



# Data to Support FDA approval of: **AQUI-S<sup>®</sup>20E and BENZOAK<sup>®</sup>**

## Potential Immediate-Release Sedatives



Molly P. Bowman, Jim Bowker, Niccole Wandelaar, and Dan Carty

U.S. Fish & Wildlife Service – AADAP Program  
Bozeman, Montana



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# What is an Ideal Sedative?

- Induction time of <15 min (preferably <3 min)
- Short recovery time (< 5 min)
- Nontoxic to fish, large safety factor
- Inexpensive
- Easy to use
- Safe to humans during normal use
- No withdrawal time
  - Immediate release



# Immediate Release Sedatives?

- **AQUI-S®20E**

- AQUI-S New Zealand, Ltd.
- 10% eugenol
- 3 d withdrawal period
- Only available under INAD 11-741
- \$299 for 1 L (approximation)



- **BENZOAK®**

- Frontier Scientific, Inc.
- 20% benzocaine
- 3 d withdrawal period
- Only available under INAD 11-740
- \$385 for 1 L (approximation)

# Easy to Use?

- Yes!
- Both can be pipetted directly into a tub of water
  - Then stir to mix



# Efficacy Studies



- **Small mountain of data required**
  - To demonstrate efficacy
  - To support FDA approval
- **AADAP and partners have completed**
  - 20 pivotal studies
  - 14 high quality supportive studies
- **All pivotal studies**
  - Conducted to under FDA/CVM approved research study protocols



# Experimental Design - Pivotal Studies

- Masking
- Positive control
  - MS-222
- Dose-verification of exposure solutions
  - $\pm 20\%$  of target dose
- For each species of fish:
  - 30 individual fish tested
- Data collected:
  - Time to handleable
  - Time to recover from the handleable stage
  - Behavior during and after sedation
  - Temperature, dissolved oxygen, and pH



# High Quality Supportive Studies

- Approved protocol used as a guideline
  - However, one or more of the criteria in the study protocol are not followed:
    - Fewer fish used
    - No dose-verification
    - No positive control
    - No masking



# Experimental Design - Pivotal Studies

- CVM wants efficacy of a product to be evaluated at the low end of the use range
  - Only one concentration tested for each of the temperature groups of fish
    - Selected a concentration that would sedate fish to handleable in <3 min



# What is Handleable?

- Similar to Stages 3 – 4 as described by Summerfelt and Smith (1990)
- Specifically:
  - Lose of equilibrium
  - Fish can be easily
    - Caught by hand,
    - Placed on a measuring board
    - Measured for length
    - Little to no movement



# What is Recovered?

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- Fish regains normal equilibrium in the water column
- Fish resumes normal swimming behavior
- Fish can avoid obstacles placed in path



# Fish Species

- **Salmonids:**
  - Rainbow trout, cutthroat trout, brown trout, lake trout, and Arctic char
- **Coolwater:**
  - Yellow perch, walleye, common carp, and fathead minnows
- **Warmwater:**
  - Blue catfish, hybrid striped bass, and channel catfish

