

IDENTIFICATION AND USE: Toluene is a colorless liquid. Toluene did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells in the presence or absence of exogenous metabolic activation. Toluene did not induce gene mutations in *Salmonella typhimurium* strain TA98, TA100, TA1535, or TA1537 with or without exogenous metabolic activation. In the mouse lymphoma assay, toluene gave an equivocal response with and without exogenous metabolic activation. In subjects exposed to 750 mg/cu m for 8 hr, fatigue, muscular weakness, confusion, impaired coordination, enlarged pupils and accommodation disturbances were experienced; at about 3000 mg/cu m, severe fatigue, pronounced nausea, mental confusion, considerable incoordination with staggering gait and strongly affected pupillary light reflexes were observed. Several case series have demonstrated that high exposure to toluene through sniffing during pregnancy induces a syndrome that closely resembles the fetal alcohol syndrome, with pre- and postnatal growth deficiency, microcephaly and developmental delay, typical craniofacial features including micrognathia, small palpebral fissures, and ear anomalies.

ANIMAL STUDIES: Rats were studied to assess the effects of acute binge-like toluene inhalations (15 or 30 min; ~5,000 ppm) on tasks that examine locomotion, exploration, balance, gait, and neurological functioning for adolescent (1 month), young adult (2–3 months), adult (5–6 months), and older adult (10–12 months) rats.

HUMAN EXPOSURE AND TOXICITY: Eye and upper airway irritation occurred after a 6.5 hr exposure to an air level of 100 ppm (377 mg/cu m) toluene, and lacrymation was seen at 500 mg/cu m. Volunteers exposed to 100 ppm (377 mg/cu m) toluene for 6 hr/day for four days suffered from subjective complaints of headache, dizziness and a sensation of intoxication. Groups of 60 male and female mice that were exposed 6.5 hours/day, 5 days/week for 2 years via inhalation at inhaled 0, 120, 600, or 1200 ppm toluene showed no biologically relevant increases for any non-neoplastic or neoplastic tissue changes. Severe renal tubular acidosis was observed in five pregnant women who were chronic abusers of paints containing toluene. Rats were dosed with 1.3 g/kg toluene subcutaneously during either week 2 (8–15 days) or week 3 (14–20 days) of pregnancy and evaluated for malformations, development of the skeleton, prenatal growth of the brain and liver, postnatal growth, and behavioral effects. The olfactory and respiratory epithelia showed signs of degeneration with nasal inflammation and metaplasia of the olfactory epithelium (principally in the females). Toluene is a component of gasoline, paints, inks, lacquers, paint thinners, adhesives, fingernail polish, cleaning agents, and rubber. BTX (a mixture of benzene, toluene, and xylene) is added to gasoline to improve octane ratings. One person exposed for 2 hr to less than 1890 ppm toluene exhibited a rapid heartbeat (sinus tachycardia), while the second person, exposed for 3 hr, exhibited a slow heartbeat (bradycardia). CYP2E1 is a versatile phase I drug-metabolizing enzyme responsible for the biotransformation of most volatile organic compounds, including toluene. However, only the duration to recover from deficits in motor functions differed among age groups, with adolescent and young adult rats requiring notably longer recovery times than older rats. Mice exposed 6 hours/day at 100 ppm toluene during days 1 to 17 of pregnancy showed no significant differences in number of implantation sites, number of fetuses, or mean fetal body weight when compared with control. Toluene is a favorite of solvent abusers, who intentionally inhale high concentrations to achieve a euphoric effect. There was maternal mortality in these groups.