
Diethylstilbestrol

CAS #56-53-1

Swiss CD-1 mice, at 0.0, 1.0, 10.0, and 50.0 PPB in feed

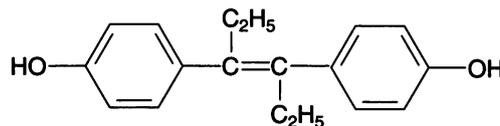
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NTIS #PB84136746



Diethylstilbestrol (DES), the least expensive and most widely used estrogen, was tested in Swiss CD-1 mice using the RACB protocol (Lamb et al., *J Am Coll Toxicol* 4(2):173-184 [1985]). This study was one of the first RACB studies conducted. DES was chosen as a known positive based on the extensive literature by MacLachlan and colleagues. There were two laboratories beginning to run RACB studies, and a DES study was performed at each of these laboratories to address the issue of interlaboratory variability. From the dose-range-finding study (Task 1), levels of 1.0, 10.0 and 50.0 ppb in feed were selected for the continuous breeding phase of the study. The estimated average

doses were approximately 0.15, 1.5, and 7.70 $\mu\text{g}/\text{kg}/\text{day}$.

No clinical signs were noted in Task 2. One male and seven females died across the groups, with no apparent relation to dose.

In the high dose group, the number of litters per pair was reduced from 4.8 (control) to 1.2, while the number of live pups per litter was reduced to approximately 20% of the control value. Adjusted pup weights in the high dose group were increased by approximately 10%.

Since adverse effects on fertility and reproduction were observed in Task 2, Task 3 was conducted to identify the affected sex, using the control and high dose groups. In the group with DES-exposed

females, the number of live pups per litter decreased by 85%. The fertility and reproductive indices of treated males were entirely unaffected.

After Task 3, the F_0 control and high dose DES females were killed and necropsied. Female body weight was reduced in the treated mice by approximately 10%; no other weight changes were noted in females. The estrous cycle was not evaluated, and males were not necropsied.

Task 4, the F_2 generation assessment, was not conducted.

This study provided a foil to set up and optimize procedures at the laboratory, and showed again that diethylstilbestrol reduced the fertility of female mice.

DIETHYLSTILBESTROL

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB84136746

Chemical: Diethylstilbestrol

CAS#: 56-53-1

Mode of exposure: Feed

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	1 PPB	10 PPB	50 PPB
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				
\bar{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		—	50 PPB	—

F ₁ generation	Dose concentration →	1 PPB	10 PPB	50 PPB
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?	Female
Study confounders:	Incomplete necropsy
NOAEL reproductive toxicity:	10 ppb
NOAEL general toxicity:	50 ppb
F ₁ more sensitive than F ₀ ?	Unknown
Postnatal toxicity:	Unknown

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