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CASWELL FILE

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

007991

JUN 19 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of an acute Inhalation LC_{50}, and a 21-Day Dermal study of Touchdown 4-LC formulation.

Tox. Chem. No.: 893C
HED Project No.: 0-1008
EPA ID No.: 10182-277
Record No.: 262149

TO: Robert J. Taylor, PM #25
Registration Division (H7505C)

THRU: Roger Gardner, Acting Section Head
Section 1, Toxicology Branch 1
Health Effects Division (H7509C) Roger Gardner 6-15-90 KB 6/15/90

FROM: Nguyen B. Thoa, Ph.D., Pharmacologist 06/15/90
Section 1, Toxicology Branch 1
Health Effects Division (H75009)

Background and Requests

ICI Agricultural Products Group has submitted, in compliance with EPA requirements for conditional registration, the two following studies:

1. ICIA0224: 4-Hour Acute Inhalation Toxicity Study in the Rat of a 480g/l SL Formulation

2. ICIA0224 4LC-E: 21-Day Dermal Study in rats

The Toxicology Branch has been asked to review them.

Recommendations and Conclusions

1. The acute inhalation study does not satisfy EPA requirements for a limit test. A nominal concentration of ICIA0224 (480g/l SL formulation) of 8.05 mg/l was used, generating only a particulate concentration of 0.83 ± 0.15 mg/kg (mean ± SD). The mass median aerodynamic diameter of the particles was 1.62 ± 1.63 (mean ± SD). Only 13.8% of the total amount of

particles were of respirable size (≤ 1um) (EPA requires 25%). It is felt however that the registrant had tried to achieve the highest attainable particulate concentration with the smallest achieved particle size. This concentration, 0.83 mg/l, when inhaled nose-only, for 4 hours, produced no death, no long lasting clinical signs, no change in organ or body weight, and no abnormal gross findings at necropsy in rats of both sexes. Consequently, the LC_{50} for the test material is defined as greater than 0.83 mg/kg (TOXICOLOGY CATEGORY 3).

2. The 21-Day Dermal study in rats was adequately conducted. The doses of ICIA0224 4LC-E used were 25, 250, and 1000 mg/kg/day. No death occured and there were no significant changes in body weight, body weight gain, food consumption or in haematology and clinical chemistry. The dose of 1000 mg/kg/day produced skin irritation and a slight increase in testes weight, both without accompanying histological changes,in male, but not in female rats. It also produced occasional sciatic nerve degeneration of unstated severity in 1 male and 2 females (out of a total number of 10 animals). Sulfosate, the active ingredient of the test material, is known to cause white matter degeneration in the spinal cord lumbar region of mice (see attached DER entitled "two-year chronic toxicity and oncogenic dietary study with SC0224 in mice", p.12). Pending further clarification of this possible neurotoxic effect, the systemic NOEL of ICIA0224 4LC-E is defined as 250 mg/kg/day. The study is classified CORE MINIMUM. Although the active ingredient of the test material, sulfosate, is an organo phosphorus, a review of one-liners did not reveal any acute delayed neurotoxicity studies in the hen (see attached one-liners on sulfoxate). This test is required before any registration of ICIA0224 4LC-E could be approved.

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Reviewed by: Nguyen B. Thoa, Ph.D 6-15-96
Section 1, Toxicology Branch 1
Secondary Reviewer: Roger Gardner R. G. 6-15-96
Section 1, Toxicology Branch 1

007991

DATA EVALUATION RECORD

STUDY TYPE: Acute inhalation toxicity in rats (Guideline 81-3)

TOX CHEM NUMBER: 893 C

MRID NUMBER: 414260-01

TEST MATERIAL: ICIA0224 ,480 g/l SL formulation (482g AI/l)

SYNONYMS: Touchdown 4-LC HERBICIDE (containing Glyphosate, trimethylsulfonium salt), formerly SC-0224.

REPORT NUMBER(S): CTL/P/2848, Study number HR 0963

SPONSOR: ICI Agricultural Products Group. Wilmington, Delaware

TESTING FACILITY: ICI Central Toxicology Laboratory, Cheshire, UK

TITLE OF REPORT: ICIA0224: 4-Hour Acute Inhalation Toxicity Study in the Rat of a 480g/l SL formulation

AUTHOR(S): A. P. Mould

STUDY COMPLETION DATE: 2-7-90

CONCLUSIONS: The acute inhalation toxicity of a ICIA0224, 480 g/l SL formulation (test material), was studied in rats. Animals of both sexes were exposed, nose- only, for 4 hours to an aerosol of the undiluted test material, at the atmospheric total particles concentration of 0.83 $\pm$ 0.15 mg/l (MMAD $\pm$ SD = 1.62 $\pm$ 1.63 um, of which 13.8% were $\leq$ 1um).

