PP-135
TXR-366

PP#003643

May 7, 1971

4(2-methyl-4-chlorophenoxy)butyric acid - MCPB

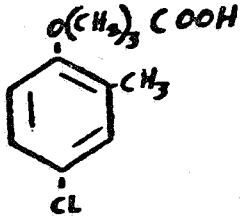
Mr. Drew M. Baker
Pesticides Tolerances Division

Pesticide Petition No. 1F1251

0.1 ppm peas (including pods)

Rhodia Inc.
Chipman Division
120 Jersey Avenue
New Brunswick, New Jersey

CHEMICAL DATA



DATA SUMMARY

Acute Rat Inhalation : LC_{50} = >100 mg/L

Acute Rabbit Dermal : LD_{50} = >1000 mg/kg

Acute Rabbit Eye Irritation: Moderate to severe irritation was produced.

90 Day Rat Feeding: Levels tested were 0, 4.0, 12, and 40 mg/kg/day. No effect level is 40 mg/kg/day (equivalent 800 ppm) or higher.

13 Week Dog Feeding: Levels tested were 0, 160, 480, and 1600 ppm. No effect level is 480 ppm.

Metabolism: MCPB is degraded to MCPA in plants and cows.

FINDINGS

A no effect subacute feeding in dogs demonstrated at 480 ppm; a no effect subacute feeding in rats demonstrated at 40 mg/kg/day (800 ppm).

SUMMARY

With the Petitions Evaluation Branch considerations permitting, the reviewed toxicological data supports the proposed tolerance of 0.1 ppm on peas.

ACUTE TOXICITY

Rat oral LD_{50} - June 20, 1969 - Hazleton Lab.

Male and female LD_{50} = 1570 and 1700 mg/kg respectively

Rat inhalation LC_{50} - November 14, 1969 - Hazleton Lab.

Male and female LC_{50} = >100 mg/L

Rabbit Dermal LD_{50} - June 12, 1969 - Hazleton Lab.

LD_{50} = 1000 mg/kg on abraded and intact skin. Gross observations showed enlarged adrenals and pitted surface of kidneys at 1000 mg/kg; small gray areas on surface of kidney at 2150 mg/kg; and white foci throughout liver at all levels.

Rabbit Eye Irritation - June 12, 1969 - Hazleton Lab.
Moderate to severe irritation was produced.

SUBACUTE TOXICITY

90 Day Rat Feeding - March 20, 1970 - Hazleton Lab.

10 young Charles River Caesarean - derived rats of each sex were fed diet levels of 0, 4.0, 12.0, and 40 mg/kg/day.

Observations and test for effects included body weight, food consumption values, physical appearance, behavior, hematological studies, mortality, clinical biochemistry findings, urine analysis, gross and microscopic pathological examination and organ weights.

Body weight gains, food consumption and survival data of test animals were comparable to control animal data. One 4.0 mg/kg level female developed a mammary adenocarcinoma considered unrelated to test material. One 4.0 mg/kg female died during ninth experimental week from unestablished causes.

The hematocrit and hemoglobin determinations, erythrocyte counts, total and differential leukocyte counts recorded at one and three months from five rats of each sex from each level revealed no significant differences from the control values.

The fasting blood sugar, BUN, total serum protein, total serum bilirubin, SG-PT, serum alkaline phosphatase, and serum electrophoresis findings recorded at one and three months plus the serum albumin, serum sodium, serum potassium, serum chlorides, carbon dioxide, serum calcium, and SG-OT taken at three months only from five rats of each sex from each level showed test and control animals to be comparable.

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The results of urine analysos taken at one and three months from pooled samples of five rats from each level showed test and control findings to be comparable.

Gross observations of the viscera at termination revealed no apparent dose related alterations. Isolated findings included a nutmeg liver (12 mg/kg/day male), a small subcutaneous tissue mass (4.0 mg/kg/day female) and two cases of yellowish tinged liver lobes (40 mg/kg/day females).

