


#8936
CASWELL, FILE

Shaughnessy No.: 128501

Date Out of EAB: MAR 1 - 1984

To: Robert Taylor
Product Manager 25
Registration Division (TS-767)

From: Samuel Creeger, Chief 
Review Section #1
Exposure Assessment Branch
Hazard Evaluation Division (TS-769)

Attached, please find the EAB review of...

Reg./File # : 476-EUP-RNE and -RNG

Chemical Name: Sulfosate

Type Product : Herbicide

Product Name : SC-0224 4-LC and -Concentrate

Company Name : Stauffer

Purpose : Response to previous review. Also additional data.

ZBB Code : other EAB #(s) : 4119 and 4120

Action Code(s): 704 TAIS Code: 60

Date Received: 12/14/83 Total Reviewing Time: 4.0 days

Date Completed: MAR 1 - 1984

Deferrals to: _____ Ecological Effects Branch
_____ Residue Chemistry Branch
_____ Toxicology Branch

1.0 INTRODUCTION

On August 18, 1983, EAB completed its initial review of Sulfosate (trimethyl sulfonium carboxymethylaminomethyl phosphonate). At that time, EAB was unable to concur with the proposed EUP use on non-crop areas, due to a number of deficiencies.

The current submission by the registrant (Stauffer, in accession 251-545) contains both a response to these issues, and additional data to support the proposed EUP.

2.0 STRUCTURE AND DIRECTIONS FOR USE

See previous review.

3.0 REGISTRANT'S RESPONSE TO ISSUES RAISES BY EAB

3.1 Issue raised by EAB

The apparent volatility of this compound (8.2 torr @ 10°C) which may lead to significant human exposure may require that additional studies be conducted (photolysis in air, human exposure analysis, reentry).

Stauffer's Response

"... the vapor pressure is due entirely to the partial pressure of water present in the technical material. ... Solid SC-0224 is hygroscopic and vapor pressure has not been determined. However, vapor pressures were determined for the related solid materials trimethylsulfonium chloride and carboxymethylaminomethyl phosphonic acid. The vapor pressures of both compounds are less than 10^{-7} at 30°C."

EAB Comment

This matter is still not clear to this reviewer. Even if the water does contribute significantly to the vapor pressure of SC-0224, EAB still has no way of knowing what ambient air levels are likely to be over treated fields. It appears from the Stauffer response that hydrated SC-0224 is the volatile moiety, and that significant amounts of this compound will be present in ambient air over treated fields (our original concern).

Therefore, this matter is still unresolved.

3.2 Issue raised by EAB

There appears to be a discrepancy between the concentration reported for the technical material (52.2% ai) and the data in the [technical data] sheet (56.7 to 60.1%).

Stauffer's Response

"...the active ingredient content of the technical material varies from 52.2 to 70.0%, with the difference consisting mainly of [REDACTED] (see Composition Limits of Typical SC-0224, Appendix 3). SC-0224 Concentrate is a proposed product with minimum active ingredient content of 52.2%; [REDACTED] is added to technical material of higher active ingredient content to ensure that the final product is consistent from batch to batch."

EAB Comment

A copy of the Composition Limits of Typical SC-0224 is appended to this review. Clearly the data in the original technical data sheet was misleading. The registrant's explanation confirms the composition of the proposed technical to be marketed, resolving EAB objections. It does not, however, justify the submission of the confusing product data sheet.

EAB considers this question to be resolved.

3.3 Issue raised by EAB

With reference to the composition limits noted above, EAB commented that the range of reported values seemed imprecise (+/- 2.9%, relative) despite presumably reliable analytical methodology for the analysis of technical materials.

Stauffer's Response

"We do not agree with the 2.9% relative variation. For the 13 numbers in the table, the average is 58.2%, the range is 56.4 to 60.1% (a difference of 3.7%) and the coefficient of variation is 2.1%. The data presented in the table was developed in an earlier stage of product development; it is not as precise as we would currently expect (EAB emphasis added) with the subsequent experience which has been developed. A recent round-robin gave a C.V. of 1.2% in the analysis of a standard. Additional variation would be expected with the amount of handling which occurred during these tests."