There were no deaths, no change in body or organ weights, and no gross findings at necropsy.

The main clinical signs included salivation, lachrymation, reduction in activity, and tail erection which were short lasting and piloerection, upward curvature of the spine, and mucoid nasal discharge which were resolved after several days.

The acute inhalation LC_{50} of the test material defined as greater than 0.83 $\pm$ 0.15 mg/l (TOXICITY CATEGORY 3).

Core Classification: This study did not satisfy the EPA requirement for a limit test (81-3). The distribution of respirable- size particles in the breathing atmosphere (13.8% of total particulate concentration) was also below the required 25%

level. However, it is felt that the best efforts were made to realize the highest attainable stable concentration of the test material which had the smallest achieved particle size. Therefore, this study is ACCEPTABLE.

MATERIALS AND METHODS

Test species: Alpk-APfSD (wistar derived) rats, approximately seven weeks of age, were used. The animals weighed 225-241 g on day one of the study.

Equipment: A glass concentric jet atomiser and size selective cyclone were used to generate the test atmosphere. The system was connected to an exposure chamber which consisted of 2 PERSPEX tubing sections (28 cm X 15 cm/ section), each having their wall drilled with 10 equidistant holes (28 cm diameter) and a sampling port. The total volume of each chamber was 27.6 liters.

A peristaltic pump drove dry, clean air (25 l/ min) through the atomiser and the exposure chamber.

Undiluted test material was pumped into the atomiser, to be aerosolized and mixed with the air, for delivery to the rats' breathing atmosphere.

Atmospheric Concentrations of the Test Material:

The test material was generated at a nominal concentration of 8.05 mg/l. This produced a total particulate concentration in the atmosphere close to the animal breathing zones (measured by gravimetry, every 30 min. during the exposure period) of 0.83 $\pm$ 0.15 mg/l. This concentration was reported to be the "highest attainable stable concentration which had the smallest achieved particle size". The mean analyzed atmospheric concentration of ICIA0224 (by HPLC with UV detection) was 0.49 $\pm$ 0.08 mg/l. The mass median aerodynamic diameter of the particles was 1.62 um, with a geometric standart deviation of 1.63. The percentage of particles with a diameter $\leq$1 um (EPA-defined respirable size) was 13.8% of total.

Experimental Procedure: Thirty minutes after the atmosphere of the exposure chamber was equilibrated at a test material total particulate concentration of 0.83 $\pm$ 0.15 mg/l, the rats (5/ sex), were positioned into restraining tubes which were inserted into the exposure chamber wall openings, for a 4- hour, nose- only, single exposure period. Control animals (5/ sex), were exposed to air only. The temperature within the chambers were 20.6 - 21.4^{o} C and the relative humidity was 17 -20% and 43 - 47% in control- and in test chambers respectively.

All animals were observed frequently for signs of toxicity and mortality during the exposure period, and twice daily thereafter

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until day 15.

Body weights were recorded prior to exposure and on days 2, 3, 8, and 15. Surviving rats were sacrificed at the end of the study, on day 15. Gross necropsy was performed on all animals, and the weights of the liver and the lungs were recorded.

Test and control data were compared statistically, using a 2-sided Student's T test.

REPORTED RESULTS

There were no deaths, no change in organ or body weights, and no post-mortem gross findings.

Control and test animals of both sexes showed wet fur, stains around the snout, and chromodacryorrhea during the exposure plus hunched posture, upward curvature of the spine, and piloerection in the period immediately following exposure.

Test animals also showed reduction in activity, deep breathing, tail erection, shaking, salivation, and lachrymation.

Most clinical signs had resolved by day 3 but test animals of both sexes still showed mucoid nasal discharge, hunched back posture, upward curvature of the spine, and piloerection which persisted for several additional days.

DISCUSSION:

Author's Discussion: An aimed for target concentration of 5 mg/l was not realized because of the nature of the test material. The highest attainable stable total particulate concentration which could be obtained with the smallest achieved particle size was 0.83 $\pm$ 0.15 mg/l. The difference observed between the nominal and the total particulate concentrations could be mainly accounted for by chamber wall losses, as expected with the type of equipment used in this study. Under the conditions of this study, the LC_{50} of the test material is greater than 0.83 mg/l.

