

Methyl isopropyl ketone

Reference	Experimental Parameters					Endpoints Assessed	Results (Effects/NOEL/LOEL)		Comments
	Chemical (Source/Purity/Preparation)	Animal Model (Species/Strain/Sex/Age) N	Study Design	Exposure (Route/Period/Frequency/Vehicle)	Doses/Concentrations		Systemic Toxicity	Reproductive and Developmental Toxicity	
Edwards 2012 WIL Research	Methyl isopropyl ketone (MIPK) Eastman Chemical Company 99.645% purity	Sprague Dawley [CrI:CD(SD)] rats; only females treated; 13 weeks old when paired for breeding with resident male breeders N = 25 bred females/group	Prenatal Developmental Toxicity Study OECD Guideline 414 OPPTS 870.3700	Inhalation Whole body inhalation; 6 h/day; 7 days/wk from GD 0 through 19 Vehicle was air	Target conc.: 0 (vehicle), 300, 750 and 1500 ppm Mean measured conc.: 0, 304, 757 and 1529 ppm	Mortality, moribundity, clinical signs, food consumption, mean body weight and mean body weight gain were recorded for dams throughout the study. At necropsy, select maternal organs were weighed and grossly examined; ovaries, uterus and live/dead fetuses were evaluated. Number of litters, number of corpora lutea, number and location of all fetuses, early and late resorptions,	No deaths among dams. There was an exposure-related increase in number of dams with no reaction to noise stimulus near the end of the exposure; no clinical findings 1h after exposure. For dams in 750 and 1500 ppm groups, mean BW gains were generally significantly lower (p<0.05 or p<0.01) for GD 0-20, mean BWs were significantly (p<0.01) lower during GD 1-20, and mean net BW, net BW gains and gravid uterine weights were significantly (p<0.05 or p<0.01) lower. At 300 ppm, mean BW gain was significantly (p<0.01) lower during GD 0-3 but similar to control for GD 3-20; overall mean BW gain was significantly (p<0.01) lower for GD	Except for 2, 1, and 1 females in the control, 750 and 1500 ppm groups, all females were gravid. No dams aborted and there were no dead fetuses. No significant differences were noted in the number of viable fetuses, early and late resorptions, pre- and post implantation losses, implantation sites, corpora lutea, or fetal sex ratio. Although mean fetal male, female and combined weights in the 750 ppm group were significantly (p<0.05) lower than concurrent controls, values were within WIL historical control ranges and values were identical to those of the 1500 ppm group which were not significantly different from concurrent control	NOAEL (maternal toxicity): <300 ppm based on clinical signs, decrease in body weights and body weight gains, and decrease in food consumption NOAEL (repro. function): 1500 ppm NOAEL (fetotoxicity): 1500 ppm NOAEL (develop. toxicity): 1500 ppm There were no significant differences in indices of embryo-fetal deaths, number of live fetuses, sex ratio, live fetal body weight, or uterus weight. There were no significant differences in external, visceral or skeletal malformations or variations.

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					<p>and total number of implantation sites were recorded. Gravid uterine weight, net body weight and net body weight changes were recorded. Uteri with no evidence of implantation were evaluated for early implantation loss.</p> <p>Live fetuses and their placentas were observed for external malformations and gross abnormalities.</p> <p>Live fetuses were weighed, sexed, and examined for visceral and skeletal malformations and variations.</p>	<p>0-20, mean BW was slightly lower ($p < 0.05$ or $p < 0.01$) for GD 3-20, and net BW gain was significantly ($p < 0.01$) lower. At 300 ppm, no effect on mean net BW or gravid uterine weight.</p> <p>Food consumption was lower ($p < 0.05$ or $p < 0.01$) for GD 0-20 in 300, 750 and 1500 ppm groups.</p> <p>No substance-related gross abnormalities noted at necropsy in any group.</p> <p>In 1500 ppm group: significantly ($p < 0.01$) higher mean adrenal gland weights (absolute and relative to brain); significantly ($p < 0.05$) lower absolute kidney weights (no effect on relative wt); no effect on liver or brain weights. At 750 ppm, mean absolute liver, kidney and brain weights were significantly ($p < 0.05$ or $p < 0.01$) lower; no effect on adrenal gland weights or any relative to brain weights. At 300 ppm, no effect on any organ weights.</p>	<p>values.</p> <p>There were no significant differences in the index of external malformations or variations, or incidence of skeletal or visceral malformations or variations.</p> <p>External malformations were seen in 0(0), 1(1), 1(1), and 1(1) (fetuses (litters)) in the control, 300, 750 and 1500 ppm groups. One fetus each in the 750 and 1500 ppm groups had microphthalmia and/or anophthalmia. Mean litter proportions were not significantly different from controls. Ectrodactyly was seen in one fetus at 300 ppm.</p> <p>Single fetuses in the 300 and 750 ppm groups had soft tissue malformations but these were not observed at 1500 ppm. A single fetus at 300 ppm had an accessory liver lobe.</p> <p>Skeletal malformations were noted in 3(3), 2(2), 4(1) and 0(0) in the control, 300, 750 and 1500 ppm groups. These were noted in single fetuses or litters, did not occur in the 1500 ppm</p>
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								<p>group, were also observed in the concurrent control group, and/or the mean litter proportions were not statistically significant compared to the concurrent control.</p> <p>Isolated incidences of skeletal variations occurred but these findings occurred infrequently, were noted similarly in the concurrent control group, and/or were not exposure-related. When evaluated on a mean litter proportion basis, values were within historical control data and/or differences from control were not statistically significant.</p>	
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