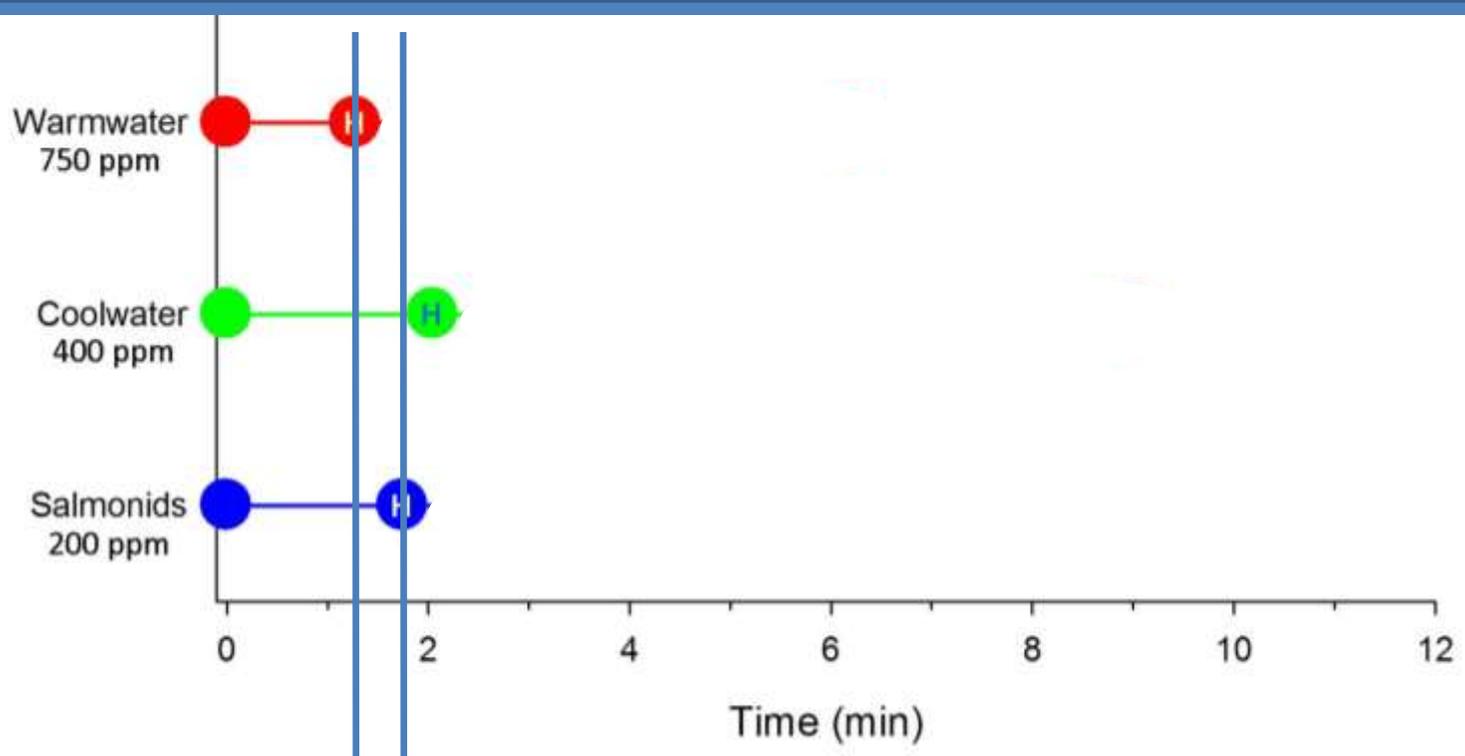


# Data Summary

Species	Product	Sedative Concentration	Water Temperature	Mean Handleable	Mean Recovery
Salmonids	AQUI-S®20E	250 ppm	13.2°C	<b>1.8 min</b> (1.3 – 2.5)	5.5 min (2.6 – 11.1)
	BENZOAK®	200 ppm	13.9°C	<b>1.8 min</b> (1.0 – 2.9)	3.8 min (0.9 – 9.2)
Coolwater	AQUI-S®20E	400 ppm	18.2°C	<b>2.5 min</b> (1.5 – 5.0)	9.9 min (4.4 – 16.8)
	BENZOAK®	400 ppm	18.0°C	<b>2.1 min</b> (1.1 – 3.3)	9.0 min (4.8 – 18.3)
Warmwater	AQUI-S®20E	600 ppm	24.3°C	<b>1.3 min</b> (0.6 – 2.4)	7.6 min (5.1 – 10.8)
	BENZOAK®	750 ppm	24.7°C	<b>1.3 min</b> (0.7 – 2.5)	6.2 min (3.7 – 9.6)