Reviewer's comments: This study did not satisfy the EPA requirement for a limit test (81-3). The distribution of respirable- size particles in the breathing atmosphere (13.8% of total particulate concentration) was also below the required 25% level. However, it is felt that the best efforts were made to realize the highest attainable stable concentration of the test material which had the smallest achieved particle size, and that there were adequate data to permit a definition of the LC_{50} of ICIA0224, 480/1SL formulation as being greater than 0.83 mg/l (TOXICITY CATEGORY 3).

Reviewed by: Nguyen B. Thoa, Ph.D NBT 6-15-90
Section 1, Toxicology Branch 1
Secondary Reviewer: Roger Gardner RG 6-15-90
Section 1, Toxicology Branch 1

007991

DATA EVALUATION RECORD

STUDY TYPE: 21 Day Dermal Study in Rats (guideline 82-2)

TOX CHEM NUMBER: 893 C

MRID NUMBER: 412099-04

TEST MATERIAL: ICIA0224 4LC-E (39.8% AI)
Batch No WF1005 A

SYNONYMS: Touchdown 4-LC HERBICIDE (containing Glyphosate, trimethylsulfonium salt), formerly SC-0224

REPORT NUMBER(S): CTL/P/2496, Study number LR 0535

SPONSOR: ICI Agricultural Products Group. Wilmington, Delaware

TESTING FACILITY: ICI Central Toxicology Laboratory, Cheshire, UK

TITLE OF REPORT: ICIA0224 4LC-E: 21 Day Dermal Study in Rats

AUTHOR(S): D. J. Tinston

STUDY COMPLETION DATE: 7-7-89

CONCLUSIONS: ICIA0224 4LC-E, 25, 250, and 1000 mg/kg, applied to the skin of rats of both sexes for 6 hrs/day/21 days, ,did not produce any significant changes in body weight, body weight gain, food consumption, or in hematology and clinical chemistry.

Both doses of 25 and 1000 mg/kg produced slight increases in testes weight, unaccompanied by any histological changes. The toxicological significance of this is unclear.

The dose 1000 mg/kg produced signs of skin irritation in male rats but not in female rats, including scabbing, erythema, edema, and desquamation. These were not accompanied by any histological changes.

This dose also induced occasional sciatic nerve fiber degeneration of unstated severity in one male and two female rats. This effect needs to be clarified since the test material is a formulation containing an organo phosphorus, sulfoxate, as the active ingredient. Pending this, the systemic NOEL of ICIA0224 4LC-E formulation is defined as 250 mg/kg/day.

Core Classification: Core minimum

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MATERIALS AND METHODS

Test Material: ICIA0224 4LC-E is a liquid formulation with a specific gravity of 1.21 g/ ml. It was stored at 20° C, and is applied undiluted to the skin.

Test species: Alpk-APfSD (Wistar derived) rats of both sexes, approximately seven weeks of age, were used. Their dorso - lumbar region (10 X 5 cm) were clipped free of hair upon their arrival at the laboratory, and only those animals with normal epidermis were used. The rats were individually housed. They weighed 225-241g (males), and 165-205g (females) , on day one of the study.

Experimental Protocol: The rats had their hair reclipped 18 to 24 hours before the start of the study. Four groups of 5 males and 5 females each were used, including one untreated control group and 3 treated groups, receiving, from day 1, dermal application of 0 (untreated controls, group 1), 25 (0.0021 ml/100 g, group 2), 250 (0.0207 ml/100g, group 3), and 1000 mg/ kg (0.0826 ml/100g, group 4) of the test material, 6 hrs/day, for 21 consecutive days. Skin contact with the test material was maintained with an occlusive dressing and adhesive bandage. Rats wore collars to prevent test material contamination. Treated skin areas were washed with water and blotted dry after each dosing period and were kept free of hair by repeated clippings.

The rats were observed twice daily, for dermal and non- dermal signs of toxicity.

Body weights were recorded daily, immediately before each dosing.

Food consumptions were recorded weekly.

The rats were sacrificed on day 22, and the following were measured and/or observed:

Haematology: hemoglobin (hb), total WBC, RBC, mean cell volume, mean cell hb, hematocrit, platelet count, differential white cell count, red cell morphology, prothrombin and kaolin-cephalin times.

