ANTIBIOTICS IN AQUACULTURE: A (FISH) VETERINARIAN’S PERSPECTIVE

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Healthful move to cut antibiotics in livestock

On Nutrition

Corrie Pennartz, Special to The Seattle Times

In late summer, the Food and Drug Administration (FDA) issued guidelines designed to reduce the use of antibiotics in livestock animals, one small part of a ramp-up effort to fight the growing threat of "superbugs," bacteria that no longer respond to treatment with common antibiotics. It's a potentially promising move for both farmers and consumers alike.

The FDA plan, which goes into effect in December 2013, will prevent veterinarians from using medically important antibiotics in food animals. Instead, the plan’s creators hope to promote a more natural cure for infections that can be treated with some antibiotics, not all of which are used in livestock.

"This is a step toward making us freer of the "superbugs" that are a growing threat to human health," said Dr. David S. Nelson, director of the CDC’s Office of Antimicrobial Resistance.

A Food and Drug Administration (FDA) official said the move would prevent antibiotics from being used in livestock animals in a manner that could lead to bacterial resistance.

"Antibiotics are a critical tool in the treatment and prevention of infections in both animals and humans," the official said. "We need to use them wisely and responsibly."
MISSION STATEMENT OF A FOODFISH VET PRACTICE:

“To assist our clients in obtaining the people, knowledge, skills, and products required to safely and consistently produce wholesome, palatable fish by the most cost-efficient methods that are available, humane, and in compliance with the regulatory agencies.”

SIMILAR TO WHAT GAA-BMP IS ENDEAVORING TO DO.
PURPOSE OF TALK

• WHAT IS BEHIND THE ANTIBIOTIC PHOBIA IN FOOD ANIMALS AND IS IT VALID?
• WHAT EXACTLY ARE ANTIBIOTICS AGAIN?
• WHAT IS BEING DONE TO MONITOR THEIR USE AND EFFECT?
• HOW CAN BEST MANAGEMENT PRACTICES HELP?
3 areas of concern regarding animals:

1. Total amount used (relative to other uses)
2. Preventative use (instead of therapeutic)
3. Use for growth promotion
• Fear seems to stem from *antibiotic resistance cases in human medicine* and how animal use might contribute to this.

• Sentiment seems to be very *sensational and reactionary* with a *simplistic understanding* of antibiotics and their use (ulterior motives?).
Estimated annual antibiotic use in US in animals is:

“TOO MUCH”

But: 45% are ionophores with no use in human medicine and 42% are tetracycline – only used 1%
In human medicine, so:

87% are never or rarely used in human medicine.

This distinction is important, because ionophores have no use in human medicine and do not have any link or possible effect on antimicrobial resistance to therapeutic antibiotics in either people or food animals.

ANTIBIOTICS, ALSO KNOWN AS ANTIMICROBIAL DRUGS, ARE DRUGS THAT FIGHT INFECTIONS CAUSED BY BACTERIA.

FIRST ANTIBIOTIC, PENICILLIN, IN 1928 BY ALEXANDER FLEMING

TRANSFORMED MEDICAL CARE AND DRAMATICALLY REDUCED ILLNESS AND DEATH FROM INFECTIOUS DISEASES.

ORIGINALLY REFERRED TO A NATURAL COMPOUND PRODUCED BY A FUNGUS OR ANOTHER MICROORGANISM KILLS BACTERIA. NOW, "ANTIBIOTICS" MAY BE SYNTHETIC COMPOUNDS.
Natural antibiotics are everywhere (SOIL, AIR and WATER) for microbial competition.

- **CLASSIFIED ACCORDING TO:**
  - THE WAY THEY ACT (BACTERICIDAL OR BACTERIOSTATIC),
  - THEIR CHEMICAL STRUCTURE,
  - THEIR MOLECULAR MECHANISMS OF ACTION,
  - WHETHER THEY ACT ON MANY BACTERIAL SPECIES (BROAD SPECTRUM) OR JUST A FEW (NARROW SPECTRUM).
TO BE CLEAR ON ANTIBIOTICS:

• DESIGNED TO **ACT ON BACTERIA, NOT HUMAN** OR ANIMAL CELLS.
• **NOT PERSISTENT** IN THE BODY OR THE ENVIRONMENT.
• **BACTERIAL RESISTANCE** IS NOT PERMANENT.
• A RESISTANT BACTERIA **DOES NOT MEAN** A MORE VIRULENT ONE.

