

# Legal and Judicious Use of Drugs and Therapeutants in Aquaculture

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**Coldwater Fish Culture Course**  
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*Drug and Therapeutant Use in Aquaculture*



# "Mechanisms" currently available for legal use of drugs in aquaculture

- FDA-approved drugs (full and conditional approvals)
- Low Regulatory Priority drugs
- Drugs with *Deferred Regulatory Status*
- Extra-label drug use policy
- Compassionate INAD exemptions
- Federally-listed T&E fish species – letter of non-enforcement



# Judicious

- ❖ **Definition**: Having or exhibiting good judgment or sound thinking
  - ❖ **Synonyms**: wise, sensible, prudent
- ❖ **AVMA Judicious Antimicrobial Use Principles**
  - **Accept responsibility for helping client design management, immunization, production unit, and nutritional programs to reduce the incidence of disease and the need for antimicrobial treatment**



# Judicious Use of Therapeutants

- ❖ Treat as a last resort
- ❖ Match “diagnosis” with situation; or utilize historical data for a given facility/fish species/time of year
- ❖ Establish a valid veterinarian-client-patient and fish health specialist relationship
- ❖ Select appropriate therapeutant to control mortality
- ❖ Deliver appropriate treatment by following all use guidelines (i.e., dose + duration + frequency) **conduct a small bioassay trial if you're unsure**



# Judicious Use of Therapeutants

- ❖ **Fate of treated fish** (possible human consumption, not harvestable, aquarium fish, etc.)
- ❖ **Food fish - adherence to withdrawal period before release or slaughter**
- ❖ **“More is not necessarily better”**
- ❖ **Adherence to discharge requirements (NPDES – Federal and state agencies)**
- ❖ **Familiar with EPA Hatchery Effluent Guidelines**



# Approved Drugs (full drug approval)



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# How does a drug get FDA approval?

## ❖ It takes:

- **An active sponsor** (traditional sponsor – Pharmaceutical/drug company; non-traditional sponsor – chemical company)
- **Time and a lot of resources**
  - Coordinators
  - Researchers
  - \$\$

## ❖ Completion of Major Technical Sections

- **Human Food Safety**
- **Environmental Safety**
- **Efficacy**
- **Target Animal Safety**
- **Product Chemistry**



# Aquaculture Drug Approvals



- “Pie-in-the-Sky” Goal

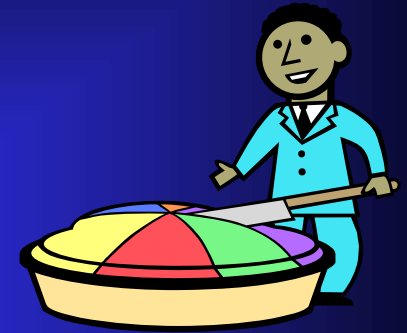
- To get as many drugs approved for use in aquaculture as possible...as quickly as possible:

- Approvals for **all finfish**
- Approvals for **all disease claims**



# Aquaculture Drug Approvals

- A more realistic Goal



- To get as many drugs approved for use in aquaculture as possible...as quickly as possible:

- Approvals for **specific species** or “groups” of species (i.e., coolwater finfish)
- Approvals for **specific disease claims**



# Approved drugs

## ❖ Romet 30<sup>®</sup> and TC<sup>®</sup>

- Catfish – enteric septicemia
- Salmonids – furunculosis

## ❖ Terramycin<sup>®</sup> 200 for Fish

- Catfish – HS, and pseudomonas disease
- Salmonids – ulcer disease, furunculosis, HS, and pseudomonas disease

## ❖ Aquaflor<sup>®</sup> - VFD Drug

- Catfish – ESC
- FW salmonids – CWD
- FW salmonids - furunculosis

## ❖ MS-222

(four families of fish)

## ❖ 35% PEROX-AID<sup>®</sup>

- Fungicide – All FW eggs
- BGD – FW salmonids
- Ex. Col. – coolwater fish/CCF

## ❖ Formalin

- Parasiticide – all FW fish
- Fungicide – all FW eggs

## ❖ Oxytet (skeletal marking)

- ❖ Immersion - (all finfish fry and fingerling)
- ❖ Feed – Pacific salmon

## ❖ Chorulon<sup>®</sup> (HCG)

(all fish)



# Approved Drugs - Summary

- There is a shortage of approved drugs  
.....particularly if you are feeling poorly and you are not a salmonid or a catfish!!
- But . . . the list is growing!



