EXECUTIVE SUMMARY

Isobornyl Methacrylate – Oral Risk Assessment CAS # 7534-94-3			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
LOAEL (lowest observed adverse effect level)	50	mg/kg-day	From a subchronic toxicity study in CD rats
$LOAEL_{HED}$ (LOAEL human equivalent dose)	12	mg/kg-day	From the LOAEL with body weight$^{3/4}$ scaling (DAF = 0.24)
Oral RfD (oral reference dose)	0.004	mg/kg-day	From a subchronic toxicity study in CD rats with a 3000x total uncertainty factor.
TAC (total allowable concentration)	0.03	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)	0.003	mg/L	From the TAC using the default 10 sources of IBOMA in drinking water
STEL (short term exposure level)	0.4	mg/L	From a subchronic toxicity study in CD rats, for a 10 kg child drinking 1 L/day

EXPOSURE SUMMARY	IBOMA is used as a reactive monomer intermediate in the manufacture of polymers. Polymers produced with IBOMA are used in paints as well as acrylic and modified acrylic plastics. Oral exposure of the general population to IBOMA may occur indirectly by food or drinking water contact with products in which IBOMA was utilized as a monomer.
KEY STUDY	Hazleton Laboratories, Inc. (1968a, as cited in OECD, 2011; ECHA, 2015). Three-Month Dietary Feeding – Rats. Isobornyl Methacrylate (IBOMA). Hazleton Project No. 417-22 for Rohm & Haas Company.
CRITICAL EFFECT	Biliary epithelial hyperplasia reported in subchronic oral feeding study in CD rats
UNCERTAINTY FACTORS	Uncertainty factors applied in calculating the oral RfD include: • 3x for interspecies extrapolation (use of human equivalent dose) • 10x for intraspecies extrapolation (lack of data to depart from default) • 10x for subchronic to chronic extrapolation (lack of chronic study, inadequate surrogate data) • 3x for LOAEL to NOAEL extrapolation (mode of action based on irritation, steep dose-response) • 3x for database (lack of reproductive, developmental studies, utilization of read-across for primary metabolites) The total uncertainty factor is therefore 3000x
TOXICITY SUMMARY	No information regarding the absorption, distribution, metabolism or elimination/excretion of IBOMA could be located in the available scientific literature. As a chemical class, alkyl-methacrylate esters are metabolized to methacrylic acid and the structurally corresponding alcohol by non-specific carboxylesterases. IBOMA has low acute oral toxicity (LD50 ≥ 2400 mg/kg) and is a slight to moderate skin and eye irritant. IBOMA is not considered to be a skin sensitizer in either humans or laboratory animals. Repeated dose toxicity of IBOMA has been evaluated in two subchronic feeding studies in CD rats and Beagle dogs. In CD rats, histopathological findings included alterations in the liver of male and female animals at all treatment levels ranging from biliary epithelial hyperplasia reported at the low-dose to severe bile duct hyperplasia at the high-dose. Renal findings included protein imbibition at the low- and mid-dose and hypertrophy of the deep proximal convoluted tubules at the high-dose. In Beagle dogs, other than significantly increased relative liver weights, no other hepatic findings were reported while renal findings included minimal to slight degenerative changes in proximal tubule epithelial cells at the high-dose. In an OECD 421 reproduction/developmental toxicity screening test in Sprague-Dawley rats, exposure of parental animals to IBOMA by gavage resulted in biliary hypertrophy and hepatocellular degeneration/necrosis at the mid-dose in male animals. At high-dose, histopathological findings in the liver included biliary hypertrophy, portal triad fibrosis, disorganization of the hepatic cords in both sexes while hepatocellular necrosis and single cell necrosis were reported in males only. Renal findings included the presence of acidophilic globules in the cortical tubular epithelium of the kidneys of the control males and all treated male animals with marginally higher incidence and severity in the treated males from the mid- and high-dose groups. No treatment-related adverse effects were reported on any reproductive or developmental parameter assessed up to the highest dose-level tested. The genetic toxicity of IBOMA was evaluated in two bacterial reverse mutation assays in an *in vitro* gene mutation assay and in an *in vitro* chromosomal aberration assay, all of which reported negative findings. Based on the weight of evidence, the available *in vitro* genotoxicity studies for IBOMA suggest low concern for genotoxicity. Due to the lack of chronic toxicity studies, there is *Inadequate Information to Assess Carcinogenic Potential* of IBOMA.
CONCLUSIONS	Based on the selected critical effect of biliary epithelial hyperplasia reported in CD rats and the application of appropriate uncertainty factors, the drinking water action levels derived in this risk assessment are protective of public health.