Antibiotics Used in Food Animals

U.S. House Briefings
February, 2012

Antibiotics Overview

• How are antibiotics regulated?
• What is the volume of use?
• What are the risks to human health?
• Coming changes in antibiotic regulation

Protecting animal and public health

REGULATION & USE OF ANTIBIOTICS
Antibiotic Use

Antibiotics approved by FDA are labeled for four different purposes:

- Disease treatment
- Disease control
- Disease prevention
- Growth promotion
WHAT IS THE VOLUME OF USE?

Making accurate comparisons

Approved Antimicrobial Drug Sales (in kg)

How much is used?

Source: FDA CVM, 2009
Use Issues

- Sales are not a measure of use
- No comparable human/animal data
- Comparisons used to scare, not to inform
- Not an indicator of public health risk

WHAT IS THE RISK TO HUMAN HEALTH?

Understanding bacteria and the food chain


**Figure:** Contribution of animal sources to the overall resistance problem

Infectious Disease Society of America’s “Facts about AR”

- Staphylococcus infections (MRSA)
- Acinetobacter baumannii
- Vancomycin Resistant Enterococcus (VRE)
- Pseudomonas aeruginosa
- Streptococcus pneumoniae
- Neisseria gonorrhoea
- Drug resistant TB, Clostridium difficile, Klebsiella species

No food-borne or animal reservoirs

CDC Diseases/Pathogens Associated with Antimicrobial Resistance

- Few organisms associated with food
- Emphasizes human-to-human spread of resistant organisms

Bacteria
- Acinetobacter
- Anthrax
- Gonorrhea
- Group B streptococcus
- Klebsiella pneumoniae
- Methicillin-resistant Staphylococcus aureus (MRSA)

COMING CHANGES IN ANTIBIOTIC REGULATION
FDA Strategy

- Issued in 2010 as a policy statement on how FDA wants to regulate feed use of antibiotics.
- Based on Congressional testimony in 2009 by FDA Deputy Commissioner Joshua Sharfstein.
  - Phase out of Growth promotion claims.
  - Increase veterinary control over use (VFD) on “medically important” antibiotics.
- FDA is seeking a voluntary approach.

Antimicrobials Approved in Feed

- Bacitracin*
- Bambermycin*
- Efrotomycin* (never marketed)
- Erythromycin
- Florfenicol* (VFD)
- Lasalocid*
- Lincomycin*
- Laidlomycin*
- Monensin*
- Neomycin*
- Novobiocin*
- Oleanomycin*
- Penicillin
- Sulfonamides
- Tiamulin*
- Tilmicosin (VFD)
- Tylosin
- Tetracyclines
- Virginiamycin

* In classes with no significant human use

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Therapeutic Use

CODEX, AVMA, FDA
AHI Response

- We welcome the opportunity to work with FDA to meet their objectives of reducing antibiotic use for growth promotion; and,
- Increasing veterinary oversight over the use of medically important antibiotics in feeds.

GOAL: All medically important antibiotics will be used therapeutically (targeted) under the supervision of a veterinarian.
Antimicrobial Resistance – Is Animal Agriculture Really the Cause?

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Antibiotic resistance risk due to on-farm antibiotic use

SUMMARY

1. Risk to humans is negligible
2. Failure to prevent or treatment illness causes unnecessary animal suffering and death
3. Animals with residual effects of illness are more likely to cause human foodborne disease
4. Action – manage the hazard
Antibiotic resistance risk due to on-farm antibiotic use

Layman’s Version

1. Long way from farm to harm
2. Animals need Medicine, just like kids
3. Healthy Animals make Safe Food
4. Action – We are managing the hazard

Why is risk negligible?

- “Long way from farm to harm”
  - Many events must occur
  - Many interventions exist to prevent those events
- Concern is NOT equivalent to risk
  - Risk requires causal chain of events
  - Risk requires set of conditions

IT’S A LONG WAY FROM THE FARM TO HARM
Filters that reduce risk

What is the problem?
Antibiotic RESISTANCE

- Increasing human infections with resistant strains
- Exposure to antibiotics selects for some resistance strains
- Livestock and their bacteria are exposed to antibiotics
- Assume a risk

Bacteria of Concern to Infectious Disease Society

- Staphylococcus infections (MRSA) – these are mainly hospital nosocomial infections, occasionally associated with schools and athletic facilities. CDC said “not a foodborne infection and cannot be acquired by eating meat.
- Acinetobacter baumannii is an opportunistic pathogen associated with a high rate of infections in soldiers wounded in Iraq.
- Vancomycin Resistant Enterococcus (VRE) hospital nosocomial infection due to extensive use of vancomycin in U.S. hospitals. Vancomycin or drugs in its class have never been approved for or used in food producing animals.
- Pseudomonas aeruginosa is another opportunistic pathogen found in intensive care units, occurs rarely in dairy mastitis
- Streptococcus pneumoniae is strictly a human pathogen that causes respiratory infections. no known connection to food producing or companion animals.
- Neisseria gonorrhoea is strictly a human pathogen that causes venereal infections transmitted through human sexual contact.
- Drug resistant tuberculosis, Clostridium difficile, and Klebsiella species are other bacteria. no known connection between these pathogens and food producing animals.

http://www.idsociety.org/Content.aspx?id=5650
What do we really mean by **RESISTANCE**?

