

Abstract

AQUI-S™ is a fish anesthetic/sedative approved for use in several countries including Australia, Chile, and New Zealand and is being pursued for use in the United States. Legal use of AQUI-S™ as an anesthetic in U.S. fish culture depends on approval by the U.S. Food and Drug Administration (FDA). To gain approval in the United States, a number of drug attributes must be characterized including (1) depletion of a drug's total residues from edible fillet tissue taken from exposed fish and (2) depletion of one primary drug residue (a marker residue) from the fillet tissue. The marker residue is selected on the basis of data generated during the total residue depletion study. Characterizing marker residue depletion allows the FDA to establish a withdrawal time for exposed fish ensuring total residue concentrations reach safe levels before fish are made available for human consumption in the U.S. Before an AQUI-S™ total residue depletion study could be conducted with rainbow trout (*Oncorhynchus mykiss*), the exposure parameters (water temperature, isoeugenol concentration, and exposure duration) that generate the greatest total AQUI-S™ residues in fillet tissue needed to be determined.

Rainbow trout were exposed to AQUI-S™ in water temperatures of 7, 12, and 17°C in one of two static exposure regimens: (1) AQUI-S™ concentrations of 14 mg/L (nominal concentration) with an exposure duration of 60 min or (2) AQUI-S™ concentrations of 34 mg/L (nominal concentration) with an exposure duration of 10 min (exposure conditions based on probable U.S. use regimens). Immediately after the end of an exposure, fish were rinsed, sacrificed, and skin-on fillets removed. The fillets were homogenized with dry ice, the homogenate extracted with acetonitrile, and extracts analyzed for isoeugenol (the active ingredient in AQUI-S™) by liquid chromatography with absorbance detection.

At common water temperatures, the tissue concentration of isoeugenol from fish exposed to 14-mg/L AQUI-S™ for 60 min was significantly greater than the isoeugenol concentration in fish exposed to 34-mg/L AQUI-S™ for 10 min ($P < 0.01$). The isoeugenol concentration (78.8 $\mu\text{g/g}$) found in fillet tissue from fish exposed to 14-mg/L AQUI-S™ for 60 min at 17°C, was significantly greater than the isoeugenol tissue concentration (57.3 $\mu\text{g/g}$) generated at 7°C ($P < 0.01$), but was not significantly greater than the isoeugenol tissue concentration (70.7 $\mu\text{g/g}$) generated at 12°C ($P = 0.22$). AQUI-S™ exposure regimens and exposure temperatures can significantly impact drug residue concentrations in fillet tissue.