of number of pigs in a production phase, feed intake per day, dose of the antimicrobial in the feed, and duration of administration. Calculations were performed for a total of 102 combinations of antimicrobials (n = 17), production phases (n = 2), and reasons for use (n = 3). Calculations were first conducted on farm-level data, and then extrapolated to the U.S. swine population. Among the nursery phase estimates, chlortetracycline had the largest estimate of use, followed by oxytetracycline and tilmicosin. In the grower/finisher phase, chlortetracycline also had the largest use estimate, followed by tylosin and oxytetracycline. As an annual industry estimate for all phases, chlortetracycline had the highest estimated use at 533,973 kg. The second and third highest estimates were tylosin and oxytetracycline with estimated annual uses of 165,803 kg and 154,956 kg, respectively. The estimates presented here were constructed to accurately reflect available data related to production practices, and to provide an example of a scientific approach to estimating use of compounds in production animals.

| | Antimicrobial | Growth Promotion | Prevention | Therapy | Any Reason 'Yearly Basis' |
|---|---|---|---|---|---|
| Antimicrobials or classes listed as Highly Important in Guidance 152 Appendix A | Chlortetracycline[2] | | | | |
| | 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[3] | 356 | 4,246 | 20,844 | 25,446 |
| | Neomycin | | | | |
| | as Neomycin/Oxytetracycline | 4,068 | 2,632 | 16,394 | 23,094 |
| | Oxytetracycline[2] | | | | |
| | as Oxytetracycline alone | 2,615 | 31,699 | 97,547 | 131,862 |
| | as Neomycin/Oxytetracycline | 4,068 | 2,632 | 16,394 | 23,094 |
| | 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[4] | 26,108 | 54,858 | 493 | 81,459 |
| Antimicrobials or classes listed as Critically Important in Guidance 152 Appendix A | Tilmicosin[5] | 1,068 | 46,906 | 22,786 | 70,761 |
| | Tylosin[5] | | | | |
| | as Tylosin alone | 25,641 | 37,893 | 91,160 | 154,694 |
| | as Tylosin/sulfamethazine | 7,500 | 149 | 3,460 | 11,109 |

Apley, et al 2012

# Nontherapeutic Use

- The term ‘nontherapeutic use’, with respect to a critical antimicrobial animal drug, means any use of the drug as a feed or water additive for an animal in the absence of any clinical sign of disease in the animal for growth promotion, feed efficiency, weight gain, routine disease prevention, or other routine purpose.’

# Delivering Antibiotic Transparency in Animals (DATA) Act

- To be introduced by Rep. Henry Waxman
- Mandate FDA "improve" the data it collects on agricultural antibiotics use.
- Require feed mills to report what antibiotics it uses in its feeds, what the drugs are used for and whether it's growth promotion or disease control and prevention.
- Require drug manufacturers to report to the U.S. Food and Drug Administration (FDA) the type, purpose and quantities of antimicrobials used on farms.

