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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MAR 29 1982

DATE: March 16, 1982

SUBJECT: Review of a Mutagenicity Study on Di-syston. EPA Reg. No. 3125-183. Acc. No. 246161. Tox Chemical No. 341

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Action Requested

A review of a dominant lethal study in mice submitted by Mobay Chemical Corporation to replace a study conducted by Industrial Bio Test (IBT).

Citation

Herbold, B. 1980. Dominant lethal study on male mouse to evaluate S-276 for mutagenic potential. Unpublished and proprietary report. Bayer AG. Institute fur Toxicologie. Report No. 9440. EPA Acc. No. 246161.

Test Substance: Disyston®. (O,O-diethyl S[2-(ethylthio)-ethyl idisulfuton) phosphorodithioate). 94.9% pure. Batch 9049/74.

Test Species: NMRI/ORIG Kislegg strain mice.

Experimental Procedure: A preliminary evaluation of the toxicity of disulfaton was conducted to determine the dose to be used in the main experiment. Single doses of 3 or 5 mg/kg were administered by gavage, and the authors reported that the effects observed were mild. No further details regarding the effects were given. The test substance was administered in aqueous Cremophor (0.5%) emulsion.

A single 5 mg disulfaton per kg body weight dose was given to the treatment group, while the untreated control mice received an equal volume of emulsion without disulfaton. Each group contained 50 males which were placed with virgin untreated female mice for a four day mating period. At the end of the first mating period females were replaced. There were 12 consecutive matings covering the 48 days following dosing.

Fourteen days after their mating period females were sacrificed and examined. Corpora lutea and implantation sites were counted. The number of viable implants and dead implants (sum of decidiomata, resorptions and dead embryos) were also recorded.

Total and dead implant data were transformed using square roots, and the angular transformation was used for the ratio of dead to total implants. These transformed data were subjected to analysis of variance, Dunett's or Tukey's tests where appropriate to determine statistical significance of differences. Frequency distributions for the parameters measured were also analyzed with the Komogorov-Smirnov test.

Reported Results: The author reported no effect on the fertility index (number of pregnant females per number mated multiplied by 100) or post implantation losses (sum of deciduomata, resorptions, and dead embryos divided by the total number of implants which is then multiplied by 100). The reported results (overall group means and ranges from 12 mating periods) are summarized as follows:

Parameter	Control	Treated
Fertility (%)	73.7 (64-82)	73.8 (60-85.7)
Corpora lutea*	10.9 (10.2-11.4)	11.0 (10.3-11.5)
Implantations*	10.5 (9.5-11.1)	10.7 (10.1-11.3)
Pre-implantation losses*	0.36 (0.08-0.76)	0.31(0.16-0.62)
Viable implants*	9.9 (9.2-10.6)	10.0 (9.3-10.5)
Dead implants*	0.60 (0.25-1.27)	0.68 (0.27-1.57)

*Per female

Discussion: The data presented in this experiment support the conclusions of the author that the test chemical does not cause dominant lethal mutations at a dose of 5 mg/kg in mice. However, the toxicological significance of the results is unclear since only one dose level was used and no positive control data were presented.

Conclusion: The study is an acceptable replacement for the invalid IBT study. However, because of the limitations mentioned above, this study cannot be evaluated by itself. According to Toxicology Branch files there are no other mutagenicity studies on Disyston. Therefore, this study alone does not satisfy minimal genetic toxicity testing needs including those for bacterial or mammalian cell point mutation chromosome damage, or DNA repair effects.

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