EAB Comment

Our objections stand, despite the recent, more careful analysis of "standard" material. If the registrant wishes to pursue this issue (a relatively minor one), they should submit statistical data to support the precision of their analytical methodology for technical (not standard) materials.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

3.4 Issue raised by EAB

(With reference to the 4LC Experimental program) ...no detailed distributional breakout of target sites/amounts to be applied was included with this submission.

Stauffer's Response

"...a table similar to that in the SC-0224 Concentrate submission was included in the 4-LC submission. The accession number for this document is 249804.

EAB Comment

Since the requisite breakout sheet has still not been provided, this EAB objection remains unresolved.

3.5 Issue raised by EAB

With reference to the submitted Hydrolysis Study, virtually no experimental detail and no raw data were submitted. In addition, the rationale for evaluation of the anion and cation separately was not discussed. Finally, analytical methodology used was not sufficiently detailed for evaluation.

Stauffer's Response

"Stauffer concurs with the reviewer's comments that the data was presented without sufficient experimental detail. As such, the report entitled 'Hydrolysis and Photolysis Degradation Studies of SC-0224' can be found in Appendix 4 (of the current submission). The analytical methods referenced in the study can be found in Appendixes 5 and 6 (in the current submission, as well)."

EAB Comment

This new study will be evaluated in this review. The rationale for separate testing of the anion and cation appears to be the differential rate of degradation each exhibits. The submitted aerobic soil metabolism studies seem to support this contention.

3.6 Issue raised by EAB

The registrant has failed to submit a study to support the aerobic soil metabolism data requirement.

Stauffer's Response

These studies can be found in Appendices 7 and 8 of this submission.

4

EAB Comment

This new study will be evaluated in section 4 of this review.

3.7 Issue raised by EAB

No data were submitted to support the accumulation in fish data requirement.

Stauffer's Response

The registrants response to this issue was quite lengthy, and is appended in its entirety to this review.

In brief, the registrant has requested a waiver of this data requirement, based on footnote 8 of 40 CFR 158.130 which states that this study will be required if significant concentrations of the active ingredient or its principal degradation products are likely to occur in the aquatic environments, and may accumulate in aquatic organisms. The registrant argues that...

- a. A company-conducted runoff study (submitted to EAB but not reviewed) showed no detectable parent anion or cation, nor its only known metabolite in any runoff water sample analyzed.
- b. The predicted bioconcentration factors (see appended table 1) based on the water solubility and octanol-water partition coefficient are very low.
- c. The label specifically prohibits application directly to bodies of water.

EAB Comment

EAB agrees with the registrant that it is unlikely that sulfosate will accumulate in fish. We therefore agree to waive the accumulation in fish data requirement.

4.0 REVIEW OF ADDITIONAL SUBMITTED DATA

- 4.1 Myers, H. W., K. S. Lee, G. G. Patchett and D. B. Katague. 1983. Hydrolysis and Photolysis Degradation Studies of SC-0224. Report No. WRC 83-53. de Guigne Technical Center, Stauffer Chemical Company, Richmond, CA. August 31, 1983. 29 pages, 8 figures, 11 tables, 10 references.

Introduction

This study was designed to evaluate the rates of both hydrolysis and photolysis of SC-0224, as well as to identify products, if any, formed by these processes.

Experimental

Unlabeled SC-0224 was prepared for each of the two experiments. For the hydrolysis part, product WRC-7746-9-1 contained 19.3% SC-0224 and 75.6% water. For the photolysis part, product WRC-8146-27-1 contained 90.9% SC-0224 and 4.2% water.

Hydrolysis:

Solutions at 10 and 100 ppm were prepared in commercial buffers of pH 5, 7, and 9. Numerous aliquots of each solution were added to teflon-sealed test tubes and maintained at 25°C in the dark for the 32 day experimental period. No distilled water (bufferless) controls were used. Neither solutions nor glassware had been sterile prior to initiation of the experiment.