Clinical chemistry: plasma urea, creatinine, glucose, triglycerides, albumin, total protein, cholesterol, calcium, phosphorus, sodium, potassium, chloride, and bilirubin levels, and plasma gamma-glutamyltransferase, alkaline phosphatase, alanine transaminase, aspartate transaminase, and creatinine kinase activities.

Pathology: The following organs were weighed: testes, liver, kidney, adrenal glands, and brain.

The abdominal, thoracic, and cranial cavities were examined at

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necropsy, and the following organs were examined, fixed and preserved (tissues marked * were stored): adrenal gland, bladder*, brain, colon*, epididymis, eye*, femur*, heart*, ileum*, kidney, liver, lung, ovary, pituitary gland*, sciatic nerve, spinal cord, spleen*, stomach*, treated skin, testis, thyroid (with parathyroid)*, and any abnormal tissue.

Tissues from groups 1 and 4 were processed for histological evaluation.

Statistical Analysis: Statistical analysis of the data were made using an analysis of variance and covariance, according to the GLM procedure in SAS (1985). Mean values of the test groups were compared with those of the control groups using a two - sided Student's t- test, based on the error mean square of the analysis.

REPORTED RESULTS

All animals survived the study.

There were no significant changes in body weight, body weight gain, or food consumption in any group, compared to the controls (one group 4 male showed poor growth and was excluded from the statistical evaluations).

Dermal reactions were only observed in group 4 males, including severe scabbing (3 rats), severe macular erythema (2 rats), edema (1 rat), and desquamation (1 rat). Scabbing and flaking of the treated skin were observed at necropsy, but there were no accompanying histological damages.

There were slight increases (9%) in testes weight in groups 2 and 4 males, also without accompanying histological changes.

There was a 39% decrease in the neutrophil count in group 4 males, compared to the control group.

Plasma aspartate transaminase and urea decreased 18% and 12% respectively in group 4 females. Plasma potassium decreased 14% in group 4 males.

Occasional sciatic nerve fiber degeneration was observed in group 4 rats (1 male and 3 females), but there were no mention of the severity.

DISCUSSION:

Author's Discussion: Daily dermal application of ICIA0224 4 LC-E for 6 hrs/day/21 days, at dose levels of 25, 250, and 1000 mg/ kg, did not produce any consistent dermal or systemic effects in the rat.

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The changes in the skin were minor and were without any accompanying histological changes. The changes in testes weight in group 4 males were neither dose- related, nor accompanied by histological changes. The hematological and clinical chemistry changes are statistically significant but do not have any toxicological meaning.

The systemic NOEL for ICIA0224 4LC-E is therefore defined as 1000 mg/ kg.

Reviewer's comments: There were no reported organ: final body weight ratios. Testes weight were slightly increased in all treated male groups, and these changes were significant for groups 2 and 4. The toxicological significance of this effect is unclear.

The occasional sciatic nerve fiber degeneration observed in 1 male and 2 females of group 4 needs clarification since the test product active ingredient, sulfoxate, is an organo phosphorus. Pending this, the systemic NOEL for ICIA0224 LC-E formulation in this study cannot be defined as 1000 mg/kg but as 250 mg/kg.

Touch down 4LC

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES/HED/SACB
TOX ONELINERS

TOXCHEM NO. 893C- Trimethylsulfonium carboxymethylamino-methylphosphonate FILE LAST PRINTED: 05/22/90

