

000635

THIS IS PHASE II CHEMICAL REVIEW PACKAGE FOR Chlorzoxipron

BRANCH PERFORMING REVIEW Toxicology BRANCH

REVIEWER RESPONSIBLE Robert C. Beverly

DATE COMPLETED 6/14/77

APPROVED BY:

BRANCH CHIEF _____ DATE _____

ISO _____ DATE _____

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CM

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COVER SHEET FORMAT

Data Review Number T VII A. I

Test Protocol ACUTE RAT INHALATION

Chemical Test#d CHLOROPICRIN

Test Species RAT

Result _____

Validation Category INVALID:

Category Repairability YES - EXECUTION of this study
PROVIDE WRITTEN PROTOCOL AND WRITEN

Registrant LITERATURE - 345-347, 1920 "SUR LA DERATISATION PAR LA
Compt. Rend. Acad. Sci. [PARIS] 170: Chloropicrine

Date Data Submitted —

Accession Number 220412

Abstract: This summary stated that an unspecified number of rats exposed to 1 gm/m³ died in 2.5 hours; rats exposed to 30 gm/m³ died in 20 minutes; rats exposed to 10 gm/m³ for one minute, died four hours post treatment and rats exposed to 10 gm/m³ for 15 minutes died in 28 minutes.

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COVER SHEET FORMAT

Data Review Number T VII A. 2.
Test Protocol ACUTE CAT INHALATION
Chemical Test@d CHLOROPICRIN
Test Species CAT
Result _____
Validation Category INVALID
Category Repairability YES PROVIDE WRITTEN PROTOCOL AND EXECUTION OF STUDY - COMPLETE IDENTIFICATION OF MATERIAL TESTED
Registrant LITERATURE - INDUSTRIAL HYGIENE & TOX VOL II
Date Data Submitted _____
Accession Number 220412

Abstract: This summary states that a level of 0.32 mg/L (48 ppm) for 20 minutes produced death after 8 to 12 days; the level of 0.51 mg/L (76 ppm) for 25 minutes produced death usually in one day.

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COVER SHEET FORMAT

Data Review Number T VII A. 3.

Test Protocol ACUTE MICE INHALATION

Chemical Tested Chloropicrin

Test Species MOUSE

Result _____

Validation Category INVALID

Category Repairability YES - PROVIDE WRITTEN PROTOCOL AND RESULTS.
COMPLETE IDENTIFICATION OF TEST MATERIAL

Registrant LITERATURE INDUSTRIAL HYGIENE + TOX. Vol II

Date Data Submitted _____

Accession Number 720412

Abstract: This summary states that a level of 0.17 mg/L (25ppm) for 15 minutes was tolerated; a level of 0.34 mg/L (50ppm) for fifteen minutes produced death after 10 days; a level of 0.85 mg/L (125ppm) for 15 minutes produced death in 3 hours to one day.

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COVER SHEET FORMAT

Data Review Number T VII A. 4

Test Protocol ACUTE DOG INHALATION

Chemical Test#d Chloropicrin

Test Species Dog

Result _____

Validation Category INVALID

Category Repairability YES PROVIDE COMPLETE IDENTIFICATION OF MATERIAL TESTED AND WRITTEN REPORT ON RESULTS

Registrant LITERATURE - INDUSTRIAL HYGIENE AND TOXICOLOGY Vol II

Date Data Submitted _____

Accession Number 920412

Abstract: This summary states that a level of 1.05 mg/l (155 ppm) for 12 minutes caused illness in a dog; a level of 0.8-0.95 mg/l (117-140 ppm) for 30 minutes produced 43% death among an unknown number of dogs; a level of 0.32 mg/l (48 ppm) for 15 minutes was tolerated in an unknown number of animals.

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COVER SHEET FORMAT

Data Review Number T VII A. 5.
Test Protocol ACUTE MICE INHALATION
Chemical Test#d CHLOROPICRIN (not completely identified)
Test Species MOUSE
Result _____
Validation Category INVALID
Category Repairability YES -
Registrant LITERATURE - Bangyo Igaku: Vol 15, 133-4, 1973
PAGE 46-7 (JAPAN)
Date Data Submitted _____
Accession Number NA

Abstract: This abstract stated that an exposure of 171 mg/M³ to mice for four hours produced 100% mortality

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Data Review Number T VII A 6
Test Protocol FOUR MONTH RAT FEEDING (INTERIM)
Chemical Test@d 100% CHLOROPICRIN ~~RESPI~~
Test Species RAT
Result NEL \leq 1000PPM (INTERIM)
Validation Category NA
Category Repairability _____
Registrant INDUSTRIAL BIO TEST LAB INC
Date Data Submitted _____
Accession Number 090104

Abstract:

Sample No: 397
Dosage Levels: 1.0, 10, 100, 1000 ppm
No animals per level: 25 of each sex

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Results: The weekly body weight gains of the control and test levels give rise to the following questions:

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1) Which numerical values represent males and which represent females?

2) Why did the test group number I gain 36 grams in the first eight days of this study ~~as~~ as compared to 0, -3.0, -4.0, and -4.0g for the ~~other~~ control and other three test levels of 1, 10, and 100 ppm? Why then did the test group I's ~~body~~ growth ~~parallel~~ body weight gains ~~parallel~~ parallel the other groups from day 15 to day 120? The lower starting weight of group I (99gms) as compared to the remaining groups (130-131gm) and the parallel growth of this dosage group as compared to the other levels from day 15 to day 20 has resulted in what appears to be an inflated body weight gain for this level by day 120. This situation ~~is~~ does not appear to be a true finding.

