
Acrylamide

CAS # 79-06-1

Swiss CD-1 mice, at 0, 3, 10, and 30 ppm, drinking water

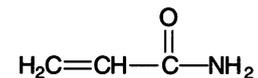
Jerrold J. Heindel, NTP/NIEHS Project Officer

Patricia A. Fail, Julia D. George, and Thomas B Grizzle,

Research Triangle Institute

Started 2/27/90; Completed 1/11/93

NTIS # 93158285



Acrylamide monomer (ACRL), used in the production of polyacrylamide, was tested in a RACB protocol in Swiss CD-1 mice to compare the relative predominance of neurotoxicity and germ cell toxicity (dominant lethality), and to evaluate reproductive effects in females (Chapin et al., *Fundam Appl Toxicol* 27:9-24 [1995]). In addition to the standard RACB end points, a dominant lethal test was performed using the F₀ males after approximately 20 weeks of ACRL treatment. For the dominant lethal test, each male was cohabited with three 11-week-old virgin females, and the male's reproductive "output" was averaged over these three females. Additionally, forelimb and hindlimb grip strength tests were administered at various times to detect neurotoxicity in the F₀ animals. A dose-range finding study was used to help identify doses

for the main study that were relatively low, to prevent debilitating neurotoxicity: 0, 3, 10, and 30 ppm in drinking water for 27 weeks. The 30-ppm dose for the F₀ mice resulted in slight reproductive toxicity (10% decreased pups per litter) and increased postimplantation loss (dominant lethal effect) in the absence of demonstrable neurotoxicity for the F₀ animals. At necropsy, the F₀ mice showed no dose-related changes in somatic or reproductive organ weights, or sperm indices. While there was a 10% decrease in the number of homogenization-resistant testicular spermatid heads in the 10- and 30-ppm groups, this was not reflected in epididymal sperm end points. There were no effects on estrous cyclicity or on female fertility evaluated during the Task 3 crossover segment. There were no effects on grip strength, and no detectable

alterations in sural or gastrocnemius nerve histology at the light microscope level.

In the second generation, the 30-ppm F₁ animals were more severely affected than their F₀ parents, with a 47% decrease in pups per litter in the presence of slight neurotoxicity (a 10% decrease in forelimb grip strength seen only at postnatal week 10 in males). There were no other treatment-related effects on fertility, pup weight, organ weights, sperm indices, or estrous cyclicity in the F₁ mice. Despite the slight effect on grip strength, there were no light-level histologic alterations in sural or gastrocnemius nerve histology.

In summary, acrylamide monomer produced dominant lethal reproductive effects in males (reduced live pups, increased resorptions) at exposure levels below those which caused neurotoxicity.

ACRYLAMIDE

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: 93158285

Chemical: Acrylamide

CAS#: 79-06-1

Mode of exposure: Water

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	3 ppm	10 ppm	30 ppm
		Male, female	Male, female	Male, female
General toxicity				
Body weight		—, —	—, —	—, —
Kidney weight ^a		↑, —	—, —	—, —
Liver weight ^a		↑, —	—, ↑	—, —
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 ^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	30 D L	—	—

F ₁ generation	Dose concentration →	3 ppm	10 ppm	30 ppm
		Male, female	Male, female	Male, female
General toxicity				
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?	Male
Study confounders:	None
NOAEL reproductive toxicity:	10 ppm
NOAEL general toxicity:	30 ppm
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.