

AQUACULTURE DRUG APPROVAL DEVELOPMENT STATUS
[NOTE: ALL APPROVAL EFFORTS ARE ON HOLD AS RESULT OF FEBRUARY 28, 2008 NTP PEER REVIEW OF MALE MOUSE STUDY]

ISOEUGENOL (AQUI-S®): RESEARCH AND DEVELOPMENT PLAN AND LABEL CLAIM MATRICES FOR ORIGINAL AND SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION (NADA) APPROVALS

1. Isoeugenol (AQUI-S®) NADA approvals (none to date)
2. Status of technical sections that support all original and supplemental NADA approvals
3. Label Claim #1: To sedate freshwater finfish to handleable condition
4. Label Claim #2: To sedate freshwater finfish for transport
5. Label Claim #3: To sedate saltwater-reared finfish to handleable condition
6. Label Claim #4: To sedate saltwater-reared finfish for transport

DEVELOPED, IN PART, UNDER THE FEDERAL-STATE AQUACULTURE DRUG APPROVAL PARTNERSHIP PROJECT, A PROJECT OF THE ASSOCIATION OF FISH AND WILDLIFE AGENCIES

Rosalie A. Schnick
National Coordinator for Aquaculture New Animal Drug Applications
Michigan State University
3039 Edgewater Lane, La Crosse, Wisconsin 54603-1088
Phone (608) 781-2205; Fax (608) 783-3507
E-mail: RozSchnick@centurytel.net
Website: <http://aquanic.org/aquadrugs>

ISOEUGENOL (AQUI-S®)
(Version 2, March 2008)

ABBREVIATIONS, ACRONYMS, & CONTACT INFORMATION FOR ENTITIES IN TABLE

AADAP	Aquatic Animal Drug Approval Partnership Program—Dr. David Erdahl, U.S. Fish and Wildlife Service, 4050 Bridger Canyon Road, Bozeman, Montana 59715; Phone: 406-994-9904; Fax: 406-582-0242; E-mail: Dave_Erdahl@fws.gov
AOI	All Other Information Technical Section, not included in any of the other sections, that is pertinent to an evaluation of effectiveness or safety [21 CFR § 514.1(b)(8)(iv)]
AQNZ	Sponsor of AQUI-S® (isoeugenol): AQUI-S New Zealand Ltd., PO Box 44 269 Lower Hutt, Unit 5, 6 Aglionby Street, Lower Hutt, New Zealand; Don Bell; E-mail: don.bell@agui-s.com ; U.S. Representative, Dr. Thomas Goodrich, Regulatory Consultant, 15110 NE 108 th Pl, Redmond, Washington, 98052; Phone: 425-922-4208; E-mail: res0099k@gte.net ;
CVM	Aquaculture Drugs Team (HFV-131), Division of Therapeutic Drugs for Food Animals, Office of New Animal Drug Evaluations, Center for Veterinary Medicine, U.S. Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855; Dr. Donald Prater; Phone: 240-276-8343; E-mail: Donald.Prater@fda.hhs.gov
Efficacy	Effectiveness Technical Section includes pivotal & supportive studies that show whether or not a drug is effective for its intended use [21 CFR § 514.1(b)(8)(i)]
FOI	Final Freedom of Information summary generated by CVM based on draft FOIs developed by researchers for each study [21 CFR § 514.11(e)(2)(ii)]
INAD	Investigational New Animal Drug exemption [21 CFR 511]
Label	Labeling Technical Section includes labeling and package inserts [21 CFR § 514.1(b)(3)]
NADA	New Animal Drug Application [21 CFR 514]
NADA Coordinator	Rosalie (Roz) Schnick, National Coordinator for Aquaculture New Animal Drug Applications, Michigan State University, 3039 Edgewater Lane, La Crosse, Wisconsin 54603-1088; Phone: 608-781-2205; Fax: 608-783-3507; E-mail: RozSchnick@centurytel.net
NTP	National Toxicology Program, U.S. National Institute for Environmental Health Sciences
NCRAC	North Central Regional Aquaculture Center—Dr. Ted Batterson, Michigan State University, 13 Natural Resources Building, East Lansing, Michigan 48824; Phone: 517-353-1962; Fax: 517-353-7181; E-mail: batters2@msu.edu
Product Chemistry	Product Chemistry Technical Section includes chemistry, manufacturing, and controls [21 CFR § 514.1(b)(4-6)]
PMF	Public Master File can contain safety and efficacy data and information generated with public funds (Guidance Document #57)
Toxicology	Part of Human Food Safety Technical Section, toxicological testing includes genetic toxicity tests and mammalian safety studies (e.g., acute, sub chronic) (Guidance Document #3)
UMESC	Upper Midwest Environmental Sciences Center—Mark Gaikowski, 2630 Fanta Reed Road, La Crosse, Wisconsin 54603; Phone: 608-783-6451; Fax: 608-783-6066; E-mail: MGaikowski@usgs.gov