The limited fertility endeavor produced with fetuses at the 0, 10, and 100 ppm levels. The 10 and 100 ppm ~~groups~~ female did not become pregnant.

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Data Review Number T VII A. 7.

Test Protocol 120 DAY CHICKEN FEEDING STUDY

Chemical Test#d 100% CHLOROPICRIN

Test Species chicken - white LEGHORN

Result NEL \geq 100ppm

Validation Category SUPPLEMENTARY

Category Repairability No

Registrant ~~INDUSTRIAL BIO TEST LAB INC~~ ~~INDUSTRIAL BIO TEST LAB INC~~

Date Data Submitted 11/9/57

Accession Number 090104

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Abstract:

PPAR ~~TEST~~ : No

SAMPLE # : 397

LEVELS TESTED : 1.0, 10, 100ppm

NO. ANIMALS PER LEVEL : 25

AGE : 5 DAYS

TESTING Lab : INDUSTRIAL Bio TEST Lab INC

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Tests and observations included were: body weight, hematologic studies eg: hemoglobin, hematocrit, lymphocytes, monocytes, neutrophils, eosinophils, and basophils, mortality, fecundity and gross and histopathology of the following tissues from five birds of each level:

brain	liver
spinal cord	spleen
heart	mesonephros
lung	stomach
large and small intestines	pancreas
ovary or testis	

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Results: All parameters ~~investigated~~ investigated are reported to be within normal biological variations. NEL = 100 ppm

*Note: This study should not be considered a neurotoxicity study, as the nature the intent of the study not the tissue taken appear.

~~can~~ to be directed toward this kind. Also, the tissue may not have been stained with an appropriate myelin-specific stain.

Tests and observations included weekly body weights, hematologic studies eg: Hemoglobin, hematocrit, lymphocytes, monocytes, neutrophils, eosinophils, and basophils, mortality, fertility and gross and histopathology of the following tissues from five birds of each level:

brain	liver
spinal cord	spleen
heart	mesonephros
lung	stomach
large and small intestines	pancreas
ovary or testis	

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Results: All parameters ~~investigated~~ investigated are reported to be within normal biological variations. NEL \approx 100 ppm

*Note: This study should not be considered a neurotoxicity study, as ~~the~~ neither the intent of the study nor the tissue taken appear

~~to~~ be directed toward this kind. Also, the tissue may not have been stained with an appropriate myelin-specific stain

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COVER SHEET FORMAT

Data Review Number T VII A 8

Test Protocol 40 DAY RAT INHALATION Study

Chemical Tested Chloropicrin

Test Species PAT

Result Subacute exposure can produce death

Validation Category COPE MINIMUM DATA (WITH RATIONALE)

Category Repairability No

Registrant TOTTORI UNIVERSITY School of MEDICINE

Date Data Submitted _____

Accession Number _____

RATIONALE: protocol does not meet COPE minimum data requirements but the information concerning data from repeated exposure is usable in hazard assessment.

Abstract: hazard assessment.

LEVEL TESTED : 0.07 ppm

No. of Animals per level: 9 or 10

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The test animals were placed in a cardboard box of 35 liters in volume with a gauze covering the top. Into the box was injected 0.35 cc of chloropicrin. ~~Post~~ Histopathology appears to have been conducted on, at least, the lung, kidney, liver, spleen, heart, skeletal muscle, brain and reproductive system.

Results: All animals died by day forty; 5 died on day 4 with the remaining deaths occurring on days 7, 19, 27 and 40. Deaths on day four were reported as being due to respiratory insufficiency. Necrotic collapse of the bronchial epithelium, inflammatory exudates, congestion, hemorrhage and edema were noted in the lungs of the day 7 death as ^{was} ~~was~~ cloudy swelling of the major renal tubules and necrosis of the epithelial cells of the kidney. The kidney pathological changes were most marked in the rat which died on day 19 ~~and day 40~~. The day 40 death showed similar pathological changes plus swelling of the hepatocytes of the central lobules of the liver and also dilatation of the sinusoid.

~~Renosclerosis was noted~~
Renosclerosis was noted in all animals.

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COVER SHEET FORMAT

Data Review Number T VII A 9

Test Protocol SIX MONTH RAT FEEDING STUDY

Chemical Tested Chloropicrin 100%

Test Species RAT

Result NEL = 100ppm

Validation Category COPE MINIMUM DATA

Category Repairability No

Registrant ~~Industrial Bio Test~~ LARVACIDE PRODUCTS INC

Date Data Submitted 1/9/57

Accession Number 090104

Abstract:

RPAR: No

TESTING Lab: INDUSTRIAL Bio TEST Lab INC

SAMPLE TESTED: # 397

LEVELS TESTED: 0, 1.0, 10, 100 ppm

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This is the final report of the preceding 4 month interim feeding study. During the additional two month hematologic studies and urinalysis determinations were conducted on day 150 and 180. Microscopic examination was conducted on five rats from each group.

Results: No mortality occurred. All other parameters investigated for the 0, 10, 10, and 100 ppm levels appear to be within normal biological variations. Within the 1000 ppm level all ~~are~~ but ~~are~~ ~~are~~ two values appear normal. These are a reduction in both absolute liver and spleen. ~~This~~ This finding in both organs is not supported by histopathology or any other parameters. However the effect appears real and must be considered as such. ~~Therefore~~ Thus the ~~no-effect~~ no-effect level for this study is 100 ppm.

NOV 1968

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