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

SEP 20 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: IMAZALIL SULFATE: EVALUATION OF SUPPLEMENT TO MRID 42593601 EMBRYOTOXICITY AND TERATOGENICITY STUDY IN ALBINO RABBITS

Barcode D 200774
S 460954
Chemical 111901
Tox Chem No. 497AB

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KB 9/14/94

ACTION: Review the submitted information in MRID 43154201 for up grading the Study in Albino Rabbits (GL 83-3).

CONCLUSIONS:

1. The data submitted have been arranged in the order of the points in question in the review by M. Ottley in memo dated Sept. 16, 1993 transmitted by J.C. Redden.

2. The study deficiencies have been adequately addressed to allow the study to be up graded to CORE: MINIMUM. The maternal NOEL and LOEL remain unchanged at 5 mg/kg and 10 mg/kg day respectively based on minimal changes (decreased body weight gain) in body weights at (1)

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5 mg/kg/day.

3. The study was stated by the registrant to have been conducted using several guidelines other than the EPA guidelines as the means with which to establish a protocol for this study

TOXICOLOGY BRANCH I EVALUATION:

Q. 4. An issue of excessive toxicity to treated does at the 20 mg/kg dose level (HDT) was raised. It was stated that this did not allow for the survival of sufficient numbers of does or fetuses at the highest dose for evaluation.

A. 4. The registrant has submitted the data from the range finding study # 2372 which was performed from Sept. 18, 1990 to Oct. 15, 1990 to support the choice of test doses in the main developmental toxicity study # 2615. Data submitted on the range finding study indicated that minimal toxicity (reduced body weight in 2 of the 4 animals tested) was observed at the lowest dose tested (20 mg/kg). Additionally, Toxicology Branch 1 concludes that since evaluation of the lower test dose groups in the main developmental study was possible despite excessive mortality at a higher dose, the study can be evaluated for that toxicity and NOELs and LOELs for maternal and developmental toxicity can be determined.

This issue has been adequately addressed.

Q. 5. There was an issue of individual fetal data on skeletal malformations not being reported in such a way that the total number of fetuses/group with effects could be determined.

A. 5. Toxicology Branch finds that data submitted by the registrant to address these questions are essentially the same as were presented in the review (HED document #010581). However, even though the data do not indicate which of the fetal skeletal variations may have been double counted, there was no statistically significant increase at the low or high dose in the total number of fetuses and the total number of litters with any particular variation relative to controls. Interpretation of the skeletal variations at the high dose was hampered by the low number of litters (4) surviving. There was no treatment related increase in visceral variations or skeletal malformations at any dose. In addition, the OECD guidelines do not provide any type of format for reporting of this type of data. Toxicology Branch does

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not consider this lack of reporting to be detrimental in the ability to draw conclusions from the data in this study.

This point has been adequately addressed.

Q. 6. There was a question of why maternal body weight change recordings were only reported on days 0, 6, 19, and 27.

A. 6. The registrant followed the OECD guidelines which do not require any specific time period for reporting the resulting body weights excepting that they must be reported. Therefore, the data are adequate for this specific chemical since an LEL and NOEL can be determined from the study.

This question has been adequately addressed.

Q. 7. There was a question of why clinical observations were being reported only for the periods of GDs 0-5, 6-18, and 19-27 and not on a daily basis.

A. 7. The registrant reported that the data had been taken daily but was only recorded into the computer at the end of the different periods of 0-5, 6-18 and 19-27 days. Toxicology Branch notes that the effects reported in the various time periods appear to be dose related. A NOEL and LEL can be ascertained from the study for these effects.

This question has been adequately addressed and does not affect the final disposition of the study .

Q. 8. There was a question concerning the omission of the age of the animals, breed, or how they were assigned to groups, and temperature, humidity, of the caging area.

A. 8. The registrant has supplied additional information indicating that the breed of rabbit used was the New -Zealand Cunistar- MDL strain from Buyens; Lichtaart. The animals were assigned to the different groups by descending body weights by C, L, M, H, H, M, L, C, L, etc.assignment.

Relative humidity was maintained between 54 and 69 % and temperature remained between 19 and 23 C during the experiment.

This question has been adequately addressed.

Q, 9. There was a question of why the uteri were not stained in attempts to account for possible early fetal losses.

A. 9. The registrant points out the staining of rabbit uteri is ineffectual and that early resorptions are best evaluated using macroscopic observations of the uterus.

This question has been adequately addressed.