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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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DATE: May 1, 1978

SUBJECT: Three-generation Reproduction Study with Pydrin (SD-43775) Caswell# 77A

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Recommendations

1. The three-generation reproduction study in rats with pydrin (SD-43775) is acceptable as core-minimum data. The NOEL for reproductive parameters is considered to be 250 ppm. The NOEL for systemic toxicity in the parents is considered to be 25 ppm based on the reduced mean body weight of the F2b parents at the high dose level.

2. The Determination of SD-43775 in the hamster diet shows that diet preparation was prepared according to specifications.

Review

Three-generation Reproduction Study in Rats (LBI Project No. 2540, final report submitted Oct. 24, 1977, revised Feb. 1978)

Test Material: SD-43775 Technical, Code 6-1-0-1; golden brown, highly viscous liquid, 98%

The test material was incorporated into the diet of weanling rats (Sprague-Dawley origin) for nine weeks prior to selection of the (F_0) parent generation. The experimental design and dose levels are outlined below for the F_0 generation:

Group No.	Number of Rats Male	Female	Dietary level ppm
1 (Vehicle control)	11	22	0
2	11	22	1
3	11	22	5
4	11	22	25
5	11	22	250

Two females and one male from the same treatment group were housed together for mating and a similar arrangement was implemented for succeeding generations as follows:

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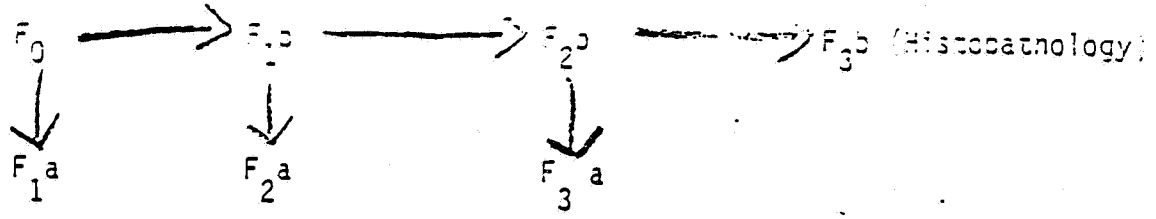
EPA FORM 1320-6 (REV. 3-76)



The following information was collected on each litter: Date of delivery, abnormalities at birth, live and dead pups - Days 1, 5 and 21, Sex ratio - Day 1, 5 and 21, Body Weights by litter - Day 1 and 21, general appearance throughout nursing. At least 10 males and 10 female F_{3b} weanlings from each treatment group were necropsied. All parent generations were necropsied. From the F_{3b} weanlings, the brain, heart, liver, and kidneys were weighed. These plus the following tissues were preserved in 10% buffered formalin:

thyroid
spleen
adrenal gland
testes
uterus
small intestine
lung
prostate
pancreas
mesenteric lymph nodes
ovaries
oviduct
stomach

Tissues from 10 male and 10 female weanlings of each dose group were submitted to A.A. Stein, M.D., Microscopy for Biological Research, LTD, Albany, N.Y., for histopathologic evaluation:

Results: Samples of prepared experimental diets were periodically sent to the Sponsor for chemical analysis of the test compound. Results are summarized below:

Desired Dose Level (ppm)	Actual (ppm)	Range (ppm)	Sample size
1	1.2	0.67-2.6	26
5	5.1	4.2-8.5	18
25	25.0	14.0-49.0	19
50	260.0	10-310	19

First generation (Parents F_0 - Offspring F_1a and F_1b)

No remarkable effects noted in F_0 parents at treatment or necropsy. No effect on reproductive parameters in F_1a and F_1b litters, except an apparent decreased fertility in females at 1 ppm dose level. However, this effect showed no dose response relationship in the higher treatment groups during the F_1 generation.

Second generation (Parents F_1b - Offspring F_2a + F_2b)

The general appearance and behavior of the parent rats of the second generation were judged to reflect no compound - related effect. The necropsy of the F_1b parents demonstrated a frequency of kidney changes (mottled, pale appearance) suggestive of a compound - related response, no effect on reproductive parameters in F_2a and F_2b litters except an apparent decrease in female fertility of the low level (1 ppm) test group. Since a dose - response relationship was not involved, this reduced reproductive capacity was not judged to be compound induced.

Third generation (Parents F_2b - Offspring F_3a and F_3b)

The mean body weights of the parents of the third generation (F_2b adults) revealed a significant reduction at the high level (250 ppm) when control and treated groups were compared. The necropsy of F_2b parents revealed gross kidney changes similar to changes noted in the F_1b parents. However the distribution with regard to dose was not judged to be consistent with a compound - related change. No effect on reproductive parameters in the F_3a and F_3b litters except an apparent decrease in female fertility of the low level (1 ppm) test group. Since a dose-response relationship was not involved, this reduced reproductive capacity was not judged to be compound induced. Histopathological examination of the F_3b weanling was unremarkable.

Conclusion: The NOEL for reproductive parameters is considered to be the high-dose level (250 ppm). The NOEL for systemic toxicity of the parents is considered, from the evidence of body weight loss of the F_2b parents, to be 25 ppm. The systemic toxicity effect observed in the F_2b parents is evidence that the highest dose level produced a toxic effect.

Classification: Core-Minimum Data

Typists:TH
RD initial G.E.Whitmore 4/26/78

E for GEW 5/8/78