Photolysis:

Solutions between 50 and 60 ppm were prepared in commercial buffers of pH 5, 7, and 9, which had previously been sterilized by passage through a 0.2µ Millipore filter. In addition, all glassware had been sterilized (method unspecified) prior to use.

Each of 3 standard preparative-size photoreactors (1300 ml) was filled with a test solution, with initial samples taken for analysis. The test solution was maintained at 40°C throughout the experimental period. Additional control aliquots were held for 30 days in a dark 40°C thermostatically-controlled bath.

The UV light source was turned on, and maintained at 24 hours/day throughout the experimental period. Considerable discussion in this study centered about the confirmation of wavelength distributions and intensities within the photoreactor. Sufficient data were submitted to confirm the pattern and intensities of the source used.

Analysis for the Carboxymethylaminomethylphosphonate (CMP) and aminomethylphosphonic acid anions was by derivitization with 9-fluorenylmethyl chloroformate followed by HPLC. The trimethylsulfonium (TMS) cation was dealkylated to dimethylsulfide, followed by GC quantification. Reported recoveries ranged from 83% to 103% for the anions and from 87% to 101% for the cation.

Results and Discussion

Hydrolysis:

Virtually no hydrolysis was measurable in all samples analyzed. In one of the 10 ppm pH 5 experiments only, some of the final data points unaccountably showed a loss of the TMS analyte. This was not seen in the matching 100 ppm experiment. In addition,

6

the dark pH 5 (photolytic) control (40°C) showed no degradation of the TMS analyte. It was therefore concluded that bacterial activity likely accounted for the observed losses.

Photolysis:

The reported data are summarized in tables 5 - 10, appended to this review. In brief, the degradation rates for anions vs. cations were found to be different. The TMS did not photolyze at

either pH 5 or pH 7. At pH 9, the first-order photolytic half-life was 31.7 days. For the CMP, halflives at pH 5, 7 and 9 were 14.6, 77.9 and 41.6 days, respectively. The only photolytic products for the CMP photolysis were phosphoric acid and aminomethylphosphonic acid (see table 11, appended).

Conclusions

EAB confirmed the statistics of the submitted data, and found them to be reliable. We conclude that both the hydrolysis and photolysis studies were carefully done and are acceptable in support of their respective data requirements.

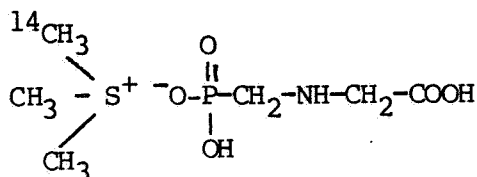
- 4.2 Dennison, J.E. and J.B. McBain. Undated. Metabolism of the SC-0224 Trimethylsulfonium Cation in Soil. Project 148193 - Herbicide SC-0224 (MIR-14-05-83). Stauffer Chemical Co. (company confidential). 11 pages (unnumbered), 8 references. 2 figures, 4 tables.

Introduction

This is the first of a two-part study (see §4.3 for review of the second part) designed to trace the fate of the trimethylsulfonium cation in soil under aerobic conditions.

Experimental

Standard SC-0224, TMS and CMAMP (carboxymethylaminomethylphosphonate) were prepared. The TMS portion of each molecule contained the radiolabel, as shown in the structure below. The ^{14}C -TMS SC-0224 had a specific activity of 20 mCi/mole and a radiopurity of 96.5% by TLC.



7

Air-dried Sorrento Loam soil (see attached table 1 for characteristics) (7.7% moisture) was sieved to pass a 3mm screen, then aliquotted to 1L biometer flasks. Each flask was treated with 10 ml of the ^{14}C -TMS SC-0224 (containing 6.0 mg SC-0224 and 1.08E8 dpm). Then, 16 ml water was added to adjust the soil to field capacity.

Two flasks were retained in a freezer as time zero controls. The remaining flasks were set up with alkali and polyurethane foam plugs, as described in figure 1 (appended) and stored at a constant 23°C in the dark. At intervals, alkali and foam plugs were taken for analysis and replaced for additional monitoring.