# Conditional Drug Approval

(under MUMS legislation)

- Provides for animal marketing after all **safety and manufacturing** components have been met.
- Only component missing is **effectiveness**.
- Sponsor has **5 yrs** to complete effectiveness component (for each claim) to achieve full drug approval



# Aquaflor<sup>®</sup>-CA1

- **News Flash – April 18, 2007!!!** Sponsor (SPAH) gained a conditional approval -- **the first of its kind for any food-animal therapeutic** -- for use of Aquaflor<sup>®</sup>- CA1 to control mortality in **catfish caused by Columnaris**.
- Sponsor may seek conditional approval for:
  - **Salmonids - Enteric Redmouth, etc.**
- Conditional approvals - VFD drug
- CVM requires **separate product labeling** and **separate “lots”** for each claim



# Why VFD's

- To more closely **control** new therapeutic products (primarily antibiotics) and their use in food animals
  - New classification applies only to new therapeutants approved after 1999 and administered in feed
  - All products approved before 1999 – still Over-the-Counter
- Obtain VFD drugs through **normal feed distribution channels** – but orders **require a signed VFD from a licensed veterinarian.**
- Falls somewhere **between Over-the-Counter and prescription drugs...**but probably closer to a prescription.



# Control???

- VFD regulations – developed by a coalition of animal health experts.
- Help reduce antibiotic resistance and prolong effectiveness of new antimicrobials through judicious use.
- Feed mill holding a Medical Feed Mill License – need to file a notification with FDA that it will be distributing VFD drugs in feed.
- No extra-label use allowed!



# Steps to obtain and feed VFD drugs

- **Contact veterinarian** for diagnosis and treatment.
- **Veterinarian works** within veterinarian-client-patient relationship to **determine need for VFD drug**.
- **Veterinarian issues a signed VFD form** to hatchery & feed mill.
- **Hatchery uses VFD form to order** medicated feed.
- **All parties** retain copies of signed VFD order for **2 yrs**.



# Low Regulatory Priority (LRP) Drugs



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# LRP Drugs

- **Consideration for LRP status originates from a request from outside of CVM**
- **Candidate drugs are typically quite innocuous (e.g., salt, ice, onion, etc.)**
- **FDA made determination based on review of all available data**
- **16 drugs are currently on the LRP list**



# LRP drugs

- **LRP status does not mean carte blanche use of a particular compound**
  - 1. Must be used for indication listed**
  - 2. Must be used according to good management practices**
  - 3. Must be used at the prescribed level**
  - 4. Must be of appropriate grade for use in food animals**
  - 5. Use only if an adverse effect on the environment is unlikely**
- **LRP drug use is not considered to be “approved” drug use, but rather low enforcement priority....regulatory action unlikely**



# LRP Drugs

- ❖ Acetic acid
- ❖ Calcium oxide
- ❖ Garlic
- ❖ Magnesium sulfate
- ❖ Onion
- ❖ Potassium chloride
- ❖ Sodium chloride
- ❖ Calcium chloride
- ❖ Fuller's earth
- ❖ Papain
- ❖ Urea or Tannic acid
- ❖ Povidone Iodine
- ❖ Sodium Sulfite
- ❖ Ice
- ❖ Carbon dioxide gas
- ❖ Sodium bicarbonate



# LRP Drugs

- ❖ Acetic acid
- ❖ ~~Calcium oxide~~
- ❖ ~~Garlic~~
- ❖ ~~Magnesium sulfate~~
- ❖ ~~Onion~~
- ❖ ~~Potassium chloride~~
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- ❖ ~~Calcium chloride~~
- ❖ Fuller's earth
- ❖ ~~Papain~~
- ❖ Urea or Tannic acid
- ❖ Povidone Iodine
- ❖ ~~Sodium Sulfite~~
- ❖ ~~Ice~~
- ❖ Carbon dioxide gas
- ❖ ~~Sodium Bicarbonate~~



# Deferred Regulatory Status (DRS) Drugs



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# Deferred Regulatory Status

- Very little specific, written guidance available
- .....verbal translation is that FDA chooses not to regulate....period!..... at this time
- For all practical purposes.....use can be carte blanche
- Ongoing efforts to gain FDA approval of DRS drugs



# DRS Drugs

## ❖ Copper sulfate ( $\text{CuSO}_4$ )

### ➤ Proposed approved uses

- For use to control mortality cause by *Ich* on catfish reared in earthen ponds
- For use to control fungus on channel catfish eggs

## ❖ Potassium permanganate ( $\text{KMnO}_4$ )

### ➤ Proposed approved uses

- For use to control mortality caused by columnaris in freshwater finfish
  - ❖ hybrid striped bass
  - ❖ Channel catfish
  - ❖ Freshwater-reared salmonids



