EXECUTIVE SUMMARY

n-Butyl Acetate – Oral Risk Assessment CAS # 123-86-4			
PARAMETER	**LEVEL**	**UNITS**	**CALCULATED**
NOAEL (no observed-adverse-effect level)	600	mg/kg-day	From a 13-week gavage study in rats
Oral RfD (oral reference dose)	0.2	mg/kg-day	From a 13-week gavage study in rats
TAC (total allowable concentration)	1	mg/L	For a 70 kg adult drinking 2 L/day with a 20% Relative Source Contribution for drinking water.
SPAC (single product allowable concentration)	0.1	mg/L	For a 70 kg adult drinking 2 L/day.
STEL (short term exposure level)	20	mg/L	From a 13-week gavage study in rats, for a 10 kg child drinking 1 L/day.

KEY STUDY	General Foods Corporation. 1978. Butyl Acetate. Ninety-Day Oral Toxicity Study in Rats. Report Number 377-004. Prepared by General Food Corporation. October 2.
CRITICAL EFFECT(S)	In both sexes, dose-related stomach lesions and reduced motor activity.
UNCERTAINTY FACTORS	Factors applied in calculating the oral RfD: • 10x for interspecies extrapolation • 10x for intraspecies extrapolation • 10x for subchronic to chronic extrapolation • 1x for extrapolation from a LOAEL to a NOAEL • 3x for database deficiencies The total uncertainty factor is therefore 3,000x.
TOXICITY SUMMARY	The critical study chosen to derive the oral RfD was a 13-week gavage study in which rats were administered 0, 600, 2,000, or 6,000 mg/kg-day of n-butyl acetate in corn oil. The low dose was considered the NOAEL. At the mid dose, which was considered the LOAEL, histopathological examination revealed slight to moderate stomach lesions, described as inflammatory infiltrates, edema, degeneration, and/or necrosis of the non-glandular and/or glandular mucosa and submucosa, and/or epithelial hyperkeratosis and acanthosis. The stomach lesions were observed in 3/20 male rats and 3/20 female rats. Reduced motor activity was also observed, but quantitative data were not provided. At the high dose, the incidence of stomach lesions and reduced motor activity increased, such that the stomach lesions were observed in 11/20 males and 10/20 females. Quantitative data for reduced motor activity were again not provided. Sedation and hypoactivity were also observed in a subchronic gavage study in mice and two subchronic inhalation studies in rats. The gavage study was chosen as the key study, since an oral study is more appropriate for calculation of the RfD. In developmental studies in rabbits and rats, statistically significant increases in retinal folds, misaligned sternebrae, and clear gallbladders were observed in the offspring of rabbit dams inhaling human equivalent doses of 2,030 mg/kg n-butyl acetate for seven hours/day during GD 1-19. In rats, a statistically significant reduction in fetal size and increased incidences of hydroureters, rib dysmorphology, and reduced pelvic ossification were observed in offspring from dams inhaling human equivalent doses of 2,030 mg/kg n-butyl acetate for seven hours/day during various gestational and non-gestational exposure paradigms. Reduced food consumption and body and/or organ weight changes were observed in both rabbit and rat dams. The mode of action of the stomach lesions is unknown. Since n-butyl acetate is rapidly metabolized to n-butanol in the blood and brain, the likely mediator of the sedation and hypoactivity caused by n-butyl acetate is n-butanol. n-Butyl acetate was not genotoxic in *Salmonella, E. coli, S. cerevisiae*, or Chinese hamster ovary cell assays.
CONCLUSIONS	The critical effects of oral exposures to n-butyl acetate in rats are stomach lesions and reduced motor activity. Due to the lack of chronic data in humans and laboratory animals, the carcinogenic potential of n-butyl acetate *cannot be determined.* The weight of genotoxicity evidence suggests that n-butyl acetate is not genotoxic. The uncertainty factors used to account for the database deficiencies, such as the lack of adequate oral studies, and two-generation reproduction or immunological data, should ensure that the drinking water action levels are protective of human health.