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Teratology Species: rat Stauffer Environ Health Cen. T-11050; 11/82	SC-0224 19.2% ai	249802	Teratogenic NOEL> 333 mg/kg/day (HDT). Fetotoxic NOEL = 100 mg/kg/day Feto Toxic LEL = 333 mg/kg/day (reduced body weight; increased resorptions). Maternal NOEL = 100 mg/kg/day Maternal LEL = 333 mg/kg/day (chromorhinorrhea, salivation, lethargy, reduced body weight, and reduced food intake.) Levels tested in SD strain by gavage - 0, 30, 100, 333 mg/kg/d in water		Supplementary 003578 Minimum 004585 Guideline 005584
Teratology Species: rabbit Stauffer Chemical T-11052; 6/21/83	SC-0224 56.2% pure Sulfosate	260966	Levels tested by gavage in Dla: (NZW) SPF on day 7 thru 19 of gestation - 0,10,40 and 100 mg/kg/day. Maternal NOEL < 10 mg/kg/day (LDT) (diarrhea, head tilt, nasal discharge, wet stains on chin, scab on mouth, red urine stain. Developmental NOEL > 100 mg/kg/day A/D ratio = 10/<100 = < 0.1		Guideline 005450
Reproduction-2 generation Species: rat Environmental Health Labs T110-51; 4/19/84	SC-0224 19.2% ai	258398	Reproductive NOEL >2000 ppm. Systemic NOEL = 150 ppm Systemic LEL =800 ppm (reduced feed intake and body weight in pups and parents; reduced absolute thymus, P1 (M,F); platelet count increase,F2B adults (M,F). Levels tested = 0,150,800,2000 ppm in CRL CD(SD) Br strain		Supplementary 005173 005690
Feeding-1 year Species: dog Stauffer Chemical ECH T-11075; 4/3/87	SC-0224 (EHC 0469-15;WRC# 8108-24-1) 56.2% pure	402140-05	Systemic NOEL = 10 mg/kg/day. Systemic LEL=50 mg/kg/day (decreased LDH). Dose levels tested: 2,10, and 50 mg kg/day. Beagle dogs; no historical control data. ~~2000mg~~		Supplementary 006337
Feeding/oncogenic-2 year Species: mice Stauffer Chemical T-11813; 4/3/87	Sulfosate tech	402140-06	Oncogenic NOEL > 8000 ppm (HDT). Systemic NOEL = 1000 ppm; LEL = 8000 ppm; effects were decreased body wt. & food consumption (both sexes); increased incidence of white matter, degeneration in lumbar bar region of spinal cord (males only), increased incidence of epithelial hyperplasia of duodenum (females only). Levels tested in Charles River Strain - 0, 100, 1000 & 8000 ppm.		Supplementary 006542
Feeding/oncogenic-2 year Species: rat Stauffer Chemical T-11082; 4/3/87	Sulfosate tech	402140-07	Oncogenic > 1000 ppm. Systemic NOEL = 100 ppm. LEL 500 ppm (effects were decreased levels of lactate dehydrogenase in males & females at 6 & 12 months). At 1000 ppm effects were decreased body wt. (both sexes), increased incidence of chronic inflammation of larynx & nasopharyngeal in males.. Levels tested in Charles River CrL: CD [SD]BR strain - 0, 100 500 & 1000 ppm.		Supplementary 006542

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TOX ONELINERS

TOXCHEM NO. 893C- Trimethylsulfonium carboxymethylamino-methylphosphonate FILE LAST PRINTED: 05/22/90

CITATION -	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Dermal-3 week Species: rabbit Hazleton HLA6142-107; 3/1/88	SC-0224 Concentrate (Containing 51.2% Sulfosate)	408937-02	Systemic NOEL = 1000 mg/kg/day. Mild erythema at application sites in all sulfosate-treated groups. Doses: 0, 10, 100, & 1000 mg/kg/day in NZ rabbits (6 hrs/day; 5 days/wk; 3 weeks).		Guideline 007063
Metabolism Species: rat Stauffer Chemical PMS-148; 2/4/85	SC-0224 14C labeled	258398	Radiolabeled trimethylsulfonium ion rapidly excreted unmetabolized in urine and feces; principal sites of localization of ion are adrenals, kidneys, bladder, liver, thyroid and stomach		Acceptable 005173
Fertility Species: rat Stauffer Chemical T-10896; 1/6/83	SC-0224 60.6% lot # EHC-0 355-19 (WRC-7549-38-00)	258398	No adverse effect on fertility or pup survival		Acceptable 005173
Mutagenic-sex link recessive Species: drosophila melanoga. Litton Bionetics Inc. 22169; 5/10/85	SC-0224	249802	Not mutagenic in SLRL test. Doses tested: 25 and 50 mg/ml		Unacceptable 003578 Acceptable 005584
Mutagenic-bone marrow cytogen. Species: rat bone marrow Stauffer Chemical T-10884; 5/10/85	SC-0224 58.5% ai	249802	Not clastogenic in the rat bone marrow cells. Doses tested: 21, 63, and 188 mg/kg		Unacceptable 003578 Acceptable 005584
Mutagenic-Ames Species: bacteria Stauffer Chemical T-10847; 5/10/85	SC-0224 lot #7269-10 and lot #7646-0901 19.2% pure by weight (90% a.i.)	249802	Not mutagenic in TA1535, TA1537, TA1538, TA98, and TA100 Tested with and without metabolic activation. Doses tested: 0.12,0.37, 1.11,3.33, and 10 mg/plate without S9 metabolic activation; 0.56,1.11, 1.67,3.33,5.0,10.0, and 15.0 mg/plate with S9 metabolic activation		Uncceptable 003578 Acceptable 005584
Mutagenic- cytogenetic Species: cho cells Stauffer Chemical T-10875; 5/10/85	SC-0224 58.5% ai lot #684 1-48-3	249802	Sister chromatid exchange not determined. Positive for the induction of chromosomal aberration in CHO cells in the absence (4 mg/ml) and presence (8,10,12 mg/ml) of S9 metabolic activation. Doses tested: 2,4, and 6 mg/ml in the absence of S9 metabolic activation; 2,4,6,8,10, & 12 mg/ml in the presence of S9 metabolic activation		Unacceptable 003578 Acceptable 005584
Mutagenic- cytogenetic Species: cho cells Stauffer Chemical T-10875; 5/10/85	SC-0224 72% ai lot #7466-18-01	249802	Increased chromosomal aberrations in activation assay at 6,7,and 8 ul/ml. No increase in sister chromatid exchanges with S-9 metabolic activation, (1 through 8 ul/ml). Dose tested: 2,4,6,8,10 and 12 mg/ml with S9 metabolic activation; 2,4, and 6 mg/ml without S9 metabolic activ.		Unacceptable 003578 Acceptable 005584