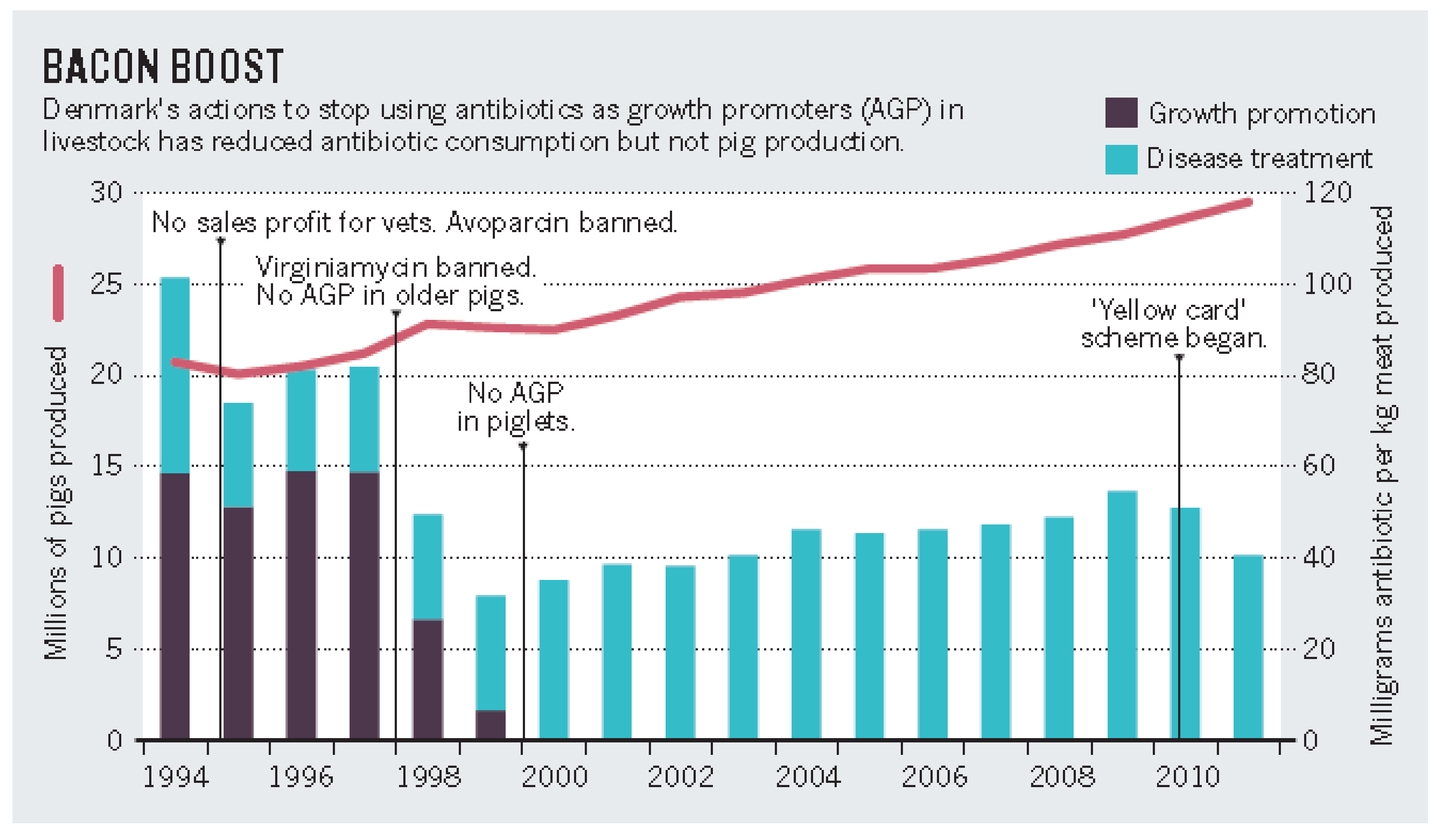
# DATA Concerns

- Sales data doesn't correlate well with on-farm use
- Feed mills will not be able to readily provide info on how drugs are used
- Manufacturers will not be able to provide estimates of use based on species, indication or quantity

# FDA Guidance 209/213

- FDA defines "production" uses (GP/FE) to be "injudicious".
- Requires enhanced veterinary oversight in the use of feed-grade antimicrobials
- Basically a "voluntary" removal of GP claims for "medically important" antimicrobials within 3 years
  - Sponsors can migrate claims to specific indications if justified
- Eliminate OTC feed grade -> VFD

# Can you regulate reductions?




28 JUNE 2012 | VOL 486 | NATURE | 465

# “The Yellow Card Initiative”

“The goal was to achieve a 10 % reduction on 2009 consumption levels as measured in kg by 2013. The yellow card initiative was – when instituted – also an incentive to help the pig producers to achieve this goal.”

**The yellow card initiative:** Each year, the DVFA will issue threshold limits for antimicrobial consumption in three age groups of pigs. The limits for 2010 were as follows:

1. Weaners (7–30 kg): 28 Animal Daily Doses (ADD) per 100 weaners per day
2. Young pigs, including young females (over 30 kg), excluding sows, gilts and boars: 8 ADD per 100 pigs per day
3. Sows, gilts and boars: 5.2 ADD per 100 pigs per day

If the average antimicrobial consumption in a holding within a nine-month period exceeds one or more of the above threshold limits, DVFA may issue an order or injunction (the yellow card) compelling the owner of the holding, in collaboration with the veterinary practitioner, to reduce the antimicrobial consumption in the holding below the threshold limits within nine months.

Danish Veterinary and Food Administration

# Veterinary Feed Directive

- FDA recognizes changes are needed
- Likely revisions:
  - Written for up to 6 months for a production site (dose, duration, refills)
  - Approximate number animals treated, not tons of feed
  - Fax, email VFD forms – no originals required
  - Records retained for 12 months
  - Decoupled from VCPR

# VCPR

- Codified in the CFR as a requirement for AMDUCA
- FDA wants to remove it from the VFD requirements
- AVMA has recently adopted some amended wording
- Appears in many state veterinary practice acts

# What's Driving Current Legislation/Regulation?

- The fear of resistance development in the human population
- Risk response disproportionate to the hazard
- Assessments often ignore the benefit side of the equation

