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CASWELL FILE

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OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No. 2097-11: Mycodex® Pet Shampoo with Allethrin. Mutagenicity study with the active ingredient.

TOX CHEM No. 25 and 25A

FROM: J.D. Doherty *J.D. Doherty 9/3/85*  
Toxicology Branch, HED (TS-769)

TO: T.A. Gardner, PM #17  
Registration Division (TS-767)

THRU: E.R. Budd, Section Head  
Toxicology Branch, HED (TS-769)

*Budd 9/3/85*  
*Heffner 9/3/85*  
*al/10/85*

The Beecham Laboratories (Bristol, Tenn.) has submitted an article from the literature reporting that allethrin, the active ingredient of their product Mycodex® Pet Shampoo, is mutagenic in a chromosome aberration test. The study was previously reviewed by Dr. M. Sochard of Toxicology Branch along with other mutagenicity data submitted separately by the manufacturer. A copy of Dr. Sochard's review of this study as it was included in a memo addressing the mutagenicity of allethrin (refer to EPA File No. 1021-1217, dated August 7, 1985, addressed to Adam Heyward, PM Team #17) is attached. In this memo Dr. Sochard indicated that allethrin was also found to be potentially mutagenic in other test systems and additional mutagenicity studies were requested from the McLaughlin Gormley King, Company the manufacturer of allethrin.

Additional comments on the mutagenicity of allethrin and how this may relate to product registrations will be made pending receipt and review of the additional mutagenicity studies requested by Dr. Sochard.

Note to PM:

The registrant also indicated that they wish to amend the formula for this product by changing from a 90% technical material which contains 8 isomers to a 93% technical preparation of d-trans-allethrin containing only 2 isomers.

TB has little or no toxicity data on the 93% d-trans-allethrin material. It should be recognized, however, that the purer d-trans-allethrin would be expected to be more toxic than the technical material containing 8 isomers. Registrations of products containing the new 93% technical material should be supported by toxicity studies using this material. The studies required will depend upon the proposed use pattern and expected exposure. As related to a pet shampoo product, such toxicity data requirements for the technical material may include but not be limited to teratology studies. Studies with the formulated product should include five acute toxicity studies to support the label signal word and precautionary statements, a dermal sensitization study and a 21 day dermal study.

2. Matsuoka, A.; Hayashi, M.; Ishidate, M. Jr. (1979)  
Chromosomal Aberration Tests on 29 Chemicals Combined with  
S-9 In Vitro. Mutation Research, 66:277-290. Submitted as  
part of Accession No. 252029.

Protocol:

A group of 29 chemicals which included allethrin, was assayed in CHL cells (chinese hamster lung cells) following treatment with S-9 mix. Test chemicals were assayed at three different doses of each, with cell cultures and chemicals incubated with shaking at 37 °C for 3 hours. Cells were then cultured in 6-cm culture dishes for 24 hours longer. Cells were colcemid treated, prepared for microscopic examination on microscope slides, and stained with Giemsa stain. One hundred well spread metaphases were counted. Chromosome aberrations were classified as follows: chromatid gaps, chromatid breaks, chromatid or chromosomal exchanges, ring formation and fragmentation, or pulverization of chromosomes. Polyploidy was also sought and recorded. Results were recorded as negative if less than 4.9 percent aberrations were seen including at high doses tested even if at sublethal concentrations.

A (+) was assigned to aberrations between 5.0 and 9.9 percent (suspicious). A positive was assigned if aberrations were at 10 to 19.7 percent (+); 20 to 49.9 percent (++) and more than 50 percent was assigned (+++). Controls included untreated and solvent-treated cells.

Results:

In the above system, with S-9 mix, allethrin was a strong positive (+++); at the 77 percent level, with chromatid gaps, chromatid breaks, chromatid or chromosome exchanges, fragmentation pulverization of chromosomes and ring formation seen at a dose-level of 0.0019 mg/ml (no other dose level results given). The conclusion was that under the circumstances reported, allethrin is mutagenic with S-9 mix. Since results are reported only for one dose level of allethrin, the study is considered unacceptable for regulatory purposes.

Core Category - Not acceptable.