- Ability to grow (on a plate) in the presence of selected antimicrobial
- Not residues
- All bacteria have some ability to grow in the presence of some antimicrobial
- DOES NOT mean clinical ineffective = Does not mean treatment failure

Resistance found many places where antibiotics never used

- Farms – even organic
- Ground water, deep ocean trenches
- Arctic and sub-artic seals
- Caves untouched 10 million years
- Permafrost, “...places which are relatively untouched by human civilization”

Hazard Does Not Mean Risk

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Example Hazardous Material

- Human Health Effects
  - cramps
  - nausea
  - dizziness
  - respiratory difficulties
  - convulsions capable of leading to death

Example Hazardous Material = Oxygen

- Human Health Effects
  - cramps
  - nausea
  - dizziness
  - respiratory difficulties
  - convulsions capable of leading to death

You too can do a risk assessment

- Risk = Pr (injury | wreck) = conditional

  - Risk of auto accident = Pr (wreck)
    - Traffic
    - Road type
    - Weather
    - Driver skill and alertness (etc)
    - Probability of wreck = a*b*c*d
Auto accident example (cont)

- Injury if in auto accident (wreck)
  - Speed at impact (continuous var)
  - Type of collision (say 5 categories)
    - Head on
    - Right angles
    - Glancing head on
    - Safety of car (H, M, L)
  - Seat belt = Y/N
- Series of conditional probabilities
- A Causal chain
- Both events must happen

Hazard to risk requires a causal pathway – failure event series

Pathway provided by FDA guidance doc 152

Pathway of Events Leading to the Risk

Release Assessment: Describes the probability that factors related to the antimicrobial use in animals will result in the emergence of resistant bacteria or resistance determinates (RzD).

Exposure Assessment: Describes the likelihood of human exposure to the RzD through particular exposure pathways.

Consequence Assessment: Describes the relationship between specified exposures to the RzD (the hazardous agent) and the consequences of those exposures (CVM-defined hazard).

Risk = 1 in 10 million per year
What does risk science say?

• No peer-reviewed scientific quantitative risk assessment has demonstrated any detectable risk of treatment failure in humans caused by current on-farm antibiotic uses in animals.

IT’S A LONG WAY FROM THE FARM TO HARM

2. Failure to prevent or treatment illness causes unnecessary animal suffering and death

• Farm is a day care and a maternity hospital
• Need medicine
• Moral and ethical issue
  – Will we deny treatment?
  – Not right to withhold veterinary care
  – How long can you wait to treat?
Antibiotics are needed

• Only 12% is used for growth promotion
  – This will decline further
• Treatment of a group requires water or feed medication
• Organic farms treat and remove →, financial penalty. How long to wait?

Group prevention needed in human & animal medicine

• Infectious individual not evident until has spread
• Can move quickly through a population
• Animals cannot “stay home” when they get sick
• Prevention prevents spread and much illness

Why take additional risk??
3. Animals with residual effects of illness are more likely to cause human foodborne illness

- Meat Inspection Act 1906
- Antemortem inspection

Largest meat recall in U.S. history due to slaughter of downer cows, February 2008

Adhesions increase chance of fecal contamination!!

Impact of pig health on foodborne Risk (Salmonella & Campylobacter)

- Healthy: Passed FSIS antemortem inspection (not visibly ill)
- Some (~7%) had internal adhesions from previous infection
- Compared to carcasses without lesions
- Two published studies
Carcass with residual illness effects present higher foodborne risk

- Pig with “peelout” is 90% more likely to be contaminated with Salmonella before entering the cooler
- Normal carcass immediately after evisceration

4. Manage the Hazard

- On-farm Quality Assurance Programs
- Veterinary oversight
- HACCP in abattoir
- Handling and cooking
- Medical practice

What farmers & veterinarians are doing?

- Assc of Swine Vets – “Purpose Driven Practice”
- Take Care – Pork Producers
- Voluntary discontinuation of “growth promotion” uses – FDA 209
- Improving oversight - AVMA
Antibiotic resistance risk due to on-farm antibiotic use

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4. Action – We are managing the hazard

Veterinarians and Antimicrobial Use

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Pew Health Professions Commission in Health America: Practitioners for 2005

“Veterinarians are more knowledgeable about the impact of animals and diseases on human health and the role and use of animals in the improvement of health and well-being than any other health professional in most communities. Thus veterinarians should be more directly available to human health providers for consultation on these subjects.”