# Extra-Label Drug Use Policy

- AMDUCA (signed into law in Oct. 1994) outlines provisions relating to extra-label use of approved New Animal Drugs (NAD)
- Is a reflection of FDA's recognized need for veterinarians to be able to treat disease conditions for which there may not be an effective, approved drug
- Applies to the extra-label use of any approved NAD or human drug by a veterinarian within the context of the veterinarian-client-patient relationship in a manner not in accordance with label directions.
- **Animal Medicinal Drug User Clarification Act of 1994**



# Extra-Label Drug Use Policy

➤ Extra-label drug use is limited by the following very specific restrictions:

1. Applies only to NAD's approved for use in other species
2. Available only thru practicing veterinarians, and mandates a valid veterinarian-client-patient relationship
3. No effective approved drug is available for use in target animal
4. Permits the use of approved over-the-counter drugs mixed in feeds  
(veterinarian order to treat a different fish species than that described on the label or for a different disease condition)
5. Not permitted for VFD drugs!
6. Does not permit the use of drugs to prevent disease, or for enhanced production (e.g., growth promotion, induced spawning)



# Investigational New Animal Drugs



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# Good ol' INADs

## "The Upside"

- Provide access to a variety of drugs...and drug uses....that are not yet approved by FDA (and that we would otherwise not have at our disposal)
- Contributes valuable efficacy and safety data that can be used to support broadening new approvals
- Treatment objectives written to be as inclusive as possible (e.g., “.....to control mortality caused by susceptible pathogens in freshwater fish”)
- .....we have been able to assemble quite a few!!



# Good ol' INADs

## "The Downside"

- Not just “use permits” like many folks initially believed
- Paperwork (and accountability) necessary for ALL involved
- Cost to participate....in either \$\$'s and/or time
- Under constant scrutiny by FDA.....as many within the “Big FDA” would like to see them go-away



# INADs

## Antibiotics

- ❖ **Aquaflor<sup>®</sup>** (florfenicol)
- ❖ **Oxytetracycline** (feed – therapy)
- ❖ **Oxytetracycline** (injection – therapy)
- ❖ **Oxytetracycline** (immersion – therapy)
- ❖ **Erythromycin** (feed – therapy)

## Marking agents

- ❖ **SE-MARK<sup>®</sup>** (calcein)
- ❖ **Oxytetracycline** (feed – marking)

## Gender manipulation

- ❖ **17- $\alpha$  MT**

## Anesthetics

- ❖ **AQUI-S<sup>®</sup>**

## Microbicides

- ❖ **35% PEROX-AID<sup>®</sup>** (hydrogen peroxide)
- ❖ **REWARD<sup>®</sup>** (diquat)
- ❖ **Chloramine-T**
- ❖ **SLICE<sup>®</sup>** (emamectin benzoate)
- ❖ **Formalin**
- ❖ **Copper sulfate**
- ❖ **Potassium permanganate**

## Spawning hormones

- ❖ **Common Carp Pituitary**
- ❖ **LHRHa** (injection)
- ❖ **Ovaplant<sup>®</sup>** (implant)
- ❖ **Catfish pituitary**

# Use of Unapproved Drugs on Federally-Listed T & E Species

- CVM letter dated December 4, 1995
- Includes USFWS and Collaborators
- Use of unapproved drugs in federally-listed T & E species will be considered to be of low enforcement priority
- Requires completion and submission to AADAP:
  - Drug receipt form
  - Drug use inventory form



# Federally-Listed T & E Species

regulatory action will not ordinarily  
be considered if:

- Treated species are not subject to legal harvest
- Service assumes responsibility with NEPA compliance
- Used only as conservation action necessary for protection and recovery of listed species
- CVM's enforcement discretion will apply to the USFWS and contract facilities utilized by the USFWS



# Summary of Legal Drug Use Options



- ...thankfully....the utility of the sum is greater than that of the individual parts
- ....a variety of options do exist
- .....but we certainly have a long way to go with respect to our goal of **approved drugs**



# Drugs most likely to be used illegally

- Clove oil
  - ❖ CVM Guidance Document #150
- MS-222 (used off-label)
  - ❖ Approved for 4 families of freshwater finfish
  - ❖ 21 d withdrawal period
- Drugs purchased from sources other than the sponsor
  - ❖ Over the internet or from supply catalogues
  - ❖ Lower quality (cheaper) grade



# Regardless of the “classification” of the accessible drugs, all drugs should be used judiciously

- ❖ Treat as a last resort
- ❖ Know what you’re treating for...don’t guess
- ❖ Use the appropriate drug correctly – more is not necessarily better
- ❖ Adhere to established withdrawal periods and hatchery discharge requirements
- ❖ Establish a valid veterinarian-client-patient relationship to gain access to VFD drugs



# Questions??



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