Plugs, alkali and soil were subjected to precipitation and/or extraction and/or combustion to quantify radiocomponents. DPM's were corrected by use of an internal standard.

Results and Discussion

Recovery data are summarized in table IV (appended). Total recoveries ranged from 72 to 88% for the combined soil/foam/NaOH. Cumulative ^{14}C recoveries for the first 165 days of the experiment are summarized in table II (appended). Overall recovery of $^{14}\text{CO}_2$ represented about 75% of applied.

No attempt was made by the authors to estimate the rate of the decline of parent SC-0224 to CO_2 and the other components.

EAB conducted a linear-log regression of the reported $^{14}\text{CO}_2$ data, plotting % remaining in the soil vs time interval. Results were as follows:

Day	% of applied Remaining	Day	% of applied Remaining
2	97.0	47	30.2
7	49.4	62	28.7
11	41.0	76	27.7
18	36.6	90	26.9
26	34.3	120	26.0
33	32.6	165	24.9

The regression curve was a very poor fit ($r^2=0.50$) with a predicted $t_{0.5}=130$ days. Testing the data for outliers, we determined that the day 2 value had a 100% probability of being an outlier at the 95% confidence level. Eliminating this value from the data set yielded an r^2 value of 0.72 (much better) and a projected halflife of 192 days.

Conclusions

It is apparent from the study that the decline of parent SC-0224 involves metabolism to CO₂. However, due to the numerous deficiencies, this study is unacceptable.

No attempt was made to identify all significant residues which occurred during the experimental period. In addition, material balance was marginal and half-life estimates were not made. Due to the necessity of eliminating the aberrant day-2 value, the EAB half-life estimate may lead to the (erroneous) conclusion that the amount of parent remaining initially was about 40%. Thus the data are proven statistically unreliable.

It is also unclear from the design of the biometer flask how sufficient oxygen could replace that used by the bacteria during metabolism, since the system appears to be essentially a closed one. A slow, constant O₂ flow-through might have yielded more reliable data.

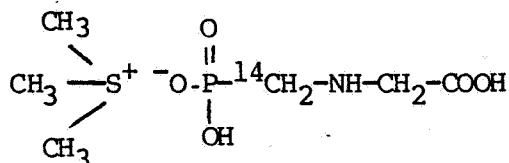
- 4.3 Dennison, J.E. and J.B. McBain. Undated. Metabolism of the SC-0224 Carboxymethylaminomethylphosphonate Anion in Soil. Project 148193 - Herbicide SC-0224 (MIR-25-8-83). Interim Report No. 1. Stauffer Chemical Co. (company confidential). 12 pages (unnumbered), 4 references. 2 figures, 5 tables.

Introduction

This second of a two-part study was designed to trace the fate of the trimethylsulfonium Carboxymethylaminomethylphosphonate anion in Soil under aerobic conditions.

Experimental

The ¹⁴C-CMAMP (¹⁴C carboxymethylaminomethylphosphonate) was prepared with the label in the phosphonomethyl moiety of the molecule (see structure below). It was found to have a specific activity of 30 mCi/mmol and a radiopurity of 96.5 ± 2.3% by TLC. Non-labeled SC-0224 was also used, and found to be 95.7% pure.



Air-dried Sorrento Loam soil (1.02% moisture) (see second table 1 for characteristics which differ from those in part one of the experiment) was sieved to pass a 3 mm screen, then aliquotted to 1L biometer flasks. Each flask was treated with 10 ml of the [¹⁴-C CMAMP] SC-0224 (containing 6.0 mg SC-0224 and 9.73E7 dpm).

Then, 28 ml water was added to adjust the soil to field capacity. The remaining experimental conditions were identical to those in part one of the experiment (see §4.2, above)

Results and Discussion

Recovery data are summarized in table IV (appended). Recoveries were excellent, ranging from 90.5% to 98.4% for combined soil/foam/NaOH. Cumulative ^{14}C recoveries for the first 30 days of the experiment are summarized in table II (appended). Overall recovery of $^{14}\text{CO}_2$ represented about 60.5% of applied.