KEY TO COLOR CODING

COLOR	STATUS
	No current plans and/or funds; problems
	In progress or planned; funded
	Submitted to CVM
	Accepted by CVM

ISOEUGENOL (AQUI-S®)

Isoeugenol (AQUI-S®) NADA approvals (none to date)

ISOEUGENOL (AQUI-S®)

Status of Technical Sections that support all original and supplemental NADA approvals

Technical Section	Entity—Data—Action	Impediments or Cost—Action
Product Chemistry (all fish & shellfish)	AQNZ (INAD #9731)—Product chemistry package—in progress	On hold because of NTP peer review results
Environmental Safety, Target Animal Safety, & Efficacy (analytical method in water/all finfish & shellfish)	AQNZ (INAD #9731)—Analytical method to detect AQUI-S® in water/all finfish & shellfish—CVM response 11/5/04; AQNZ in-depth response 4/18/05; CVM requested more information	On hold because of NTP peer review results
Environmental Safety (studies/pond, flow-through, & net-pen systems)	AQNZ (INAD #9731)—Environmental Safety/studies/photodegradation, solubility, and disassociation constant studies/freshwater & saltwater—CVM accepted 11/14/05	None
Environmental Safety (pond, flow-through, & net-pen systems)	AQNZ (INAD #9731)—Environmental Safety/ecotoxicity studies—in progress	On hold because of NTP peer review results
Environmental Safety (pond, flow-through, & net-pen systems)	AQNZ (INAD #9731)—Environmental Safety/environmental assessment/pond, flow-through, & net-pen systems—planned in the future	On hold because of NTP peer review results
Human Food Safety (toxicology)	AQNZ (INAD #9731)—Human Food Safety/toxicology/isoegenol NTP studies—Teratology/rat study—accepted 6/13/05; NTP multigenerational reproduction/rat study—accepted 6/24/05	None
Human Food Safety (toxicology)	AQNZ (INAD #9731)—Human Food Safety/toxicology/Isoegenol NTP studies—90-day toxicology/rat study—completed	On hold because of NTP peer review results
Human Food Safety (toxicology)	AQNZ (INAD #9731)— Human Food Safety/toxicology/isoegenol NTP studies—2-year carcinogenicity/rat & mouse studies—NTP final report peer review—accepted results as clear carcinogen in male mouse 2/28/08	NTP peer review of results causes all efforts to cease in USA
Human Food Safety (toxicology)	AQNZ (INAD #9731)—Human Food Safety/toxicology summary—planned in the future	On hold because of NTP peer review results
Human Food Safety (residue chemistry/Atlantic salmon)	AQNZ (INAD #9731)—Human Food Safety/residue studies/radiolabeled metabolite study/Atlantic salmon (proprietary & confidential)—CVM accepted as supportive 11/2/05	None
Human Food Safety (residue chemistry/freshwater salmonids)	UMESC (PMF #5695)—Human Food Safety/analytical method development/isoegenol & its metabolites/rainbow trout tissue—completion report in progress	On hold because of NTP peer review results
Human Food Safety (residue chemistry/freshwater)	UMESC (PMF #5695)—Human Food Safety/Total residue depletion study using radiolabeled material/rainbow trout as surrogate for all	None—pending acceptance by CVM—base & NCRAC funds obtained 2/04

