EXECUTIVE SUMMARY

Triclosan – Oral Risk Assessment CAS # 3380-34-5			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
NOAEL (no-observed-adverse-effect level)	10	mg/kg-day	From a 18-month repeated dose study in CD-1 mice
$NOAEL_{HED}$ (NOAEL human equivalent dose)	1.4	mg/kg-day	From the NOAEL with body weight$^{3/4}$ scaling
Oral RfD (oral reference dose)	0.047	mg/kg-day	From the $NOAEL_{HED}$ with a 30x total uncertainty factor
TAC (total allowable concentration)	0.3	mg/L	For a 70 kg adult drinking 2 L/day using a 20% relative source contribution for drinking water
SPAC (single product allowable concentration)	0.03	mg/L	From the TAC, using the default 10 sources of triclosan in drinking water
STEL (short term exposure level)	0.7	mg/L	From a 13-week repeated dose study in CD-1 mice, for a 10 kg child drinking 1 L/day

EXPOSURE SUMMARY	Triclosan is used as an antimicrobial agent in a wide range of consumer products/applications. Oral and dermal exposures to triclosan occur predominantly through the use of consumer products containing triclosan.
KEY STUDY	Pharmaco LSR. 1995. An 18-month oral oncogenicity study of triclosan in the mouse via dietary administration. Final Report. Study No. 93-2260. Pharmaco LSR, Mettlers Road, East Millstone, NJ.
CRITICAL EFFECT	Co-critical effects of decreased erythroid parameters and hepatic toxicity reported in mice following subchronic and chronic exposure to triclosan
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD include: • 3x for interspecies extrapolation • 10x for intraspecies extrapolation • 1x for subchronic to chronic extrapolation • 1x for LOAEL to NOAEL • 1x for database deficiencies The total uncertainty factor is therefore 30x.
TOXICITY SUMMARY	Available human safety studies reported no signs of overt toxicity in over 3,000 subjects exposed to triclosan-containing toothpaste for periods ranging from 12 weeks to 3 years. In humans and laboratory animals, triclosan is well absorbed following oral ingestion and undergoes extensive first-pass metabolism with conversion to a glucuronide and sulfate conjugate with the ratio of the primary metabolites being influenced by both exposure concentration and species. Triclosan is predominantly eliminated by urinary excretion in humans while the primary route of excretion in laboratory animals varies by species. Triclosan has low acute oral toxicity and has been reported to produce both skin and eye irritation while having a low skin sensitization potential. In repeated dose oral studies in laboratory animals, adverse effects of triclosan were reported predominantly in the liver, kidney and blood. Hepatic tumors were reported in mice following 18-month exposure to triclosan but the available data suggest that such tumors were likely due to mouse-specific PPARα activation; additionally, no evidence of carcinogenicity was reported in long-term dietary studies in both rats and hamsters. Reproductive and developmental effects reported following exposure to triclosan were at concentrations at which maternal (or parental) toxicity was typically present. Recent studies in rats have demonstrated consistent reductions in serum T_4 concentrations following exposure to triclosan. Based on liver histopathology and decreased erythroid parameters in the 18-month dietary study in mice, the $NOAEL_{HED}$ of 1.4 mg/kg-day was selected as the point of departure, and was determined to be adequately protective against other adverse effects considered, including thyroid disruption and renal toxicity. A weight of evidence evaluation that considers both *in vivo* and *in vitro* genotoxicity studies suggests low concern for genotoxicity. Triclosan is *Not Likely to Be Carcinogenic to Humans* based on U.S. EPA (2005) guidelines.
CONCLUSIONS	Based on the hepatic and hematological toxicity reported in CD-1 mice and the application of appropriate uncertainty factors, the drinking water action levels derived in this risk assessment are protective of public health.