# A little science

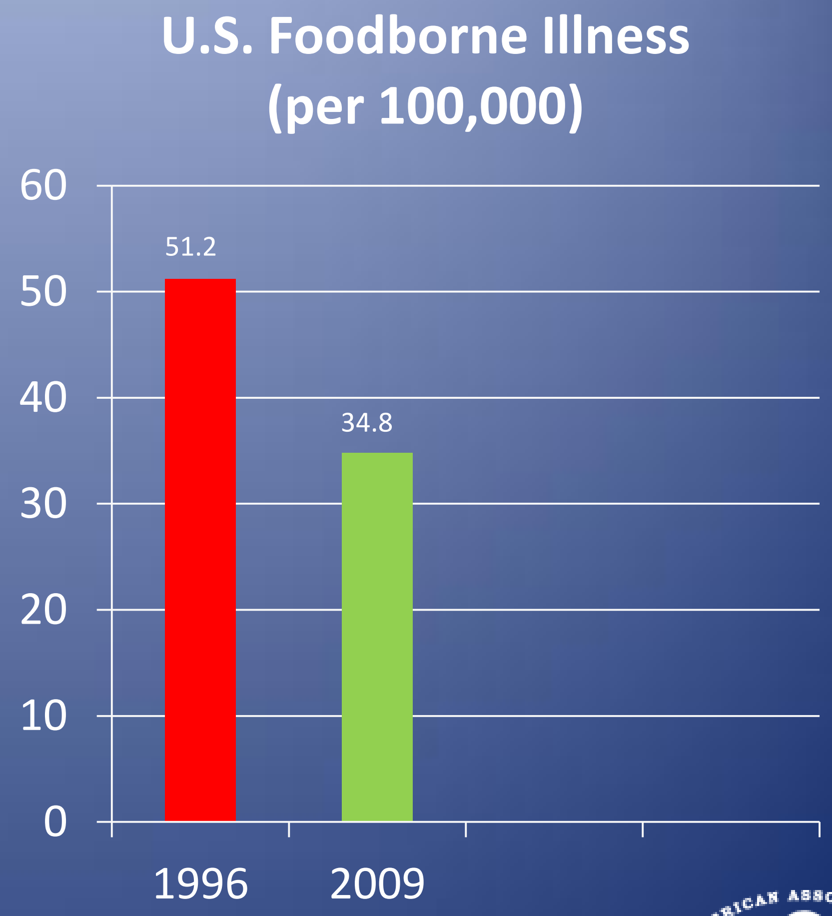
- Guidance 152 called for evaluating risk to establish a "reasonable certainty of no harm" – NOT "no risk"
- Have to differentiate between "might" and "likely"
- A lot of steps between abtic use in livestock and increased human illness resulting from resistance

# FDA RISK ASSESSMENT
# - Assumes this causal pathway


Hurd, 2010

# Risk – Benefit
# The Other Half of the Equation

- Peel out carcasses are 90% more likely to be contaminated with salmonella – Hurd
- Very minor changes in microbial load due to reduced poultry health could have relatively large impacts on human health. Singer *et al.* 2007




FDA, 2009

# Risk Assessments

- All scientific risk assessments conducted to date have shown the risk associated with antimicrobial use in livestock to be low to near zero.

# Risk Assessment Results

| Risk (High to Low) | Yearly probability | Outcome measured |
|---|---|---|
| Enrofloxicin use in poultry to treat disease | 1 in 30,000 | Compromised treatment<br>*By FDA, <u>overestimated</u> attributable fraction* |
| Enrofloxicin use in poultry to treat disease | Removal is more hazardous to health | By Cox and Popken |
| All macrolide uses (cattle, swine, poultry) | 1 in 10 million | Compromised treatment<br>By Hurd *et al.*, Alban in Denmark |
| Streptogramin/Virginiamycin use | ~ 100 in 100 million | Impaired treatment<br>*By FDA, still a draft* |
| Penicillin growth promoter | ~4 in billion | Excess mortality<br>Cox and Popken |
| Baytril ® use in dairy heifers | ~1 in 61 billion | Compromised treatment |

Source: Dr. Scott Hurd

# Put that in perspective…

- Chance of dying
  - Car crash

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- Chance of dying
  - Car crash – 1 in 6,700

# Put that in perspective…

- Chance of dying
  - Car crash – 1 in 6,700
  - Commercial plane crash

# Put that in perspective…

- Chance of dying
  - Car crash – 1 in 6,700
  - Commercial plane crash – 1.27 in 100,000 flight hours

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- Chance of dying
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  - Commercial plane crash – 1.27 in 100,000 flight hours
  - Bicycling – 1 in 140,845
  - Running