No attempt was made by the authors to estimate the rate of decline of parent SC-0224 to CO_2 .

EAB conducted a linear-log regression of the reported $^{14}\text{CO}_2$ data, plotting % of applied remaining in the soil vs time. Results were as follows:

Day	% of applied Remaining
2	82.27
5	69.12
9	58.32
16	49.10
23	44.31
30	39.50

The regression curve was a good fit ($r^2=0.94$) with a predicted $t_{0.5}=27.9$ days.

Conclusions

It is apparent from the study that the decline of parent SC-0224 involves metabolism to CO_2 . The EAB half-life estimate, based on evolved CO_2 , was 27.9 days. However, due to the numerous deficiencies, this study is unacceptable.

No attempt was made to identify all significant residues which occurred during the experimental period. In addition, reported half-life estimates were inaccurate.

It is also unclear from the design of the biometer flask how sufficient oxygen could replace that used by the bacteria during metabolism, since the system appears to be essentially a closed one. A slow, constant O_2 flowthrough might have yielded more reliable results.

10

5.0 EXECUTIVE SUMMARY

The issues in §3.1 and 3.4 remain unresolved.

The submitted hydrolysis and aqueous photolysis studies were acceptable, in support of their respective data requirements.

For purposes of this EUP, EAB agrees to waive the accumulation in fish data requirement, based on the computed low potential for SC-0224 to accumulate in fish.

The two studies submitted in support of the aerobic soil metabolism data requirement contained numerous deficiencies; therefore, this data requirement is still unsatisfied.

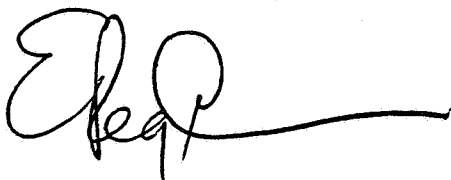
6.0 CONCLUSIONS

EAB cannot concur with the EUP at this time, due to the issues delineated in this review, and as summarized above.

7.0 RECOMMENDATION

The registrant should be informed of the EAB conclusions, and should provide an acceptable aerobic soil metabolism study for EAB review.

Since EAB has little information on the relative persistence, water solubility and octanol/water partition coefficient of the major degradates of SC-0224, the accumulation in fish study may be required for full registration. Pivotal information may be drawn from an acceptable aerobic soil metabolism study.



Emil Regelman
Chemist
EAB/HED
February 29, 1984

Self-inside Review

Page 12 is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

- ☒ Identity of product inert ingredients.
 - ☒ Identity of product inert impurities.
 - _____ Description of the product manufacturing process.
 - _____ Description of quality control procedures.
 - _____ Identity of the source of product ingredients.
 - _____ Sales or other commercial/financial information.
 - _____ A draft product label.
 - _____ The product confidential statement of formula.
 - _____ Information about a pending registration action.
 - _____ FIFRA registration data.
 - _____ The document is a duplicate of page(s) _____.
 - _____ The document is not responsive to the request.
-

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

6.1.3. Accumulation in Fish

Stauffer does not agree that a fish accumulation study should be considered a requirement for the EUPs or any other subsequent registration activities. Footnote 8 of 40 CFR 158.130 indicates that this study is required if significant concentrations of the active ingredient or its principal degradation products are likely to occur in aquatic environments and may accumulate in aquatic organisms.

Proposed uses of SC-0224 do not include direct application to water. In fact, the proposed EUP label includes precautionary language to prevent this type of application. In order to assess the significance of a runoff potential occurring from some of the proposed uses, Stauffer conducted a runoff study (Accession No. 249804, Appendix D-2 and a subsequent letter of July 6, 1983 detailing rainfall and irrigation). With the concerns expressed by the reviewer in section 7.0 of the EAB reviewer's comments, it is unclear why the submitted study was not reviewed.

