

US EPA ARCHIVE DOCUMENT

CASE

PM

CHEM Chlorsulfuron

002650

BRANCH TB

DISC

TOPIC 90-Day Feeding - Rat

FORMULATION Technical

FICHE/MASTER ID

CONTENT CAT

Ninety-Day Feeding Study With 2-Chloro-N-[(4-Methoxy-6-Methyl-1,3,5-Triazin-2-Yl)Aminocarbonyl]Benzenesulfonamide (INW-4189) In Rats, Haskell Laboratory Report No. 80-80, Wood, C. K.

SUBST. CLASS =

OTHER SUBJECT DESCRIPTORS

DIRECT RVW TIME =

3 1/2 hours

START-DATE

END DATE

REVIEWED BY: J. C. Summers

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DATE: November 11, 1980

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TITLE:

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DATE:

Conclusion:

- A. Core Minimum (Number of animals tested; 10 vs. 20 rats/sex/dose).
- B. A NOEL of 100 ppm based on decreased urine pH in males was found when technical chlorsulfuron was fed to rats for about 90 days at dietary levels of 0, 100, 500, or 2500 ppm. No gross or histopathological abnormalities that could be attributed to chlorsulfuron were observed at any test level.
- C. This study generally conforms to EPA Proposed Guidelines in section 163.82-1 Subchronic oral dosing studies (43 Federal Register 37363, 8/22/78) with some modifications.

Methods:

Four hundred-seventeen male and four hundred twenty-one female rats were received from Charles River Breeding Laboratories, Wilmington, Massachusetts. Following an 11-day pretest, 40 rats of each sex, selected on the basis of weight gain, and freedom from any clinical signs of disease or injury, were divided by randomization into four groups of 10 males and 10 females and housed in pairs, sexes separate. Groups were fed ground Purina® Laboratory Chow diets containing 0, 100, 500, or 2500 ppm chlorsulfuron for about 90 days. Diets were prepared fresh weekly and stored under refrigeration until used. Rats received test diet and water ad libitum.

All rats were examined at least once daily for abnormal behavior and clinical signs of toxicity. Rats were weighed once a week and the amount of diet consumed by each group of rats was determined at each weighing interval. Mortality of rats was recorded. One, two, and three months after initiation of the study, all rats were subjected to clinical chemistry, hematological, and urine analytical examinations. Tail blood was evaluated for alkaline phosphatase, SGOT, and SGPT activities, BUN, creatinine, uric acid, glucose, and total plasma protein. Urine was examined for volume, pH, sugar, protein, bilirubin, urobilinogen, occult blood, color, appearance, and sediments. Blood was examined for erythrocyte, leukocyte, and differential leukocyte counts, hematocrits, and hemoglobin concentrations. Mean corpuscular hemoglobin, mean corpuscular volume, and mean corpuscular hemoglobin concentrations were calculated. Blood smears were prepared at the end of the study.

After 98 or 99 days, the survivors from all groups were sacrificed and necropsied. The brain, heart, spleen, thymus, stomach, pituitary adrenals, lungs, liver, kidneys, and testes were weighed and mean final body weights, organ weights, and organ to body weight ratios were calculated. The tissues noted above and the following tissues were examined microscopically for histopathologic changes: spinal cord, sciatic nerve, aorta, mesenteric vessels, femoral bone marrow, sternal bone with marrow, lymph nodes, eye, skin, skeletal muscle, salivary, and exorbital lacrimal glands, esophagus, duodenum, jejunum, ileum, cecum, colon, pancreas, thyroid, and parathyroid glands, trachea, urinary bladder, prostate, epididymis, mammary gland, ovary, uterus, vagina, and all gross lesions.

Results:

Mean body weights, weight gains, food consumption, and food efficiency were comparable between dose and control groups although a malfunction in the automatic watering device caused a temporary decrease in female body weights on day eighty-four. There was neither mortality nor compound-related clinical observations. Male rats fed 500 or 2500 ppm exhibited slight decreases in plasma creatinine, decreased urine pH and slightly increased hematocrits. Only the decrease in urine pH was considered related to the presence of chlorsulfuron, and it was considered of unclear biological significance. Female rats fed 2500 ppm exhibited slightly decreased erythrocyte counts. Glucose variations noted between test groups were not dose-related and thus were not considered compound-related. Gross pathological and histopathological examination of rats at all levels revealed no abnormalities or lesions that could be attributed to the dietary presence of chlorsulfuron. The no observable effect level was 100 ppm based on decreased urine pH in males.

MALE

<u>Dose,</u> <u>ppm</u>	<u>One</u> <u>Month</u>	<u>Two</u> <u>Month</u>	<u>Three</u> <u>Month</u>
0	7.75	7.55	6.92
100	6.83	7.70	6.71
500	6.64	6.90	6.34
2500	6.49	6.45	6.50

Discussion:

The methods and materials, scientific principles, validity of conclusions, and adequacy of data for conclusions were adequate for the study. Ten rather than twenty rats/sex/test group as noted in the guidelines were used in the study. This did not affect the validity of the study, particularly since no adverse effects were seen when all rats were examined histologically at all dose levels. Results of the 2-year rat feeding study, Report No. 557-81, also support the findings in this study.