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TOX ONELINERS

TOXCHEM NO. 893C- Trimethylsulfonium carboxymethylamino-methylphosphonate FILE LAST PRINTED: 05/22/90

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Mutagenic- lymphoma mutation Species: mouse lymphoma Stauffer Chemical T-10848; 5/10/85	SC-0224 90% & 58.5% ai lots 7269-10 & 6841-48-3	249802	Positive mutagenicity observed at the thymidine locus under S-9 rat liver metabolic activation. Dose levels tested: 0.375,0.75,1.50, 3.0,6.0,8.0,8.5,9.0,9.5 and 10 mg/ml in the presence of S-9 metabolic activation.		Unacceptable 003578 Acceptable 005584
Mutagenic Species: balb/3t cells Stauffer Chemical T-10848; 5/10/85	SC-0224 est. 90% tech lot #7269-10	249802	Negative responses at 0.313, 0.625, 1.25,2.50, and 5.0 mg/ml in the BALB/3T cells transformation assay		Unacceptable 003578 Acceptable 005584
Mutagenic-Ames Species: salmonella typhimur. Stauffer Chemical T-12660; 9/25/85	SC-0224 55.6% pure lot # JHC 8865-20-1	260966	Not a mutagen up to 40 ul/plate with TA1535, TA1537, TA98, and TA100 strains of salmonella typhimurium in either the standard plate assay or the preincubation assay with and without the metabolic activation. Concentrations tested: 2.5,5.0,10.0,20.0, and 40.0 ul/ml.		Acceptable 005450
Mutagenic- lymphoma mutation Species: mouse Stauffer Chemical EHC T-12661; 12/19/85	SC-0224 55.6% pure lot # JHC 8865-20-1	260966	Mutagenic effect was observed under the standard test procedure with and without the metabolic activation at the concentrations tested (3.5 through 5.0 ul/ml). Concentrations tested: 1 through 5.4 ul/ml under the nonactivation assay system; 2.5 through 5.0 ul/ml under the activation assay system.		Acceptable 005450
Mutagenic- cytogenetic Species: L5178Y cells Stauffer Chemical EHC T-12662; 12/19/85	SC-0224 55.6% pure lot # JHC 8865-20-1	260966	(A) Chromosomal Aberration Assay Under the standard test procedure positive clastogenic effect was observed at the concentration of 5 ul/ml under the nonactivation assay and at the concentrations of 3 to 5 ul/ml under the activation assay. Concentrations tested: 1 through 5 ul/ml under the nonactivation assay; 3 through 5 ul/ml under the activation assay. (B) Sister Chromatid Exchange Assay Under the standard test procedure, the test compound was a positive inducer of SCE at the concentration of 5 ul/ml under the nonactivation assay and at the concentrations of 3 to 5 ul/ml under the activation assay. Concentrations tested: 1 through 5 ul/ml under the nonactivation assay; 3 through 5 ul/ml under the activation assay.		Acceptable (A) 005450 Acceptable (B) 005450
Mutagenic- cytogenetic Species: cho cells Stauffer Chemical EHC T-12663; 12/18/85	SC-0224 55.6% pure lot # JHC 8865-20-1	260966	(A) Chromosomal Aberration Assay. Not a clastogen up to 10 ul/ml under the adjusted acidic test condition with and without the metabolic activation system. Concentrations tested: 4 through 10 ul/ml under the nonactivation or the activation system. (B) Sister Chromatid Exchange Assay; Not an inducer up to 10 ul/ml under the adjusted acidic test condition with and without the metabolic activation system. Concentrations tested: 4 through 10 ul/ml under the nonactivation or the activation system.		Unacceptable (A) 005450 Unacceptable 005450

