

# Legal and Judicious Use of Drugs and Therapeutants in Aquaculture

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*Drug and Therapeutant Use in Aquaculture*



# Once upon a time...and not all that long ago.....

- Fisheries manager's access to drugs and chemicals was limited only by their active and inventive imaginations
- If you could get your hands on it, you could use it!!
- Home and Ranch, Chemical Supply Companies, local discount stores, hardware stores, etc. were all “fair game” in the quest for needed drugs and chemicals



However, in the early 1990's a decree went out that changed everything.....and feast became famine

- FDA...who had very conveniently been looking the other way....decided the time had come for aquaculture to be regulated
- FDA's decision left aquaculture with only 3 therapeutants and a single anesthetic that were “approved” for use...and use of these drugs was severely restricted by species, life stage, specific pathogen, and use-pattern



# “Mechanisms” currently available for legal use of drugs in aquaculture

- FDA-approved drugs
- Low Regulatory Priority Compounds
- Compounds with *Deferred Regulatory Status*
- Extra-label drug use policy
- Compassionate INAD exemptions
- For use on specific Federally-listed T & E species



# 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 and/or 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
- ❖ Food fish - adherence to withdrawal time 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



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# Approved drugs

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

(in feed; limited use)

❖ **Terramycin<sup>®</sup> for Fish**

(in feed; limited use)

❖ **Aquaflor<sup>®</sup>**

(in feed; limited use)

❖ **OTC (immersion marking)**

(all fish)

❖ **MS – 222**

(all fish)

❖ **Chorulon<sup>®</sup> (HCG)**

(all fish)

❖ **Formalin**

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



# Approved Drugs

## Romet TC (in feed)

- Control of enteric septicemia in catfish
- Control of furunculosis in salmonids
- ✓ Palatability issues associated with Romet-B have been resolved



# Approved Drugs

## Terramycin (OTC) for Fish (in feed)

- Control of bacterial hemorrhagic septicemia and pseudomonas disease in catfish
- Control of ulcer disease, furunculosis, bacterial hemorrhagic septicemia, and pseudomonas disease in salmonids ( $\geq 9^{\circ}\text{C}$ )
- Marking of skeletal tissue in Pacific salmonids



# Approved Drugs

## Aquaflor (in feed)

- To control mortality in catfish due to enteric septicemia (ESC) – **Approved Nov, 2005**



# Approved Drugs

## Oxytetracycline (immersion marking agent)

- Skeletal marking of all finfish
- 3 products available
  - OTC HCL Soluble Powder - Phoenix Scientific, Inc
  - OxyMarine - Pharmaq, Inc.
  - Terramycin 343 - Pfizer, Inc.



# Approved Drugs

## Tricaine methanesulfonate (MS-222)

- Temporary immobilization (i.e., anesthetic)
- All finfish
- 21-day withdrawal period before fish can be released, stocked, or harvested



# Approved Drugs

## Chorulon

### (Human Chorionic Gonadotropin -HCG)

- Spawning aid in broodfish (i.e., induced gamete maturation)
- All finfish



# Approved Drugs

## Formalin

- **Control of external parasites - all finfish**  
*Approved November, 2002*
- **Control of fungi - eggs of all finfish**





# Approved Drugs

## Sulfamerazine for Fish (in feed)

- Control of furunculosis in rainbow trout, brook trout, and brown trout
- ✓ *Unfortunately Not Available.....oh well!!*



# Approved Drugs - Summary

- .....obviously, there is an extreme shortage of approved drugs.....particularly if you are feeling poorly and you are not a salmonid or a catfish!!



# Low Regulatory Priority (LRP) Drugs



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# LRP Compounds

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



# LRP Compounds

- **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. 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
- ❖ Hydrogen Peroxide
- ❖ 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



# 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
- Copper sulfate and potassium permanganate only 2 such compounds
- For all practical purposes.....this is “carte blanche”





# DRS Drugs

- ❖ Copper sulfate ( $\text{CuSO}_4$ )
- ❖ Potassium permanganate ( $\text{KMnO}_4$ )



# Extra-label Drug Use Policy

- AMDUCA (signed into law in Oct. 1994) outlines provisions relating to extra-label use of approved New Animal Drug (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 vet within the context of the vet-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. 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 Downside"

- Not just “use permits” like many folks initially believed
- .....a bit....ok, maybe more than a bit...of 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



# Good ol' INADs

## "The Upside"

- Contribute 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 bacterial pathogens in freshwater fish”)
- .....we have been able to assemble quite a few!!
- INADs are providing access to a variety of drugs...and drug uses....that we would otherwise not have at our disposal



# INADs

- ❖ **Aquaflor<sup>®</sup>**
  - ❖ **OTC** (feed – therapy)
  - ❖ **OTC** (injection – therapy)
  - ❖ **OTC** (immersion – therapy)
  - ❖ **Erythromycin** (feed – therapy)
  
  - ❖ **SE-MARK<sup>®</sup>** (Calcein)
  - ❖ **OTC** (feed – marking)
  
  - ❖ **17 alpha-MT**
  
  - ❖ **Slice**
- ❖ **Formalin**
  - ❖ **Hydrogen peroxide**
  - ❖ **Chloramine-T**
  - ❖ **Diquat**
  - ❖ **Copper Sulfate**
  - ❖ **KMnO<sub>4</sub>**
  
  - ❖ **CCP**
  - ❖ **LHRHa** (injectable)
  - ❖ **sGnRH** (implant)
  
  - ❖ **AQUI-S**



# Total Number of Drugs Available

7 approved drugs

17 LPR drugs

2 DRS drugs

17 INADs (+ H<sub>2</sub>O<sub>2</sub>)

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Total = 38 drugs





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

- CVM letter dated Dec. 4, 1995
- Includes FWS and Collaborators
- Use of unapproved drugs in 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



# 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 Service and contract facilities utilized by the Service



# 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**



# Summary

## ...or “what’s this all mean??”

- ❖ Yeah, you’re right, “we” don’t have many approved aquatic animal drugs to chose from...
- ❖ However, access to INADs, LRP drugs, and DRS drugs enhances our medicine chest...
- ❖ Provide us more options to treat fish than we might have previously thought.



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



# Questions??



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