EXECUTIVE SUMMARY

1-HEXANOL– Oral Risk Assessment CAS # 111-27-3			
PARAMETER	**LEVEL**	**UNITS**	**DERIVED**
NOAEL (no-observed-adverse-effect level)	1127	mg/kg-day	From a subchronic feeding study with albino rats
$NOAEL_{HED}$ (NOAEL human equivalent dose)	270	mg/kg-day	From the NOAEL with body weight$^{3/4}$ scaling (DAF = 0.24)
Oral RfD (oral reference dose)	0.3	mg/kg-day	From the $NOAEL_{HED}$ with a 1000x 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 1-hexanol in drinking water
STEL (short term exposure level)	30	mg/L	From a subchronic feeding study, for a 10 kg child drinking 1 L/day

EXPOSURE SUMMARY	1-Hexanol is used as a plasticizer, solvent, defoamer, food additive, and food flavoring agent; it is produced for use in perfumery and for antiseptics and hypnotics. General population exposure can occur due to its residual presence in products with drinking water contact. Other sources of potential exposure include inhalation of vapor and use of household wax products and other consumer goods. Oral exposure may include ingestion of foods which contain 1-hexanol naturally or as a direct food additive.
KEY STUDY	Scientific Associates, Inc. 1966a. Final report on thirteen-week subacute feeding of Alfol 6 and Alfol 16 to rats (as cited in ECHA, 2015).
CRITICAL EFFECT	No specific critical effect was identified for the point of departure for 1-hexanol, based on the available toxicity data. The 13-week study in rats did not identify any statistically significant toxic responses to 1-hexanol administration and the 13-week study in dogs failed to identify systemic effects when the test substance was administered in the feed, in spite of the presence of localized gastrointestinal tract irritation.
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD include: • **3x** for interspecies extrapolation • **10x** for intraspecies extrapolation • **10x** for subchronic to chronic extrapolation • **1x** for LOAEL to NOAEL • **3x** for database deficiencies The total uncertainty factor is therefore 1000**x**.
TOXICITY SUMMARY	1-Hexanol is rapidly and efficiently absorbed through the gastrointestinal tract (WHO, 1999). In the body, 1-hexanol is oxidized to hexanal, which is then rapidly oxidized to hexanoic acid (WHO, 1999). In rabbits, conjugation with glucuronic acid is a possible minor route of metabolism (Kamil *et al.*, 1953). 1-Hexanol and its metabolites may be excreted in the urine and feces and exhaled via the lungs (HSBD, 2015). The acute oral LD_{50} values for 1-hexanol are ≥720 mg/kg in rats, ≥1950 mg/kg in mice, and ≥1500 mg/kg in rabbits. 1-Hexanol is not likely a skin irritant in humans, but is a mild skin irritant and ocular irritant in rabbits. In a 13-week oral feeding study in albino rats, no statistically significant toxic responses to 1-hexanol administration were reported at doses up to 1127 mg/kg-day. In a 13-week oral study in Beagle dogs, at the highest dose administered in a gelatin capsule (1000 mg/kg-day), signs of central nervous system depression, difficult respiration, testicular atrophy, decreased oogenesis, and mortality were reported, and are attributed to the method of test substance administration, which is considered less relevant to exposure of 1-hexanol in drinking water. When lower doses were administered to dogs in the daily diet (190 mg/kg-day and 370 mg/kg-day), no systemic effects were identified, but localized gastrointestinal tract irritation was reported. 1-Hexanol and the other members of the long chain alcohols category do not contain any structural alerts for mutagenic activity. *In vitro* genetic toxicity tests across the range of category members, including bacterial reverse mutation, comet, and micronucleus assays with 1-hexanol, are negative. *In vivo* studies were not identified for 1-hexanol; however, SAR analysis and results from *in vivo* studies with the analogue 2-ethylhexanol suggest a lack of genotoxic activity for these aliphatic alcohols. In the absence of epidemiology or chronic studies, there is *Inadequate Information to Assess Carcinogenic Potential* of 1-hexanol based on U.S. EPA (2005) guidelines.
CONCLUSIONS	1-Hexanol and similar saturated aliphatic acyclic linear primary alcohols have a low order of toxicity associated with repeated oral exposure. Based on the studies reviewed and the uncertainty factors applied, the drinking water action levels derived in this risk assessment are protective of public health.