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U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES/HED/SACB
TOX ONELINERS

TOXCHEM NO. 893C- Trimethylsulfonium carboxymethylamino-methylphosphonate FILE LAST PRINTED: 05/22/90

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Mutagenic-micronucleus assay Species: mouse bone marrow Stauffer Chemical EHC T-12689; 4/23/87	SC-0224 (EHC0701-25;lot # JHC8865-20-1) 55.3% pure	402140-04	Failed to induce significant increase in the number of PCE containing micronuclei. Dose levels tested: 700, 900, & 1100 mg/kg for males & 400, 600, & 800 mg/kg for females. Charles River D-1 strain; no range finding test to set a cytotoxic dose		Unacceptable 006337
Mutagenic- lymphoma mutation Species: mouse lymphoma Stauffer Chemical EHC T-12661; 12/19/85	SC-0224	260966	Mutagenic in this assay with and without metabolic activation under the PH unadjusted test condition. (PH 5.62-7.07)-1 through 5 ul/ml. 3/20/87 Addendum: Not a mutagen in this assay with and without metabolic activation under the PH adjusted test condition (PH 7.4)-5 through 10 ul/ml conc. used. L51781 mouse cells.		Acceptable 006337
Mutagenic- cytogenetic Species: mouse lymphoma Stauffer Chemical EHC T-12662; 12/19/85	SC-0224	260966	Clastogenic in these assays with and without metabolic activation under the PH unadjusted test condition (PH5-62-7.07)-3 through 5 ul/ml. 3/20/87 Addendum: Not a clastogen in these assays with & without metabolic activation under the PH adjusted test condition (PH 7.4)-4 through 10 ul/ml. L51781 mouse cells.		Acceptable 006337
Mutagenic- cytogenetic Species: cho cells Stauffer Chemical T-12663; 12/18/85	SC-0224	260966	3/20/87 Addendum. Not a clastogen in these assays with and without metabolic activation under the PH adjusted test condition (PH 7.4 to 7.6). Concentrations tested: 4 through 10ul/ml.		Acceptable 006337
Acute oral LD50 Species: rat Stauffer Chemical T-11185; 11/82	SC-0224 62% ai	249802	LD50 = 748 mg/kg (male) = 755 mg/kg (female) Toxic signs = depression, prostration, ptosis, slow, shallow respiration, tremors.	3	Minimum 003578
Acute oral LD50 Species: rat Stauffer Chemical 11189; 11/82	SC-0224-4LC Formulation 41.4% ai [redacted]	249803	LD50 (male) = 846 mg/kg. (female) = 805 mg/kg depression, ptosis, atoxia, tremors, and prostration	3	Minimum 003578
Acute oral LD50 Species: rat Stauffer Chemical T-12589; 2/12/87	SC-0224 4-LCE (containing 39.9% sulfosate)	408938-02	LD50 (M) = 1760 mg/kg , LD50 (F) = 1298 mg/kg	3	Guideline 007074
Acute Dermal LD50 Species: rabbit Stauffer Chemical T-11185; 11/82	SC-0224 62% ai	249802 260508	LD50 > 2000 mg/kg intact and abraded skin. Toxic signs: abraded - mild to severe depression in some rabbits. Mild to moderate erythema intact - mild depression mild erythema.	3	Minimum 003578 Supplementary 005584

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INERT INGREDIENT INFORMATION IS NOT INCLUDED

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES/HED/SACB
TOX ONELINERS

TOXCHEM NO. 893C- Trimethylsulfonium carboxymethylamino-methylphosphonate FILE LAST PRINTED: 05/22/90