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- Chance of dying
  - Car crash – 1 in 6,700
  - Commercial plane crash – 1.27 in 100,000 flight hours
  - Bicycling – 1 in 140,845
  - Running – 1 in 1 million

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- Chance of dying
  - Car crash – 1 in 6,700
  - Commercial plane crash – 1.27 in 100,000 flight hours
  - Bicycling – 1 in 140,845
  - Running – 1 in 1 million
  - Dance party

# Put that in perspective…

- Chance of dying
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  - Bicycling – 1 in 140,845
  - Running – 1 in 1 million
  - Dance party – 1 in 100 million

# Put that in perspective…

## Food Security in 2050

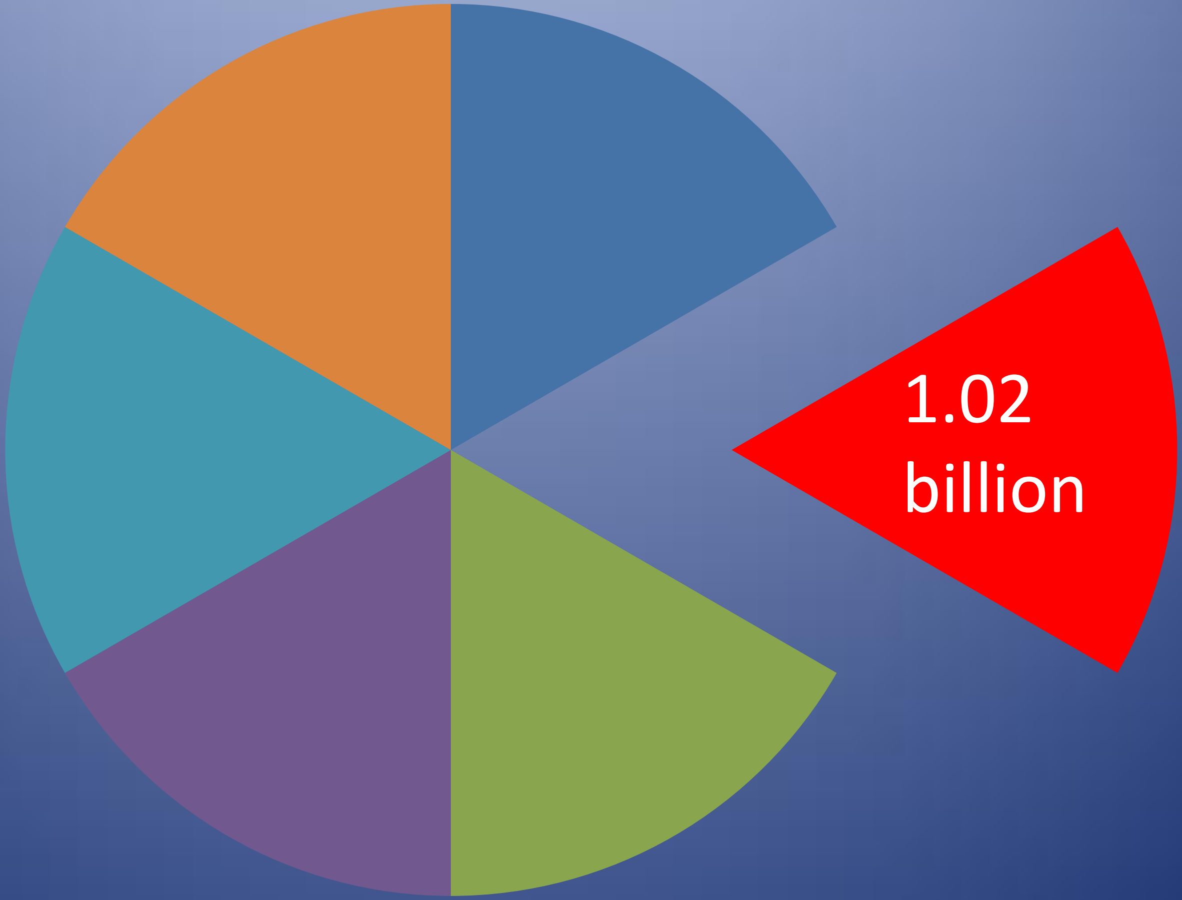
World population = 9 billion

Requires 100% more food

70% from efficiency-improving technologies

# Put that in perspective…

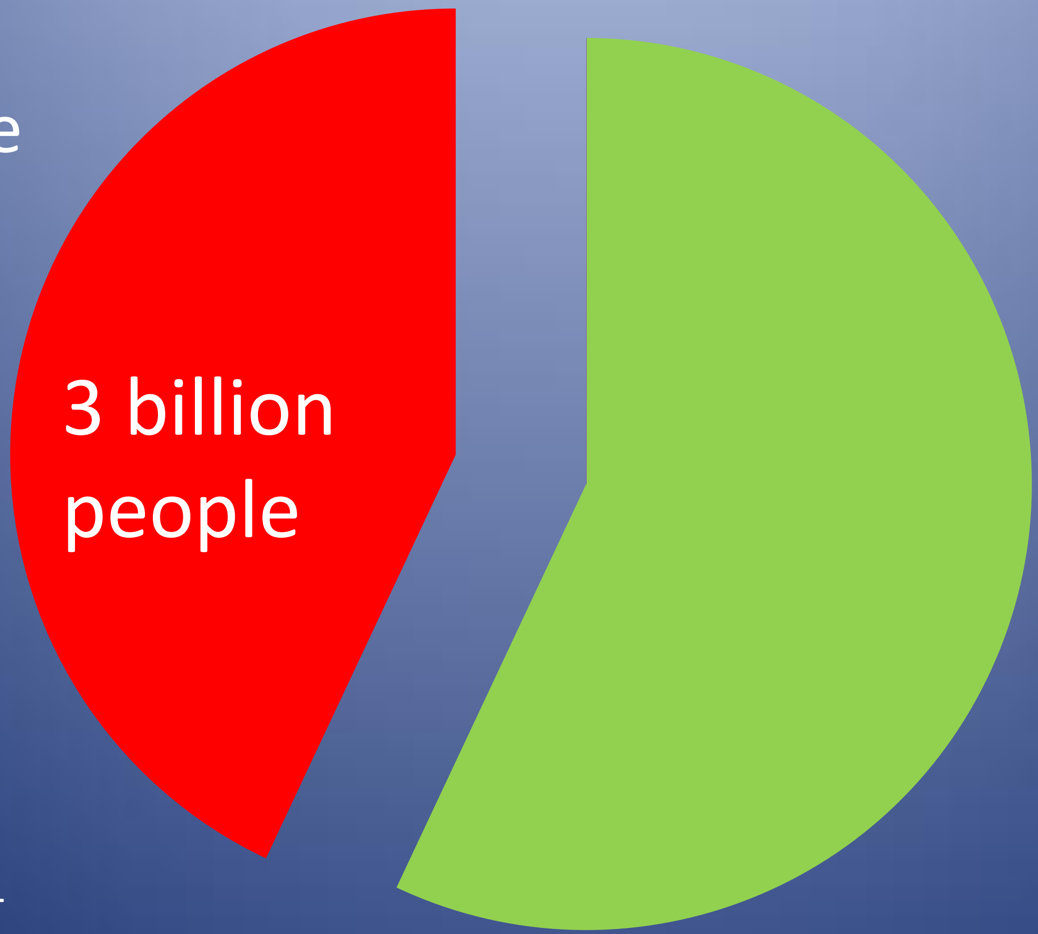
1 in 6 people went hungry in 2010




FAO, 2010

# Put that in perspective…

43% Live on less than $2USD




UNICEF, 2011

# Put that in perspective…
## Pork production efficiency (1959 – 2009)


Pork Checkoff, 2012

# Economic Impact of AGP Loss

- Dermott Hayes and Helen Jensen examined results from Denmark and Swedish study
- Extrapolated findings to estimate economic impact on U.S. swine producers

# Economic Assessment

| Description | Cost/animal |
|---|---|
| Weaning | $1.25 |
| Finishing | $1.05 |
| Veterinary cost | $0.25 |
| Vaccine | $0.75 |
| Sort loss | $0.65 |
| Capital cost (increased post-weaning & sow space) | $0.55 |
| Total cost per animal (first year) | $4.50 |

Hayes, 2003

# Economic Assessment

- Total cost over 10 year period: >$700 million
- Increase cost to consumers: approx. 2% retail

Inc cost → dec production → fewer producers

Hayes, 2003

# Science messages

- All scientific risk assessments published to date have shown a negligible risk to humans
- Failure to prevent or treat animal illness causes unnecessary suffering and death
- Animals with residual effects of illness are more likely to cause human foodborne illness
  - Peel out carcasses are 90% more likely to be contaminated with salmonella – Hurd
  - Very minor changes in microbial load due to reduced poultry health could have relatively large impacts on human health. Singer *et al.* 2007

# Science messages

- Volume of use has no relevance to resistance development
  - Key focus should be bug/drug interaction
  - Then evaluating the chance that resistant bacteria somehow migrate from livestock to humans and result in elevated levels of illness

# That's

# dENDdogram