In this study, SC-0224 4-LC was applied at a rate of 6 lbs. a.i. per acre to plots located on a 20° slope at the bottom of which were plastic lined trenches for water collection. A total of 13" of water was applied to these plots over a 60 day period by irrigation or natural rainfall. Most of the applied water (10.2") occurred as heavy irrigation immediately prior to sampling from the trenches. Neither the parent cation, anion nor its only known soil metabolite could be detected in any of the water samples removed from the runoff trenches.

Additionally, it is well known that the bioaccumulation of a chemical in aquatic organisms is strongly dependent on the physical properties of the chemical such as water solubility and the ability of the chemical to partition into lipids. For many chemicals, excellent correlations have been shown between the bioconcentration factor (BCF) in fish and the water/octanol partition coefficient and/or the molar water solubility (see references 1-6). The BCF for SC-0224 was estimated using published methods as shown in Table 1. The estimated BCF values for SC-0224 ranged from 0.32 to 4.6. These calculations clearly indicate that SC-0224 would not be expected to accumulate in aquatic organisms. The very low bioaccumulation potential of SC-0224 predicted by these estimates is further supported by the high water solubility (430 g/100 ml) and very low water/octanol partition coefficient ($\ll 10$).

Subdivisions N and E guidelines clearly indicate that a fish accumulation study would not be appropriate for SC-0224 since it has a low potential for accumulation (low octanol/water partition coefficient, low bioconcentration factor and high water solubility) and residues are not likely to reach water under the proposed uses (no residues are detected in the runoff study).

TABLE 1

ESTIMATION OF BIOCONCENTRATION FACTOR FOR SC-0224

Octanol/Water Partition Coefficient (Kow) ^a	LOG Kow	Molar Water Solubility (s) ^b	Log S	Estimation of Bioconcentration Factor (BCF)			
				Briggs ^c	Veith ^f	Chiou ^d	Neely ^e
<<10 ^a	1	17.6 x 10 ⁶ g	7.25	0.32	1.4	0.53	4.6

^a In measuring the water/octanol partition coefficient, no SC-0224 (<0.1 ppm) could be measured in the octanol phase. Therefore, the Kow was reported as 10 according to EPA guidelines.

^b Molar water solubility = Solubility of SC-0224 in umoles/L.

^c Calculated according to Briggs (1): $\text{Log BCF} = \text{Log Kow} - 1.5$

^d Calculated according to Chiou, et al. (2): $\text{Log BCF} = 3.41 - 0.508 (\text{Log S})$.

^e Calculated according to Neely, et al. (5): $\text{Log BCF} = 0.542 \text{ Log Kow} + 0.124$.

^f Calculated according to Veith, et al. (6): $\text{Log BCF} = 0.85 \text{ Log Kow} + 0.70$.

^g The molecular weight of SC-0224 is 245 g/mole. The solubility of SC-0224 in water is 430 g/100 ml.

REFERENCES

1. Briggs, G. G. Theoretical and experimental relationships between soil absorption, octanol-water partition coefficients, water solubilities, bioconcentration factors and the parachlor. *J. Ag. Fd. Chem.* 29:1050-1059 (1981).
2. Chiou, C. T., Freed, V. H., Schmedding D. W., and Kohnert, R. L. Partition coefficient and bioaccumulation of selected organic chemicals. *Environ. Sci. Technol.* 11:475-478 (1977).
3. Kenaga, E. E. and Goring, C. A. I. Relationship between water solubility, soil absorption, octanol-water partition coefficient, and concentration of chemicals in biota. *Aquatic Toxicology ASTM Stp 707*. J. Eaton, P. R. Parrish, and A. C. Hendrik, eds. American Society for Testing of Materials (1980).
4. Leo, A., Hansch, C., and Elkins, D. Partition coefficients and their uses. *Chem. Reviews.* 7:525-616 (1971).
5. Neely, W. B., Branson, D. R., and Blau, G. F. Partition coefficient to measure bioconcentration potential of organic chemicals in fish. *Environ. Sci. Technol.* 8:1113-1115 (1974).
6. Veith, E. D., DeFoe, D. L., and B. V. Gergsteadt. Measuring and estimating the bioconcentration factor of chemicals in fish. *J. Fish. Res. Bd. Can.* 36:1040-1048 (1979).
7. Pesticide Assessment Guidelines. Subdivision E: Hazard Evaluation: Wildlife and Aquatic Organisms Section 72-6. Aquatic Organism accumulation Tests (p. 82). EPA 540/9-82-024, October, 1983.