Organ weights of the heart, liver, spleen, kidneys, thyroid and testes revealed a significant decrease in thyroid absolute and ratio weight for 4.0 mg/kg/day male and female and 12 mg/kg/day females. The 40 mg/kg/day males showed a significant increase in kidney absolute and ratio weights. No dose related pattern is indicated in these findings.

The microscopic examination of the pituitary, thyroid, heart, liver, spleen, kidney, adrenal, stomach, pancreas, small and large intestine, mesenteric lymph node, urinary bladder, testis, ovary and bone marrow from five of each sex of the control and 40 mg/kg/day level revealed the absence of definite compound related histopathological alterations. A similar examination of the liver and kidney from five of each sex of the 4.0 and 12 mg/kg/day levels proved unremarkable.

From these data it can be concluded that rats can ingest 40 mg/kg/day for 90 days without exhibiting definite compound related effects.

13 Week Dog Feeding - March 25, 1970 - Hazleton Labs.

Four young adult purebred beagles of each sex were fed diet levels of 0, 160, 480, and 1600 ppm.

Observations and tests for effects included appearance, behavior, body weights, food consumption, hematological studies, urine analysis, gross examination of viscera, organ weights and microscopic pathological examination.

Body weight gains of 160 and 480 ppm dogs was unaffected. Body weight gain of both sex was inhibited at 1600 ppm.

Hematological studies conducted initially and at four and thirteen weeks included: hematocrit and hemoglobin determinations, erythrocyte count, and total and differential leukocyte counts. No compound related variations were noted between or within the control and test levels.

Blood chemistry studies conducted initially and at four and thirteen weeks included: fasting blood sugar, BUN, total serum protein and bilirubin, serum albumin and potassium, bromsulphalein liver function test, serum chloride, carbon dioxide, serum calcium, SG-PT, serum alkaline phosphatase, SG-OT and serum electrophoresis.

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The 1600 ppm males and females showed a significant increase in bromsulphalein retention at 13 weeks.

Urine analysis conducted initially and at 4 and 13 weeks produced values within normal limits.

Gross observation of the viscera at termination of the study revealed a 1600 ppm male to exhibit small testes. Other findings were incidental and not dose related.

Weights of the thyroids, heart, liver, spleen, kidneys, adrenals and testes with epididymis revealed a significant decrease in the testes weight and weight ratio at 1600 ppm.

Control and 1600 ppm level tissues examinated microscopically included thyroids, heart, liver, gallbladder, spleen, kidneys, adrenals, stomach, pancreas, small intestine, large intestine, messenteric lymph node, urinary bladder, testis, ovary and bone marrow. Tissues examined from the 160 and 480 ppm included liver, kidneys, prostate, and testis. A compound related change showing a curtailment in spermatogenic activity was evident in all males of the 1600 ppm level. Tubular atrophy was also noted at 1600 ppm. Prostates of the male 1600 ppm level presented an immature or atrophic appearance. Biliary epithelial proliferation was noted in 1600 ppm male.

From these data, it can be concluded that ingestion of 1600 ppm by dogs for 13 weeks produces significant testes and prostate tissue alterations. Although unsupported by organ weights or microscopic pathology, hepatic stress is also indicated at 1600 ppm. The no effect level is 480 ppm.

3 Week Rabbit Dermal - May 18, 1970 - Hazleton Labs.

Ten New Zealand White strain rabbits of each sex received 14 applications of the material at field dilution and 5 times field dilution.

Observations and tests for effect included mortality, toxic effects, irritation, body weights, hematological studies, urine analysis and microscopic examination of the liver, kidneys and skin.

Histological changes of acanthosis, hyperatosis and dermatitis which were more severe than the controls were noted.

Metabolism - By means of beta oxidation of the butyric side chain MCPB is converted to MCPA in plants (Wain) and cows.

003643

± via crotonic and B-hydroxy

sgv
Ides

cc:
OGFitzhugh
JCCummings
Perrine Br.
Atlanta Br. (CLewis)
PRD/EPA
Branch Files

XRDCoberly/ccw
5/7/71

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