CASE PM

CHEM Chlorsulfuron

002636

BRANCH TB DISC TOPIC 90-Day Feeding - Mouse

FORMULATION Technical

FICHE/MASTER ID CONTENT CAT

Ninety-Day Range-Finding Feeding Study With 2-Chloro-N-[(4-Methoxy-6-Methyl-1,3,5-Triazin-2-Yl)Aminocarbonyl] Benzenesulfonamide (INW-4189) In Mice, Haskell Laboratory Report No. 69-80, Smith, L. W.

SUBST. CLASS =

OTHER SUBJECT DESCRIPTORS

DIRECT RVW TIME = 2 1/2 hours START-DATE END DATE

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Conclusion:

A. Core Supplementary (species tested)
B. A NOEL of 2500 ppm based on lower erythrocyte and higher MCU and MCH in males and fewer neutrophols and more lymphocytes in females was found when technical chlorsulfuron was fed to mice for 90 days at dietary levels of 0, 500, 2500, 5000, or 7500 ppm. No gross pathologic findings were observed in any test level. No histopathologic findings that could be attributed to chlorsulfuron were found in the 7500 ppm level, the only dose level evaluated.
C. This study provides supplemental information and is not needed to satisfy EPA Proposed Guidelines. It was run to evaluate subchronic toxicity and to establish appropriate levels for two-year mouse study. It generally follows the guideline in Section 163.82-1 Subchronic Oral Dosing Studies (43 Federal Register 37363, 8/22/78).

Methods:

Sixty two male and sixty-two female weanling ChR-CD®-1 mice were received and evaluated during an 11-day pretest. Fifty mice of each sex were selected on the basis of weight gain and freedom from clinical signs of disease and divided by randomization into five groups of ten males and five groups of ten females and housed individually. Groups were fed ground Purina® Laboratory Chow diets containing 0, 500, 2500, 5000, or 7500 ppm chlorsulfuron for about 90 days. Mice were examined daily for any abnormal behavior or clinical signs of toxicity. Mice were weighed once a week and group diet conumption was measured weekly. Food efficiency and dose were calculated. Mortality was recorded.

Hematological exams were run on all mice after 87 days. This included hemoglobin concentration, hematocrit, erythrocyte count, leukocyte count, and differential leukocyte count. Mean corpuscular hemoglobin, mean corpuscular volume and mean corpuscular hemoglobin concentrations were calculated. Alkaline phophatase, SGPT, and SGOT activities, total protein, BUN, and plasma creatinine were scheduled on all animals after approximately 90 days. Of this series only the total protein was determined because of equipment malfunction. After 91 and 92 days on test surviving mice were subjected to gross pathological examinations. The brain, heart, liver, kidneys, and testes were weighed. Microscopic examination of tissues from the control and high dose group included the following: stomach, duodenum, jejunum, ileum, cecum, colon, pancreas, liver, gall bladder, kidney, heart, brain, esophagus, spleen, bone marrow, thymus, testis, epididymis, urinary bladder, seminal vesicle, prostate, lung, eye, lymph node, thyroid, salivary gland, trachea, adrenal ovary, uterus, skin and medinstinal tissue.

Results:

The final body weights of male mice fed 2500 or 7500 ppm were significantly lower (6%) than those of the control males. Due to the small magnitude of this difference and the absence of a dose-response relationship, this effect was not considered biologically significant. No significant differences between control and treated groups were found in body weight gains, food consumption, and food efficiency. Except for slight, transient weight loss, there were no clinical signs of toxicity. The only mortality

was one 500 ppm male mouse which died on day 87 during hematological examination. Death was not considered compound-related. Male mice fed 5000 or 7500 ppm had significantly lower erythrocyte counts than control males; thus mean corpuscular volumes and mean coruscular hemoglobins were higher in these mice. Female mice fed 5000 or 7500 ppm had significantly fewer nertrophilic granulocytes and more lymphocytes than control females. No effects were seen in the 500 or 2500 ppm levels. Variations in absolute and/or relative liver, brain and heart weights in the 2500 5000, and 7500 ppm levels were not considered compound-related in the absence of pathological effects in these organs. Gross pathological findings at all feeding levels and mircroscopic findings in mice fed 7500 ppm were considered to be spontaneous or the result of intercurrent disease. The NOEL was 2500 ppm based on lower erythrocyte and higher MCV and MCH in males and fewer neutrophils and more lymphocytes in females compared to controls.

	Male - 3 Months		
Dose, ppm	Erythrocytes, X 10^6/mm^3	MCU, U3	MCH NG
0	7.45	74	23
500	7.47	76	23
2500	7.20	75	24
5000	6.79	82	25
7500	6.84	81	25

	Female - 3 Months	
	Neutrophils, %	Lymphocytes, %
0	19	79
500	14	85
2500	21	78
5000	15	84
7500	14	85

Discussion:

The methods, materials, scientific prinicples, validity of conclusions, and adequacy of data for conclusions were adequate for the study. Liver and brain relative organ weight effects reported in the Results section appear to be reversed, but this does not affect the validity of the study since they are not considered to be compound-related.