salmonids)	freshwater-reared salmonids— submitted 3/24/06	
Technical Section	Entity—Data—Action	Impediments or Cost—Action
Human Food Safety (residue chemistry/(freshwater salmonids)	UMESC (PMF #5695)—Human Food Safety/determinative method development & validation for marker residue/freshwater salmonids—in progress	On hold because of NTP peer review results
Human Food Safety (residue chemistry/coolwater & warmwater finfish)	UMESC (PMF #5695)—Human Food Safety/determinative method development & validation for marker residue/coolwater & warmwater finfish—in progress	On hold because of NTP peer review results
Human Food Safety (residue chemistry/freshwater salmonids)	UMESC (PMF #5695)—Human Food Safety/marker residue depletion study/rainbow trout as surrogate for all freshwater-reared salmonids—planned in the future	On hold because of NTP peer review results
Human Food Safety (residue chemistry/cool & warmwater finfish)	UMESC (PMF #5695)—Human Food Safety/marker residue depletion studies/cool & warmwater finfish—planned in the future	On hold because of NTP peer review results; Multi-State Conservation Grant funds obtained 9/15/05
Human Food Safety (residue chemistry/all finfish)	AQNZ (INAD #9731) & IAFWA—Human Food Safety/confirmatory method development for marker residue/all finfish (CVM needed 2/22/05)—planned in the future	On hold because of NTP peer review results; base funds
Target Animal Safety (Atlantic salmon)	AQNZ (INAD #9731)—Target Animal Safety/study/Atlantic salmon (proprietary & confidential)—CVM accepted as supportive 5/17/05	None
Target Animal Safety (freshwater salmonids)	AADAP (INAD #10-541)—Target animal safety/study/rainbow trout & one other freshwater-reared salmonid species—in progress	On hold because of NTP peer review results
Target Animal Safety (coolwater & warmwater finfish)	AADAP (INAD #10-541)—Target animal safety/studies/coolwater & warmwater finfish—planned in the future	On hold because of NTP peer review results; Multi-State Conservation Grant funds obtained 9/15/05
Target Animal Safety & Efficacy (Gibbs Method)	AQNZ (INAD #9731)—Target animal safety & efficacy studies validation study of dose verification method (Gibbs Method)—accepted with conditions 1/15/08	On hold because of NTP peer review results

ISOEUGENOL (AQUI-S®)

LABEL CLAIM #1

SPECIES: FRESHWATER FINFISH

INDICATIONS: [To sedate freshwater finfish to handleable condition](#)

DIRECTIONS FOR USE: Apply 5-60 ml AQUI-S® per 1000L of water [ml/m³; equivalent to parts per million (ppm)] to achieve sedation for 1-60 minutes. Depth of sedation achieved will be dependent on water temperature, exposure time and species.

Technical Section	Entity—Data—Action	Impediments or Cost—Action
Efficacy (freshwater finfish)	AADAP (INAD #10-541)—Efficacy/freshwater finfish—accepted as complete 11/28/06	None
Label	AQNZ (INAD #9731) & NADA Coordinator—Label—planned in the future	On hold because of NTP peer review results
FOI	CVM—FOI—planned in the future with input from AQNZ, UMESC & AADAP	On hold because of NTP peer review results
AOI	AQNZ (INAD #9731) & NADA Coordinator—AOI—planned in the future	On hold because of NTP peer review results
NADA Package	AQNZ (INAD #9731) & NADA Coordinator—NADA package—planned in the future	On hold because of NTP peer review results

ISOEUGENOL (AQUI-S®)

LABEL CLAIM #2

SPECIES: FRESHWATER FINFISH

INDICATIONS: [To sedate freshwater finfish for transport](#)

DIRECTIONS FOR USE: Apply ___ ml AQUI-S® per 1000L of water [ml/m³; equivalent to parts per million (ppm)] to achieve sedation for ___ minutes. Depth of sedation achieved will be dependent on water temperature, exposure time and species.

