

Ethylene Glycol Monomethyl Ether

CAS #109-86-4

Swiss CD-1 mice, at 0.0, 0.1, 0.2, 0.4%, drinking water

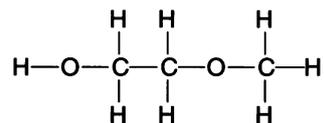
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Ethylene glycol monomethyl ether (EGME), a common chemical and solvent used in industry and in consumer goods, was tested for reproductive toxicity in Swiss CD-1 mice using the RACB protocol (Morrissey et al., *Fundam Appl Toxicol* 13(4):747-777 [1989]). It was part of a series of glycol ethers and congeners evaluated for structure-activity correlations using this design. In a preliminary study using concentrations of 0.5% to 2.0% EGME in drinking water, all treated mice were infertile. Thus, follow-up study was designed to more accurately define the dose-response curve. Data from the previous study, plus body weights, clinical signs, and food and water consumption during the dose-range-finding segment (Task 1) were used to set concentrations for the main study (Task 2) at 0.1, 0.2, and 0.4% EGME in drinking water. These concentrations produced calculated consumption estimates of approximately 159, 336, and 619 mg/kg/day.

During Task 2, 1 male died in the control group, and 2, 1, and 4 females died in the control to high dose EGME groups, respectively. Only 1 of the remaining 16 high-dose pairs had a litter, while the fertility rate in the other groups was unchanged

by EGME consumption. Female body weight during Task 2 was reduced, which reflects the lack of pregnancy-induced body weight increases. The number of litters per pair was reduced by 30% at 0.2% EGME, while the number of live pups per litter was reduced by 18 and 77% in the low dose and middle dose groups, respectively. No live pups were delivered at 0.4% EGME. Pup weight adjusted for litter size was reduced by 6% in the middle dose group. Cumulative days to litter was increased for all litters at all doses; for the 0.1 and 0.2% EGME groups, the last litter was delivered 8 and 11 days after the controls, respectively.

The middle dose group was used in a Task 3 crossover to determine the affected sex. There was a 66% reduction in pups delivered to treated females, and the pup adjusted body weight was reduced by 6%. No adverse effects were seen in litters of treated males. After delivery and assessment of the litters, these F_0 mice were killed and necropsied. Body and organ weights were unaffected by 0.2% EGME consumption, but estrous cycle length was increased from 4.85 days (controls) to 5.63 days.

For a second generation mating, there were only sufficient mice from the 0.1% EGME group. Thus, F_1 mice from the last

litter of the control and 0.1% EGME groups were reared to mating at 74 ± 10 days of age. Only 5 of 20 EGME pairs mated and only 2 of 20 bore a litter (versus 19 of 20 for controls for both end points). In those two litters, 75% of the pups were live-born (vs 99% for controls). Other changes were not significant, probably due to the low number of animals involved.

After litter delivery and subsequent vaginal lavage, the F_1 mice were killed and necropsied. While female body weight was unchanged by 0.1% EGME consumption, adjusted liver weight was reduced by 11%. In males, no body weight difference was found, but EGME consumption reduced weights of seminal vesicles, epididymis and prostate by 11, 12, and 20%, respectively. Epididymal sperm parameters and estrous cycle length were unchanged by 0.1% EGME exposure.

In summary, these concentrations (0.1-0.4%) of ethylene glycol monomethyl ether produced marked reductions in fertility and reproductive indices, while leaving body weights unchanged. Because of the reduced liver weight in the F_1 females, it must be concluded that the reproductive effects seen in this study occurred in the presence of some somatic toxicity.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

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Chemical: Ethylene Glycol Monomethyl Ether

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Mode of exposure: Drinking water

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	0.1%	0.2%	0.4%
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, ↓
Kidney weight ^a		•, •	—, —	•, •
Liver weight ^a		•, •	—, —	•, •
Mortality		—, —	—, —	—, —
Feed consumption		•, •	•, •	•, •
Water consumption		—, —	—, —	—, —
Clinical signs		—, —	—, —	—, —

Reproductive toxicity				
x litters/pair		—	↓	↓
# live pups/litter; pup wt./litter		↓, —	↓, ↓	↓, ↓
Cumulative days to litter		↑	↑	↑
Absolute testis, epididymis weight ^a		•, •	—, —	•, •
Sex accessory gland weight ^a (prostate, seminal vesicle)		•, •	—, —	•, •
Epidid. sperm parameters (#, motility, morphology)		•, •, •	—, —, —	•, •, •
Estrous cycle length		•	↑	•

Determination of affected sex (crossover)		Male	Female	Both
Dose level		—	0.2%	—

F ₁ generation	Dose concentration →	0.1%	•	•
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		—	•	•
Mortality		—	•	•
Adult body weight		—, —	•	•
Kidney weight ^a		—, —	•	•
Liver weight ^a		—, ↓	•	•
Feed consumption		•	•	•
Water consumption		—, —	•	•
Clinical signs		—, —	•	•

Reproductive toxicity				
Fertility index		↓	•	•
# live pups/litter; pup wt./litter		—, —	•, •	•, •
Absolute testis, epididymis weight ^a		—, ↓	•, •	•, •
Sex accessory gland weight ^a (prostate, seminal vesicle)		↓, ↓	•, •	•, •
Epidid. sperm parameters (#, motility, morphology)		—, —, —	•, •, •	•, •, •
Estrous cycle length		—	•	•

Summary information	
Affected sex?	Both
Study confounders:	None
NOAEL reproductive toxicity:	Couldn't determine
NOAEL general toxicity:	Couldn't determine
F ₁ more sensitive than F ₀ ?	Yes
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.