EXECUTIVE SUMMARY

BROMINE/BROMIDE – Oral Risk Assessment CAS #s 7726-95-6/24959-67-9			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
NOAEL (no-observed-adverse-effect level)	7	mg/kg-day	From a 12-week repeated dose study in human volunteers
Oral RfD (oral reference dose)	0.7	mg/kg-day	From a 12-week repeated dose study in human volunteers with a 10x total uncertainty factor
TAC (total allowable concentration)	10 (total)*	mg/L	For a 70 kg adult drinking 2 L/day using a 50% relative source contribution for drinking water
SPAC (single product allowable concentration)	1 (total)*	mg/L	From the TAC, using 10 sources of bromine/bromide in drinking water.
STEL (short term exposure level)	10 (total)*	mg/L	From a 12-week repeated dose study in human volunteers, for a 10 kg child drinking 1 L/day
*The total concentration of bromine and bromide.			

EXPOSURE SUMMARY	Bromine is a bromide-releasing antimicrobial pesticide and is also used as a bactericide and fungicide on surfaces. It is registered for use in drinking water disinfection aboard ships and gas drilling/production platforms. The primary source of general population exposure to bromine/bromide is from the diet.
KEY STUDY	Van Gelderen et al. (1993) and Sangster et al. (1983) studies in healthy human volunteers given sodium bromide at up to nominally 9 mg/kg-day for at least 12 weeks.
CRITICAL EFFECT	Sedation, absent in female volunteers administered 7 mg/kg-day bromide.
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD include: 1x for interspecies extrapolation 10x for intraspecies extrapolation 1x for subchronic to chronic 1x for LOAEL to NOAEL 1x for database deficiencies The total uncertainty factor is therefore 10x.
TOXICITY SUMMARY	Bromine disproportionates in water and physiological systems to bromide (stable) and hypobromite (unstable) ions; consequently exposure in living organisms is principally to the bromide ion. According to U.S. EPA (2010c) the only bromine residue of toxicological concern is bromate which has an MCL of 0.01 mg/L (10 µg/L). Concentrated bromine is a potent irritant and systemic exposure is therefore limited. There is extensive clinical experience with various bromide salts based on their use as sedative-hypnotics and in treatment of seizures disorders. Repeated oral exposure in various mammalian species is associated with central nervous system effects expressed as behavioral and EEG changes. Repeated oral dosing also causes a hypothyroid effect that is specific to rats and not observed clinically or when assessed in volunteers. When male and female volunteers were administered sodium bromide capsules for 12 weeks at nominally 9 mg Br-/kg-day, serum thyroxine, triiodothyronine, and related hormone levels remained within normal limits. A small effect on EEGs of volunteers given 9 mg/kg-day (nominally) was reproducible but within normal limits. A dose-related incidence of nausea occurred shortly after the ingestion of the capsules, and no longer occurred when the capsules were taken during a meal. After adjusting the dose for bromide intake, the human systemic NOAEL was 7 mg/kg-day, based on the absence of sedation and EEG changes within normal limits. In a rat three-generation study with sodium bromide administered via the diet, fertility and viability of offspring were affected at doses of 186 mg/kg-day; the respective NOAELs for reproductive and parental effects were ~48 and ~12 mg Br-/kg-day. In developmental toxicity studies by the gavage route, the NOAELs for both parental and developmental effects were 77 and 196 mg Br/kg-day, in rats and rabbits, respectively. Chronic (two-year) administration of potassium bromide or methyl bromide via the diet of rats did not result in treatment related adverse findings with the exception of modestly lowered (3-6%) body weights in males, after consuming methyl bromide fumigated diets at 16 mg Br/kg-day. Sodium bromide was not mutagenic in bacterial reverse mutation assays, did not induce chromosomal aberrations in human lymphocytes *in vitro*, and did not produce evidence of DNA damage in a mammalian cell DNA repair assay. In the context of drinking water exposure to the bromide ion, the weight of evidence conclusion is that bromine/bromide is *Not Likely to Be Carcinogenic to Humans* based on U.S. EPA (2005) guidelines.
CONCLUSIONS	The derived action levels for the total concentration of bromine and bromide are protective of human health. Values apply specifically to elemental bromine and inorganic bromide ion and not to organobromine compounds or bromate, which have individual regulatory levels.