Technical Section	Entity—Data—Action	Impediments or Cost—Action
Efficacy (freshwater finfish)	AADAP (INAD #10-541)—Efficacy/freshwater finfish—accepted as complete 11/28/06	None
Label	AQNZ (INAD #9731) & NADA Coordinator—Label—planned in the future	On hold because of NTP peer review results
FOI	CVM—FOI—planned in the future with input from AQNZ, UMESC & AADAP	On hold because of NTP peer review results
AOI	AQNZ (INAD #9731) & NADA Coordinator—AOI—planned in the future	On hold because of NTP peer review results
NADA Package	AQNZ (INAD #9731) & NADA Coordinator—NADA package—planned in the future	On hold because of NTP peer review results

ISOEUGENOL (AQUI-S®)

LABEL CLAIM #3

SPECIES: SALTWATER-REARED FINFISH

INDICATIONS: To sedate saltwater-reared finfish to handleable condition

DIRECTIONS FOR USE: Apply ___ ml AQUI-S® per 1000L of water [ml/m³; equivalent to parts per million (ppm)] to achieve sedation for ___ minutes. Depth of sedation achieved will be dependent on water temperature, exposure time and species.

Technical Section	Entity—Data—Action	Impediments or Cost—Action
Efficacy (Atlantic salmon)	AQNZ (INAD #9731)—Efficacy/Atlantic salmon (proprietary & confidential)—CVM accepted as supportive 5/17/05	None
Efficacy (saltwater-reared finfish)	AADAP (INAD #10-541)—Efficacy/saltwater-reared finfish—planned in the future	On hold because of NTP peer review results
Label	AQNZ (INAD #9731) & NADA Coordinator—Label—planned in the future	On hold because of NTP peer review results
FOI	CVM—FOI—planned in the future with input from AQNZ, UMESC & AADAP	On hold because of NTP peer review results
AOI	AQNZ (INAD #9731) & NADA Coordinator—AOI—planned in the future	On hold because of NTP peer review results
NADA Package	AQNZ (INAD #9731) & NADA Coordinator—NADA package—planned in the future	On hold because of NTP peer review results

ISOEUGENOL (AQUI-S®)

LABEL CLAIM #4

SPECIES: SALTWATER-REARED FINFISH

INDICATIONS: [To sedate saltwater-reared finfish for transport](#)

DIRECTIONS FOR USE: Apply ___ ml AQUI-S® per 1000L of water [ml/m³; equivalent to parts per million (ppm)] to achieve sedation for ___ minutes. Depth of sedation achieved will be dependent on water temperature, exposure time and species.

Technical Section	Entity—Data—Action	Impediments or Cost—Action
Efficacy (Atlantic salmon)	AQNZ (INAD #9731)—Efficacy/Atlantic salmon (proprietary & confidential)—CVM accepted as supportive 5/17/05	None
Efficacy (saltwater-reared finfish)	AADAP (INAD #10-541)—Efficacy/saltwater-reared finfish—planned in the future	On hold because of NTP peer review results
Label	AQNZ (INAD #9731) & NADA Coordinator—Label—planned in the future	On hold because of NTP peer review results
FOI	CVM—FOI—planned in the future with input from AQNZ, UMESC & AADAP	On hold because of NTP peer review results
AOI	AQNZ (INAD #9731) & NADA Coordinator—AOI—planned in the future	On hold because of NTP peer review results
NADA Package	AQNZ (INAD #9731) & NADA Coordinator—NADA package—planned in the future	On hold because of NTP peer review results