• **EVERY ANTIBIOTIC HAS BACTERIA THAT IS RESISTANT** (RIGHT FROM THE START).
TO BE CLEAR ON USING ANTIBIOTICS (2):

• ALL HAVE A SPECIFIC WITHDRAWAL TIME TO ENSURE NONE IN MEAT.
• RESISTANCE CAN HAPPEN WITHOUT MISUSE (OR USE!).
• EARLY (PROPHYLACTIC USE?) MAY ACTUALLY BE MORE EFFICIENT AND LEAD TO LESS RESISTANCE.
• GROWTH PROMOTING ANTIBIOTICS ARE NOT INTENDED FOR THERAPY AND IT IS A MEDICAL APPROACH TO ALTER THE GUT FLORA TO ALLOW FOR MORE EFFICIENT NUTRIENT ABSORPTION AND ASSIMILATION - WHICH MAY MEAN LESS OF A “CARBON FOOTPRINT”.
FDA PACKAGE REQUIRED FOR FOOD ANTIBIOTIC APPROVAL

- EFFICACY TECHNICAL SECTION
- TARGET ANIMAL SAFETY TECHNICAL SECTION
- HUMAN FOOD SAFETY TECHNICAL SECTION – TOXICOLOGY AND RESIDUES
- CHEMISTRY, MANUFACTURING AND CONTROLS TECHNICAL SECTION (GMP COMPLIANCE)
- ENVIRONMENTAL SAFETY TECHNICAL SECTION
- LABELING TECHNICAL SECTION
- FREEDOM OF INFORMATION
- ALL OTHER INFORMATION
- ANALYTICAL METHOD VALIDATIONS MAY BE PART OF EACH OR ALL OF THE ABOVE
THE FDA and Aquaculture Antibiotics

- No new aquaculture antibiotics in the US since 2004.
- No new aquaculture antibiotics foreseeable in the next decade.
- Continuous examination and response to concerns regarding antibiotic resistance.

- E.g.: FDA implemented “Guidance for Industry GFI#152” in 2003
  - Assigns a high ranking for intended administration to flocks or herds of animals, it is virtually impossible for FDA to approve antibiotics for use in feed or water if those same antibiotics are also used in humans.
  - A “no risk policy”: antibiotics with a reasonable certainty of no harm to human health are rejected.

This is actually troubling because antibiotics approved decades ago may be the only ones available in flocks, herds, and schools to combat infectious diseases and safeguard the food supply.
There ARE **multiple monitoring and surveillance systems in place in the US** that recognize impactful events and trigger further investigation to determine the level of associated risks:

1. FDA Adverse Event reporting system – treatment failure
2. National Antimicrobial Resistance Monitoring System (NARMS)
   - Monitors resistance in:
     - A) foodborne human enteric pathogens
     - B) resistance in animals (overrepresentation of samples)
3. Post-harvest HACCP based pathogen reduction programs
4. Many specific antimicrobial risk assessments have been performed.

**The question of what the nature and magnitude of the risk to humans can only be answered by performing systematic risk assessments.**
Risk assessments actions:

1. Allow continued availability of product with no changes
2. Withdraw drug
3. Review by Veterinary Medicine Committee
4. Limitations of use / under only certain conditions
Risk assessments actions EXAMPLES:

1. 1998 Fluroquinolone resistant Campylobacter in poultry
   - Outcome: withdrawal  Result: human cases continue to rise

2. 2004 - Virginiamycin as a growth promoter in food animals contributes to resistant strains of E. fecium in humans
   - Outcome: found inconsistent resistant genes; 14 in 100 million risk IF it were to occur
   - Result: None  (banned in Denmark since 1998, but resistance still greater than in U.S.)

- One risk assessment actually concluded that withdrawal of macrolide and fluroquinolone use would cause more illness days than it would prevent.
Efforts on the Part of the American Veterinary Medical Association

National Antimicrobial Resistance Monitoring System (NARMS)

The AVMA recognizes the importance of NARMS as a valuable resource for information on resistance monitoring of bacterial isolates from animal, food products, and humans. Therefore, the AVMA recommends that the USDA, FDA, and CDC budget for adequate and equitable funding of the resistance monitoring systems and for the timely reporting of results in order to be able to provide a current and relevant antimicrobial resistance information for best practice.

National Antimicrobial Resistance Monitoring System (NARMS)

The AVMA Antimicrobial Use Task Force

AVMA Task Force for Antimicrobial Use Data Collection in Animal Agriculture

Approval and Availability of Antimicrobials for Use in Food-Producing Animals

The AVMA recognizes that it is essential to support the efforts of the U.S. Food and Drug Administration’s (FDA) Center for Veterinary Medicine (CVM) to ensure that adequate information is available to health care providers regarding appropriate antimicrobial use in animals. The AVMA supports the National Antimicrobial Resistance Monitoring System (NARMS). The AVMA Antimicrobial Use Task Force is working to ensure that recommendations for the use of antimicrobials in food-producing animals are evidence-based and supported by the latest data from NARMS.

AVMA Strategy Regarding Antimicrobial-Resistant Bacteria

Extralabel Use of Cephalosporins in Food-Producing Animals

Testimony of

The National Advisory Committee on Immunization Practices (NACI) is committed to providing recommendations that are evidence-based and support the best available data. The NACI recognizes the importance of monitoring antimicrobial resistance and provides recommendations to healthcare providers and public health officials to ensure that appropriate antimicrobial use is maintained.

