Methyl Salicylate

CAS #119-36-8
Swiss CD-1 mice, at 0.0, 100, 250, and 500 mg/kg by gavage
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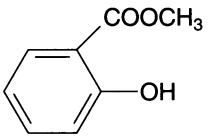
NTIS #PB85164283/AS



Methyl salicylate (MS) is used as a fragrance and flavoring agent, but is lethal at sufficient doses and is teratogenic in rodents. MS was tested to update and expand the reproductive toxicity database, and used, in part, as a known positive: it was simultaneously tested by two different laboratories at different doses, using the RACB protocol and Swiss mice (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). Food and water consumptions, clinical signs, and body weights were used in the Task 1 dose-range-finding study to set doses for the continuous cohabitation phase (Task 2) at 100, 250, and 500 mg/kg/day by gavage in corn oil.

Deaths occurred at a rate of three, two, two, and four mice per group in the control to high dose groups, respectively. The causes of death varied and were ultimately not considered because of MS exposure. There were no effects of MS exposure on body weights during Task 2.

There was a 9% reduction in the mean number of litters per pair at the high dose and a 31% reduction in the number of live pups per litter (from a control value of 11.3, to 7.8 pups per litter). While the viability and sex ratio of these pups was not altered, the pup weight adjusted for litter size in the middle and high dose groups was decreased by 3 and 6%, respectively. MS exposure increased the time to deliver each litter in the high dose group, starting with the second litter, by 2 to 3 days.

These effects led to Task 3 in an attempt to define the affected sex using the control and high dose groups. MS exposure caused no discernible effects on the proportion of pairs mating or delivering pups, nor on the number, viability, or adjusted weight of those pups. Because only 5 of 17 control × control pairs delivered any young, Task 3 was repeated. Though 7 of 17 pairs delivered young, the same lack of MS effects were observed as in the first trial.

It was decided that the animals should be killed and discarded. No necropsy was performed, and the second generation was not evaluated.

In summary, MS exposure, at dose levels that did not alter body weight or produce adverse clinical signs, adversely affected reproduction (reduced numbers of litters per pair, and number of pups per litter) in Swiss CD-1 mice.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85164283/AS**
Chemical: **Methyl Salicylate**
CAS#: **119-36-8**
Mode of exposure: **Gavage**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	100 mg/kg	250 mg/kg	500 mg/kg
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			
x̄ 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	—	—	—

F_1 generation — Dose concentration →	•	•	•
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?	Unclear
Study confounders:	None

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