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# Methacrylamide

CAS #79-39-0

Swiss CD-1 mice at 0, 24, 80, 240 ppm, drinking water

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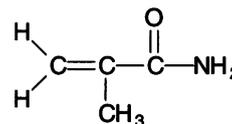
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Methacrylamide (MACR), a congener of acrylamide, was tested for reproductive toxicity, neurotoxicity, and dominant lethal effects in Swiss CD-1 mice using the Continuous Breeding protocol. MACR was one of a series of structural congeners chosen to represent a varying degrees of reproductive and neural toxicities. MACR was previously reported to have more neurotoxicity than reproductive toxicity. A dose-range-finding study was used to identify concentration levels that were expected to produce only slight neurotoxicity: 0, 24, 80, 240 ppm in drinking water for up to 27 weeks. Water consumption was unchanged by MACR; consumption of MACR was calculated at approximately 4, 15, and 49 mg/kg for the  $F_0$  mice.

Methacrylamide induced no changes in fertility or pup end points at any dose in  $F_0$  animals. There were no treatment-related differences in body weights. Grip strength was variably changed and significantly (12%) increased in males at week 15. Consistent with the lack of reproductive effects in Task 2, MACR produced no change in the dominant lethal test after Task 2. In the absence of detectable effects on fertility end points, Task 3 (crossover mating to determine the affected sex) was not conducted. At necropsy, sperm concentration was reduced by 21% at 80 ppm, and sperm motility was reduced by approximately 42% at 240 ppm.

In the  $F_1$  animals, there was slight neurotoxicity at postnatal day 21, measured as

decreases in forelimb grip strength in males (26–29%) and hindlimb grip strength (12–31%). These decrements in grip strength were not apparent by week 5, nor were they seen again as the animals matured. At cohabitation at approximately postnatal day 74, male body weights were significantly reduced approximately 5% in all treated groups. In the  $F_1$  mating trial, there were no treatment-related effects on any reproductive end point, nor were any necropsy end points meaningfully altered.

In summary, methacrylamide at these concentrations was without effect on  $F_0$  body weights, neurotoxicity, or reproduction, and had only transient effects on body weight and grip strength in  $F_1$  mice, with no alterations in fertility of the  $F_1$ s.

METHACRYLAMIDE

**Summary:** NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: 93149284

Chemical: Methacrylamide

CAS#: 79-39-0

Mode of exposure: Water

Species/strain: Swiss CD-1 mice

F <sub>0</sub> generation	Dose concentration →	24 ppm	80 ppm	240 ppm
		Male, female	Male, female	Male, female
General toxicity				
Body weight		↓, —	—, —	—, —
Kidney weight <sup>a</sup>		↑, —	—, —	—, —
Liver weight <sup>a</sup>		—, —	—, —	—, —
Mortality		—, —	—, —	—, —
Feed consumption		—, —	—, —	—, —
Water consumption		—, —	—, —	↑, ↑
Clinical signs		—, —	—, —	—, —

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

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

F <sub>1</sub> generation	Dose concentration →	24 ppm	80 ppm	240 ppm
		Male, female	Male, female	Male, female
General toxicity				
Pup growth to weaning		—, —	—, —	—, —
Mortality		—, —	—, —	↓, —
Adult body weight		↓, —	↓, —	—, —
Kidney weight <sup>a</sup>		—, —	—, —	—, —
Liver weight <sup>a</sup>		—, —	—, —	—, —
Feed consumption		—, —	—, ↑	↑, —
Water consumption		—, —	—, —	↓, —
Clinical signs		—, —	—, —	—, —

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

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	240 ppm
NOAEL general toxicity:	24 ppm based on the decrease in male F <sub>1</sub> body weights, which demands replication.
F <sub>1</sub> more sensitive than F <sub>0</sub> ?	Yes. Based on the decrease in male F <sub>1</sub> body weights.
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. <sup>a</sup>Adjusted for body weight.