AVMA Antimicrobial Use Task Force

AVMA says Pew Commission report is flawed

The AVMA Task Force for Antimicrobial Use Data Collection in Animal Agriculture

The Role of the Veterinarian in Animal Antimicrobial Use

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.
DISEASE DAM

- Good fish strains & genetic improvement
- Vaccination
- Minimization of risk factors
- Reduction in infectious pressure
- Vigilant surveillance & early treatment
ONLY THREE IN U.S. AQUACULTURE!
(one more in Canada)

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<thead>
<tr>
<th>Species</th>
<th>Indication</th>
<th>Dosing</th>
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<tbody>
<tr>
<td>Pacific salmon</td>
<td>Control of ulcer disease (Aeromonas salmonicida)</td>
<td>250 mg/kg per fish per day</td>
</tr>
<tr>
<td>Salmonoids</td>
<td>Control of ulcer disease (Aeromonas salmonicida)</td>
<td>25.0 mg/kg per fish per day</td>
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<tr>
<td>Freshwater-reared Onchocerca mykiss</td>
<td>Control of mortality due to cold-water disease caused by Flavobacterium psychrophilum</td>
<td>3.75 mg/kg per 100 fish per day</td>
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<tr>
<td>Catfish</td>
<td>Control of mortality due to columnaris disease (F. columnaris)</td>
<td>3.75 mg/kg per 100 fish per day</td>
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<tr>
<td>Freshwater-reared salmonids</td>
<td>Control of bacterial hemorraghic septicaemia (A. salmonicida) and pseudomonas disease (Pseudomonas spp.)</td>
<td>2.5 - 3.75 mg/kg per 100 fish per day</td>
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**Sulfadimethoxine & Ormetoprim**

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<tr>
<td>Salmonids</td>
<td>Control of furunculosis due to Aeromonas salmonicida</td>
<td>50 mg/kg per fish per day</td>
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<tr>
<td>Catfish</td>
<td>Control of enteric septicaemia due to Edwardsiella tarda</td>
<td>50 mg/kg per fish per day</td>
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**TERRAMYCIN®**

First approved in 1970's

![Chemical Structure of TERRAMYCIN®](image)

**FLORFENICOL**

First approved in 2004

![Chemical Structure of FLORFENICOL](image)

**ROMET® 30 and ROMET® TC**

First approved in 1984

![Chemical Structure of ROMET® 30 and ROMET® TC](image)
Veterinarians treating food fish with antimicrobial drugs have four primary responsibilities:

- To optimize stock production for those who own and care for food fish through effective disease prevention;
- To diagnose and then treat or control disease in their patients through the safe and effective use of therapeutants;
- To ensure that fish harvested for food meet established safety standards; and,
- To ensure that antimicrobial drug administration does not adversely impact the environment receiving production facility effluent
Judicious Therapeutic Use of Antimicrobials

Position Statement
When the decision is reached to use antimicrobials for treatment, control, or prevention of disease, veterinarians should strive to optimize therapeutic efficacy and minimize resistance to antimicrobials to protect public and animal health and well-being.

Objectives
- Support development of a scientific knowledge base that provides the basis for judicious therapeutic antimicrobial use.
- Support educational efforts that promote science-based judicious antimicrobial use.
- Maintain efficacy of antimicrobials by minimizing potential for development and transmission of resistance.
- Foster an atmosphere within industry research and development programs and government regulatory bodies that facilitate current and future availability of veterinary antimicrobials.
1. Emphasize disease prevention strategies, such as appropriate husbandry and hygiene, routine health monitoring and immunization.

2. Obtain accurate disease diagnosis prior to initiating disease treatment.

3. Ensure bacteria causing the aquatic animal disease are sensitive to the antimicrobial considered for use.

4. If medicated feed is used, ensure aquatic animals are feeding before treatment is applied.

5. Limit therapeutic exposure according to label instructions.

6. Observe all required withdrawal times.


8. Use good waste management practices.
IN CONCLUSION, THERE IS A DILEMMA:

SHOULD BMP PROGRAMS INCORPORATE ANTIBIOTIC USE?

• BMP’S ARE MAKING AQUACULTURE PRODUCE MORE ACCEPTABLE – GOOD!
• THERE IS A SIMPLISTIC AND IRRATIONAL FEAR OF ANTIBIOTIC USE IN FOOD ANIMALS BY THE CONSUMER – BAD!
• SUPPLIERS CAN PANDER TO THIS FEAR TO SELL PRODUCT (EG: PEPSI & ASPARTAME; CHINESE RESTAURANTS AND MSG; GLUTEN-FREE, ETC.) – BAD!
• BY DOING THE ABOVE, THE INDUSTRY WILL BE HURT IN THE LONG RUN AND POTENTIALLY PUBLIC HEALTH – BAD!
• AT THE VERY LEAST ADOPT AND PROMOTE JUDICIOUS USE PRACTICES – GOOD!
• BUT HOW DO WE EDUCATE THE PUBLIC? WHO SHOULD DO IT? AND IS THIS A POINTLESS TASK?

THE GOOD IS IN THE DETAILS BUT WHO CARES ABOUT DETAILS?
THANK YOU. QUESTIONS/COMMENTS?