

tert*-Amyl Methyl Ether [994-05-8]*Results of Testing**

Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
<i>tert</i> -Amyl methyl ether	994-05-8	HEADME Pilot study for Metabolism, Distribution and Pharmacokinetics	40 CFR 795.230	rats	inhalation, nose-only, single, 6 hours	2500 ppm	4	Over 95% of radioactivity recovered for up to 7 days was excreted by 48 hours after exposure. The majority of radioactivity was found in charcoal traps (44% of total recovered) and in urine (51%), with a minor amount in feces (1%) and KOH traps (3%). Less than 0.5% of the total recovered radioactivity was in the carcass.	62 FR 51858; 10/3/97; Docket OPPTS-44643
<i>tert</i> -Amyl methyl ether	994-05-8	HEADME Pharmacokinetics, blood	40 CFR 795.230	mice	inhalation, nose-only, single, 6 hours	100, 500, 2500 ppm	Not reported	The concentration of TAME in blood following exposure to 100 ppm was 1.5 µg/ml. The half-life was between 13 and 48 minutes. Acetone was elevated above background levels at all exposure concentrations. Acetone elevation at 500 or 2500 ppm was up to six times greater than that measured after the 100 ppm exposure.	62 FR 51858; 10/3/97; Docket OPPTS-44643
<i>tert</i> -Amyl methyl ether	994-05-8	HEADME Pharmacokinetics, blood	40 CFR 795.230	rats	inhalation, nose-only, single, 6 hours	100, 500, 2500 ppm	Not reported	The concentration of TAME in blood following exposure to 100 ppm was 3 µg/ml. The half-life was between 33 and 84 minutes. Acetone was elevated above background levels at all exposure concentrations.	62 FR 51858; 10/3/97; Docket OPPTS-44643
<i>tert</i> -Amyl methyl ether	994-05-8	HEADME Metabolism and distribution	40 CFR 795.230	rats	inhalation, nose-only, single, 6 hours; additional group whole-body inhalation, 5 days.	100, 500, 2500 ppm (nose-only); 500 ppm (whole-body)	Not reported	For inhalation exposures, rats had a linear response for the total (0-48 hr following exposure termination) exhaled TAME and <i>tert</i> -amyl alcohol (TAA) as a function of exposure concentration. A decrease in the amount (0-48 hr) of expired TAME was observed for rats, but not mice, following 5 days of inhalation exposure to 500 ppm TAME as compared with 1 day of exposure.	62 FR 51858; 10/3/97; Docket OPPTS-44643
<i>tert</i> -Amyl methyl ether	994-05-8	HEADME Metabolism and distribution	40 CFR 795.230	mice	inhalation, nose-only, single, 6 hours; additional group whole-body inhalation, 5 days.	100, 500, 2500 ppm (nose-only); 500 ppm (whole-body)	Not reported	For inhalation exposures, mice had an increase in exhaled TAME and TAA (normalized by body weight and exposure concentration) observed with an increase in exposure concentration. A decrease in the amount (0-48 hr) of expired TAME was observed for rats, but not mice, following 5 days of inhalation exposure to 500 ppm TAME as compared with 1 day of exposure.	62 FR 51858; 10/3/97; Docket OPPTS-44643
<i>tert</i> -Amyl methyl ether	994-05-8	HEADME Metabolism and distribution	40 CFR 795.230	rats	oral, gavage	10, 100 mg/kg	Not reported	Female rats had an increase in exhaled TAME (normalized by body weight and amount administered) following gavage at the high dose, as compared with the low dose.	62 FR 51858; 10/3/97; Docket OPPTS-44643

G102
tert-Amyl Methyl Ether [994-05-8]

Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
tert-Amyl methyl ether	994-05-8	HEADME Metabolism and distribution	40 CFR 795.230	mice	oral, gavage	20, 100 mg/kg	Not reported	Male and female mice had an increase in exhaled TAME (normalized by body weight and amount administered) following gavage at the high dose, as compared with the low dose.	62 FR 51858; 10/3/97; Docket OPPTS-44643
tert-Amyl methyl ether	994-05-8	HEGETOXCHRM Mutagenicity: Chromosomal aberrations	40 CFR 798.5375	Chinese hamster, ovary cells	<i>in-vitro</i>	313-5000 µg/mL	Not applicable	The test substance was positive for mutagenic effect in the S-9 activated system.	61 FR 42611; 8/16/96, Docket OPPTS-44629
tert-Amyl methyl ether	994-05-8	HEGETOXMUTA Mutagenicity: CHO/HGRT assay	40 CFR 798.5300	Chinese hamster, ovary cells	<i>in-vitro</i>	1000 to 5000 µg/mL	Not applicable	The test substance was negative in the CHO/HGPRT mutagen assay.	61 FR 42611; 8/16/96, Docket OPPTS-44629
tert-Amyl methyl ether	994-05-8	HENEUR Neurotoxicity screen	40 CFR 795.247	rats	inhalation, whole-body, 5 d/wk, 13 weeks	0, 250, 1500, 3500 ppm	51 (0, 3500 ppm); 41 (250, 1500 ppm)	Exposure to 3500 ppm resulted in neurological effects including depression of central nervous system activity and neuromuscular impairment, one hour after acute exposure; these effects were no longer evident 6 and 24 hours after acute exposure and were not seen after repeated exposure to the test substance. The NOEL for acute neurobehavioral effects was 250 ppm in males and 1500 ppm in females. The NOEL for subchronic neurotoxicity was 3500 ppm in both males and females.	62 FR 51858; 10/3/97; Docket OPPTS-44643
tert-Amyl methyl ether	994-05-8	HERTOXTERA Developmental toxicity	40 CFR 870.3700	rats	inhalation, 6 hr/d, gestation day 6 - 19	0, 250, 1500, 3500 ppm (target)	25	No dams died, aborted, or delivered early. Maternal body weight was significantly reduced at 3500 ppm. Treatment-related clinical observations included ataxia, dazed appearance, lethargy, eye(s) squinting or closed, and slow respiration at 3500 ppm, and lethargy and piloerection at 1500 ppm. Developmental toxicity was present at 3500 ppm, specifically reduced fetal body weights per litter. There were no treatment-related changes in the incidence or severity of fetal external, visceral, skeletal or total malformations or variations in this study. The NOAEL for maternal toxicity was 250 ppm and for developmental toxicity was 1500 ppm under the conditions of this study.	62 FR 18350; 4/15/97, Docket OPPTS-44639

G102
***tert*-Amyl Methyl Ether [994-05-8]**

Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
<i>tert</i> -Amyl methyl ether	994-05-8	HERTOXTERA Developmental toxicity	40 CFR 870.3700	mice	inhalation, 6 hr/d, gestation day 6 - 16	0, 250, 1500, 3500 ppm (target)	25	Four dams died at 3500 ppm. Treatment-related clinical observations included mortality, ataxia, prone positioning, gasping, rough coat, lethargy, eye(s) squinted, head tremors and slow respiration at 3500 ppm, and eye(s) half closed and head tremors at 1500 ppm. Developmental toxicity was present at 3500 ppm, specifically significantly increased incidence of late fetal deaths, significantly reduced fetal body weights per litter, and increased incidences of cleft palate and enlarged lateral ventricles of the cerebrum. At 1500 ppm, fetuses also exhibited an increased incidence of cleft palate. The NOAEL for maternal and developmental toxicity was 250 ppm under the conditions of this study.	62 FR 18350; 4/15/97, Docket OPPTS-44639