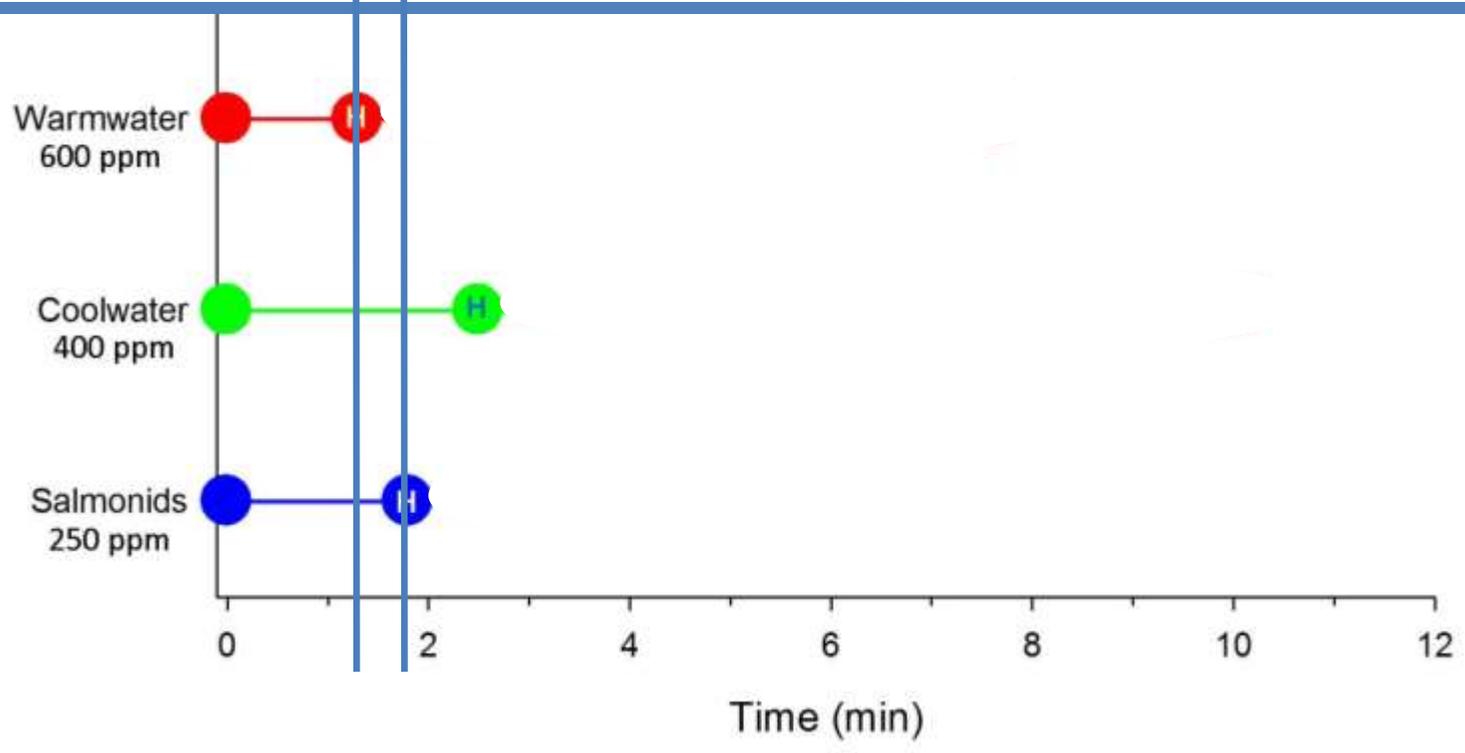
**BENZOAK<sup>®</sup>**

**20% Benzocaine**



**AQUI-S<sup>®</sup> 20E**

**10% Eugenol**

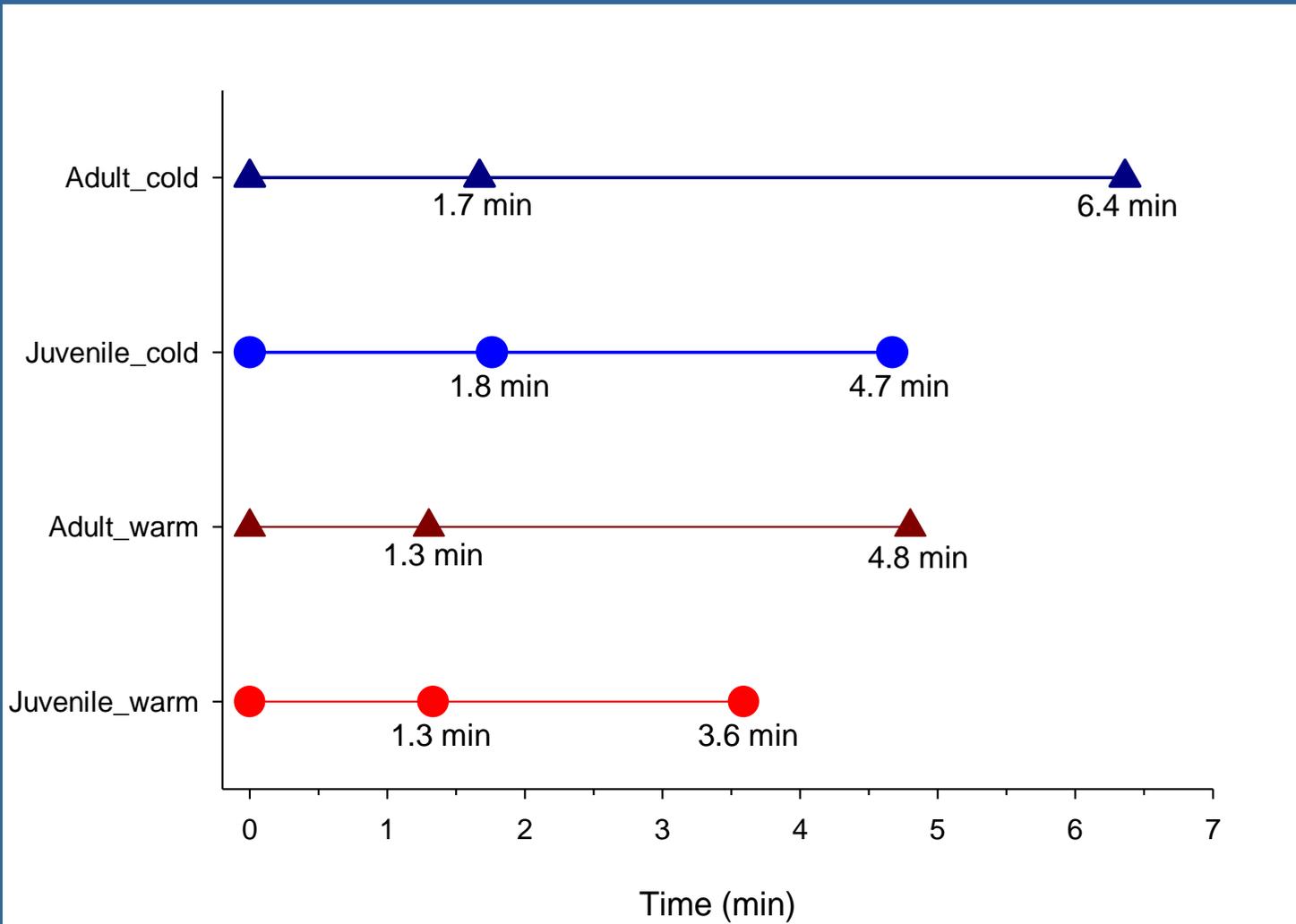


# Effect of Size and Temperature

- **High Quality Supportive Study**
  - Rainbow trout
    - 250 ppm AQUI-S®20E (25 ppm eugenol)
  - Two life-stages
    - Adult, 40 cm and 0.9 kg
    - Juvenile, 17 cm and 55 g
  - Two water temperatures
    - 10 or 16°C



# Overview of Data



# Summary

- Fish become handleable in an ‘ideal’ period of time
  - Less than 3 min
- Fish recover faster after exposure to BENZOAK<sup>®</sup> than AQUI-S<sup>®</sup>20E
  - Recovery times ‘less-than-ideal’,
  - However, a conservative measure of recovery was used
- Both products are easy to use and work well
  - Add products directly to tub of water and stir
  - Sedated a variety of species, life-stages and water temperatures
- No fish died during or after any studies
  - Normal behavior
    - Some piping
    - Some head shaking



# A Big Thanks To.....

- **Fort Richardson State Fish Hatchery**
  - Alaska Department of Fish & Game
- **Dr. Jesse Trusenski and students**
  - Southern Illinois University – Carbondale
- **Alan Johnson**
  - Iowa DNR Rathbun Fish Culture Research Facility
- **Jeff Meinertz and staff**
  - USGS Upper Midwest Environmental Sciences Center
- **Hatchery staff**
  - USFWS Bozeman Fish Technology Center



# Status

- Results from 7 studies
  - Submitted to CVM for review
- Results from the rest of the studies
  - Will be submitted this winter
- Request that the effectiveness technical section be considered complete
  - No more data necessary to demonstrate effectiveness
- Conduct studies to demonstrate that the effective doses are safe
  - Three studies required



**Questions??**

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