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Acute Dermal LD50 Species: rabbit Stauffer Chemical 11189; 11/82	SC-0224-4LC Formulation 41.4%	249803	LD50 = 1279 mg/kg (abraded and intact) Mild to moderate erythema and edema	2	Minimum 003578
Acute Dermal LD50 Species: rabbits Stauffer Chemical T-12589; 2/12/87	SC-0224 4-LCE (containing 39.9% sulfosate)	408938-02	LD50 (M&F) > 2000 mg/kg	3	Guideline 007074
Acute inhalation LC50 Species: rat Stauffer Chemical T-11084; 9/82	SC-0224 62% ai	249802	LC50 > 6.9 mg/L/4 hours (actual measured concentration) No necropsy findings related to treatment.	3	Minimum 003578
Acute inhalation LC50 Species: rat Environmental Health Labs T-11728; 5/6/86	SC-0224 56.2%	258398	LC50 > 0.81 mg/L/4 hrs (male, female	3	Guideline 005173 007063
Acute inhalation LC50 Species: rat Environmental Health Labs T-11870; 5/9/84	SC-0224-4LC 41.2%	258398	LC50 = 1.30 mg/L (male). LC50 = 1.56 mg/L (female)	2	Guideline 005173
Acute inhalation LC50 Species: rat Stauffer Chemical T-12983; 6/22/87	SC-0224 4-LCE (containing 39.9% sulfosate)	408938-03	A respirable aerosol could not be produced for the test due to high viscosity and foaming properties of the test material. No test animals were exposed.		Supplementary 007074
Primary eye irritation Species: rabbit Stauffer Chemical T-11185; 11/82	SC-0224 62% ai pH 5.65	249802	No corneal involvement Unwashed eyes - mild irritation in 1 rabbit and mild conjunctivitis in all 6 at 24 hrs., all eyes clear at 7 days. Washed eyes - mild conjunctivitis in 2/3 at 24 hrs., all clear at 3 days.	3	Minimum 003578
Primary eye irritation Species: rabbit Stauffer Chemical 11189; 11/82	SC-0224-4LC Formulation 41.4% pH = 4.77	249803	Corrosive. Severe corneal opacity, moderate iritis and conjunctivitis through 10-14 days, clearing in most rabbits at 24 days. Washing eyes reduces effects. Severe reaction apparently caused by the inert [redacted]	1	Minimum 003578

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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TOX ONELINERS

TOXCHEM NO. 893C- Trimethylsulfonium carboxymethylamino-methylphosphonate FILE LAST PRINTED: 05/22/90

CITATION	MATERIAL	ACCESSION/ MRID NO.	RESULTS	TOX CAT	COREGRADE/ DOCUMENT#
Primary eye irritation Species: rabbit Stauffer Chemical T-12589; 2/12/87	SC-0224 4-LCE (containing 39.9% sulfosate)	408938-02	Moderate iritis and mild to moderate conjunctival irritation; cleared by day 7.	3	Guideline 007074
Primary dermal irritation Species: rabbit Stauffer Chemical T-11185; 11/82	SC-0224 62% ai pH 5.65	249802	24 hour exposure: Draize score 0.67 4 hour exposure: Draize score 0.19 A mild dermal irritant.	4	Minimum 003578
Primary dermal irritation Species: rabbit Stauffer Chemical 11189; 11/82	Sc-0224-4LC Formulation 41.4% pH = 4.77	249803	Moderate dermal irritant. Erythema and edema at 24 hrs. in intact and abraded skin. Mild edema and scar tissue at 72 hrs. PIS = 2.92 at 24 hours.	3	Minimum 003578
Primary dermal irritation Species: rabbit Stauffer Chemical T-12589; 2/12/87	SC-0224 4-LCE (containing 39.9% sulfosate)	408938-02	Non-irritating (4-hour exposure)	4	Guideline 007074
Dermal sensitization Species: guinea pig Richmond Toxicology Lab T-11420; 10/22/84	SC-0224 41.2%	258398	Slight sensitization		Guideline 005173
Dermal sensitization Species: guinea pig Richmond Toxicology Lab T-11269; 10/12/84	SC-0224 4LC 56.3%	258398	Slight sensitization.		Guideline 005173
Dermal sensitization Species: guinea pig Stauffer Chemical T-12588; 8/4/87	Sc-0224 4-LCE (containing 39.9% sulfosate)	408938-04	Negative for skin sensitization using modified Buehler procedure.		Guideline 007074

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