G102
***tert*-Amyl Methyl Ether [994-05-8]**

Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
<i>tert</i> -Amyl methyl ether	994-05-8	HERTOXTERE Reproduction and Fertility	40 CFR 870.3800	Sprague- Dawley rats	inhalation	0, 250, 1500 and 3000 ppm	30/sex/group	<p>F₀ Generation - There is evidence of toxicity to offspring at the 1500 ppm and 3000 ppm TAME exposure levels; significant reductions in pup body weight by litter at both concentrations. In both sexes at 3000 ppm, there were persistent decreases in mean body weight gain, body weights and feed consumption. Most animals exhibited transient ataxia at 3000 ppm and some animals were effected at 1500 ppm. The NOAEL for the study is 250 ppm for both adult and offspring systemic toxicity.</p> <p>F₁ Generation - For F₁ males, the age at acquisition of preputial separation was significantly delayed at exposure to 1500 and 3000 ppm. For F₁ females, the age at acquisition of vaginal patency was significantly delayed at 250, 1500, and 3000 ppm. For both sexes there were persistent reductions in body weight gains and feed consumption. Increased relative liver weight was reported for both males and females exposed to 3000 ppm and for males only exposed to 1500 ppm.</p> <p>F₂ Generation - F₂ offspring of the 3000 ppm group exhibited decreased survival indices at pnd 4 and 21. At 1500 ppm, the total was 101 F₂ pups of which approximately 90 pups died between pnd 0 -4. At 3000 ppm, the pup body weights from F₁ parents were significantly reduced at all timepoints measured. At 1500 ppm, F₂ offspring exhibited significantly reduced body weights on pnd 14 & 21 only. In F₂ male offspring the age at acquisition of preputial separation was significantly delayed at 3000 ppm. For F₂ females, the age at acquisition of vaginal patency was significantly delayed at 3000 ppm.</p>	63 FR 25040; 5/6/98, Docket OPPTS-44648

G102
***tert*-Amyl Methyl Ether [994-05-8]**

Chemical Name	CAS No.	Study Code/Type	Protocol/Guideline	Species	Exposure	Dose/Concentration	No. per Group	Results	Reference
<i>tert</i> -Amyl methyl ether	994-05-8	HESTOX 90-Day Subchronic toxicity	40 CFR 798.2450 (Amended to include mitogenesis, special staining and immunochemistry)	rats	inhalation, whole-body, 5 d/wk, 13 weeks	0, 250, 1500, 3500 ppm	51 (0, 3500 ppm); 41 (250, 1500 ppm)	Exposure to 3500 ppm resulted in low incidence of mortality (2/102), abnormal clinical signs (lethargy and prostration), decreased body weight and body weight gain, effects on hematology (increased platelet counts), effects on clinical chemistry (increases in protein, albumin and globulin), and effects on organ weights. Microscopic examination revealed increased intracytoplasmic eosinophilic/hyaline droplets in proximal convoluted tubules in male kidneys which contained alpha-2u-globulin immunoreactivity. There was also increased kidney proliferation and increased neuropathy. Based on these findings, the NOEL for female rats was 250 ppm and for male rats was not established.	62 FR 51858; 10/3/97; Docket OPPTS-44643
<i>tert</i> -Amyl methyl ether	994-05-8	HESTOX 90-Day Subchronic toxicity	40 CFR 798.2450 (Amended to include mitogenesis, special staining and immunochemistry)	mice	inhalation, whole-body, 5 d/wk, 13 weeks	0, 250, 1500, 2500 ppm	46 (0, 2500 ppm); 36 (250, 1500 ppm)	Exposure to 2500 ppm resulted in mortality, abnormal clinical signs (prostration, lethargy, decreased activity), effects on clinical chemistry and increased absolute and relative liver weights. Cell proliferations studies in the liver showed increased labeling index of hepatocytes and there was microscopic evidence of centrilobular hepatocellular hypertrophy in males and females. The NOEL for males was 250 ppm and the NOEL for females was not established.	62 FR 51858; 10/3/97; Docket OPPTS-44643