EXECUTIVE SUMMARY

Diethylene Glycol Dibenzoate – Oral Risk Assessment CAS # 120-55-8			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
NOAEL (no observed adverse effect level)	324	mg/kg-day	From a two-generation reproductive toxicity study in Sprague-Dawley rats
$NOAEL_{HED}$ (NOAEL human equivalent dose)	75	mg/kg-day	From the NOAEL with body weight$^{3/4}$ scaling (DAF = 0.23)
Oral RfD (oral reference dose)	0.25	mg/kg-day	From a two-generation reproductive toxicity study in Sprague-Dawley rats with a 300x total uncertainty factor.
TAC (total allowable concentration)	2	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)	0.2	mg/L	From the TAC using the default 10 sources of diethylene glycol dibenzoate in drinking water
STEL (short term exposure level)	8	mg/L	From a two-generation reproductive toxicity study in Sprague-Dawley rats, for a 10 kg child drinking 1 L/day

EXPOSURE SUMMARY	Diethylene glycol dibenzoate (DEGDB) is a high solvating plasticizer used in several applications including PVC, vinyl flooring, adhesives, elastomers, latex caulks and sealants, some of which have drinking water contact applications. Exposure of the general population to DEGDB may occur through contact with products which contain DEGDB.
KEY STUDY	Huntingdon Life Sciences, 2001 (as cited in Velsicol Chemical Corporation, 2001a; U.S. EPA, 2015b; ECHA, 2015) Benzoflex 2-45. Study of Reproductive Performance in Sprague-Dawley Rats Treated Continuously through Two Successive Generations by Dietary Administration. Unpublished.
CRITICAL EFFECT	Decreased pup body weight gain from a dietary two-generation reproductive toxicity study in Sprague-Dawley 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) • 3x for subchronic to chronic extrapolation (fetotoxicity during sensitive exposure period, lack of chronic data) • 1x for LOAEL to NOAEL extrapolation (NOAEL utilized) • 3x for database (lack of developmental study in second species) The total uncertainty factor is therefore 300x
TOXICITY SUMMARY	Diethylene glycol dibenzoate (DEGDB) is well absorbed following oral administration. In animal studies, doses of DEGDB were absorbed, metabolized and predominantly excreted in the urine within 24 hours of administration. Following absorption, DEGDB is completely metabolized by the hydrolysis of the ester bonds to benzoic acid which then undergoes conjugation with glycine (primary route) or glucuronic acid (minor route). DEGDB has low acute toxicity (LD50 > 2000 mg/kg) and is non-irritating in guideline compliant studies examining eye and skin irritation. In a guideline compliant subchronic feeding study in CD rats, reported toxicology effects included significant decreases in body weights at dose concentrations ≥1750 mg/kg-day in addition to hemosiderosis, reduced erythrocyte parameters and liver effects (increased relative weight, periportal hepatocyte hypertrophy) at 2500 mg/kg-day. Both the erythrocyte and liver effects were found to be fully reversible following a 4-week recovery period indicative of adaptive responses to DEGDB exposure. Two other subchronic feeding studies examining the toxicity of DEGDB in animals reported no adverse effects at the highest doses tested in either CD rats (1000 mg/kg-day) or Beagle dogs (451 mg/kg-day). In a guideline compliant two-generation reproductive toxicity study (dietary) in Sprague-Dawley rats, no adverse effects were reported in the parental animals or in any of the reproductive parameters evaluated up to the highest dose tested (males: 861 mg/kg-day, females: 980 mg/kg-day). A significant decrease in body weight gain in F2 offspring from birth to weaning was reported at the high-dose resulting in a developmental NOAEL of 324 mg/kg-day. In a guideline compliant developmental toxicity study (gavage) in Sprague-Dawley rats, no adverse effects were reported in maternal animals up to the highest dose of 1000 mg/kg-day. A slight, but significant, decrease in fetal weight in addition to increased incidences of incomplete ossification and cervical ribs were reported at 1000 mg/kg-day, resulting in a developmental NOAEL of 500 mg/kg-day. The genetic toxicity of DEGDB has been assessed in three separate guideline compliant studies (*in vitro* cell transformation assay, bacterial reverse mutation assay, and *in vitro* mammalian chromosome aberration assay) all of which reported negative findings. Based on the weight of evidence, the available *in vitro* genotoxicity studies for DEGDB suggest low concern for genotoxicity. Due to the lack of chronic toxicity studies, there is *Inadequate Information to Assess Carcinogenic Potential* of DEGDB.
CONCLUSIONS	Based on the decreased pup body weights reported in Sprague-Dawley rats and the application of appropriate uncertainty factors, the drinking water action levels derived in this risk assessment are protective of public health.