Role of the Veterinarian

- AVMA Role of the Veterinarian Policy: Veterinarians should be involved in the decision-making process for the use of antimicrobials in animals regardless of the distribution channels through which the antimicrobials were obtained.
- Additionally, the FDA references the veterinarian's role in their Guidance for Industry #209 - The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals in defining greater veterinary oversight.
  - *Veterinary involvement* in the decision-making process associated with the use of medically important antimicrobial drugs is an important aspect of assuring appropriate use, including judicious prevention use.
- AVMA Judicious Use Policy: “When the decision is reached to use antimicrobials for therapy, veterinarians should strive to optimize therapeutic efficacy and minimize resistance to antimicrobials to protect public and animal health.” ... “Judicious use of antimicrobials, when under the direction of a veterinarian, should meet all requirements of a veterinarian-client-patient relationship.”

VCPR = oversight

The veterinarian-client-patient relationship (or VCPR) is the basis for interaction among veterinarians, their clients, and their patients.
- the veterinarian is personally acquainted with the keeping and care of the patient
- The veterinarian provides oversight of treatment, compliance and outcome
- Patient records are maintained
Model Veterinary Practice Act

The AVMA Model Veterinary Practice Act is to serve as a set of guiding principles for state regulation of the practice of veterinary medicine.

- The commentary to the model act explains that states may wish to further specify that when establishing a VCPR in the case of large operations, “sufficient knowledge” of the patient can be supplemented by means of:
  1. examination of health, laboratory, or production records;
  2. consultation with owners, caretakers, or supervisory staff regarding a health management program for the patient; or
  3. information regarding the local epidemiology of diseases for the appropriate species.

Principles of Veterinary Medical Ethics

- Regardless of practice ownership, the interests of the patient, client, and public require that all decisions that affect diagnosis, care, and treatment of patients are made by veterinarians.
- The responsibilities of the veterinary profession extend to society in general. Veterinarians are encouraged to provide their services for activities that protect public health.
- Dispensing or prescribing a prescription product requires a VCPR. Without a VCPR, veterinarians merchandising or using any pharmaceutical is unethical.
- Veterinarians are responsible for choosing the treatment regimens for their patients.
- It is against our ethics to:
  - be influenced by considerations other than the needs of the patient, the welfare of the client, and the safety of the public.
  - allow medical judgment to be influenced by agreements by which they stand to profit through ...products.

How Vets work with Producers

Within the Veterinarian-Client-Patient-Relationship (VCPR) - the producer is the “client” component of that relationship,
- assist producers in complying with their industry’s quality assurance programs (that also contain the concepts below)
- work closely with producers to ensure the health and welfare of their animals
- AVMA Judicious Use Policy: “Veterinarians should work with those responsible for the care of animals to use antimicrobials judiciously regardless of the distribution system through which the antimicrobial was obtained.”
AVMA Efforts
Veterinary Foresight and Expertise in Antimicrobial Discussions

**AVMA Policy:** AVMA recognizes that veterinarians need to be involved in discussions relative to judicious use of antimicrobials and food supply veterinary medicine... to ensure that risks and benefits to both humans and animals are given due consideration.

AVMA Efforts
Numerous issue specific Task Forces and Steering Committees as well as standing Councils and Committees to provide guidance on these issues.

- **2009-2010 AVMA’s Antimicrobial Use Task Force**
- **2010-present AVMA Steering Committee for FDA Policy on Veterinary Oversight of Antimicrobials.**

Streamlining the VFD

The AVMA’s Steering Committee for Veterinary Oversight:

- engaged with the FDA as it proposed changes to the Veterinary Feed Directive (VFD) to make it more workable and to gain greater veterinary oversight. Much of the feedback provided by the Steering Committee was incorporated into the FDA’s VFD Draft Text for Proposed Regulation published in July 2012
- The Veterinary Feed Directive (VFD) is the primary vehicle for greater veterinary oversight of antimicrobials in feed
- continues to collaborate with the FDA to provide guidance from the veterinary perspective and clarify veterinarians’ role in the oversight of antimicrobial use in animals as regulatory changes are made to address antimicrobial resistance.
Listening Sessions on VFD

- The FDA has organized, in conjunction with USDA, 5 listening sessions to be held throughout the country to hear input on the proposed changes to the Veterinary Feed Directive as the VFD is the primary vehicle for increasing veterinary oversight of antimicrobials in feed.
- AVMA has been invited and will be participating in these sessions given the importance and role of the veterinary workforce in implementing changes.
- Information gleaned from these listening sessions will be provided to AVMA decision makers (in addition to FDA and USDA) to enhance understanding of the concerns associated with the newly proposed VFD process as we all continue working to enhance veterinary oversight.

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