Substantive Review

Page _____ is not included in this copy.

Pages 16 through 28 are not included in this copy.

The material not included contains the following type of information:

- _____ Identity of product inert ingredients.
 - _____ Identity of product inert impurities.
 - _____ Description of the product manufacturing process.
 - _____ Description of quality control procedures.
 - _____ Identity of the source of product ingredients.
 - _____ Sales or other commercial/financial information.
 - _____ A draft product label.
 - _____ The product confidential statement of formula.
 - _____ Information about a pending registration action.
 - ☒ FIFRA registration data.
 - _____ The document is a duplicate of page(s) _____.
 - _____ The document is not responsive to the request.
-

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.



CASWELL FILE

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

FEB 8 1984

MEMORANDUM

TO: Robert Taylor, PM 25
Registration Division (TS-767)

THRU: Robert B. Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

SUBJECT: 476-EUP-RNE and 476-EUP-RNG for SC-0224 4-LC Nonselec-
tive Foliar Systemic Herbicide for Weed Control in
Non Food Crop Areas. Trimethylsulfonium carboxymethyl-
aminomethylphosphonate. R-50224. CASWELL # 893C
Accession Nos. 249801, 249802, 249803, 249804.

Applicant: Stauffer Chemical Company
1200 S. 47th Street
Richmond, California 94804

OK for RBD 12-16-83
WBS 01/84

Stauffer Chemical Company requests an experimental use permit for SC-0224 4-LC non-selective foliar systemic herbicide for weed control in non food areas. The use will include railroad, highway, and other rights of way use patterns in the states of Colorado, Iowa, Kansas, Minnesota, Nebraska, North and South Dakota, Missouri, Illinois, Indiana, Michigan, Wisconsin, Conn., Delaware, Kentucky, Maine, New Jersey, New York, Ohio, Pennsylvania, Virginia, Florida, Georgia, North and South Carolina, Tennessee, Louisiana, Mississippi, New Mexico, Oklahoma, Texas, Arizona, Nevada, Utah, Idaho, Montana, Oregon, Washington, and Wyoming; 41 of the 50 states. The data are needed to support future registrations of SC-0224 4-LC. The proposed experimental program is from Sept. 1, 1983 to September 1, 1985.

29

10. Acute Dermal Toxicity of SC-0224-4-LC Formulation in Rabbits:
- a. LD₅₀, intact and abraded skin = 1279 mg/kg. OK
 - b. Toxicity Category II. See TAB 12
p 8-11
 - c. Core Minimum Data
11. Primary Dermal Irritation of SC-0224-4-LC Formulation in Rabbits: OK
- a. Formulation is a Moderate Dermal Irritant
 - b. Toxicity Category III.
 - c. Core Minimum Data.
12. Primary Eye Irritation of SC-0224-4-LC Formulation in Rabbits: OK
- a. Formulation is very corrosive to the eye, producing corneal opacity, iritis, and severe conjunctivitis. This contrasts with the technical chemical, which is only mildly irritating to the eye.
 - b. The irritation and corrosiveness is reduced somewhat by washing the eyes.
 - c. Toxicity Category I.
 - d. The data are Core Minimum.
13. The proposed labels for both the "concentrate" and for the 4 LC formulation are satisfactory, and accurately reflects the corrosive nature of the formulation to the eyes, in the case of the formulation.

Roland A. Gessert

Roland A. Gessert, D.V.M.
Veterinary Medical Officer
Toxicology Review Section I

TS-769:GESSERT:s11:X73710:9/19/83
11/7/83

card 7

Acute Oral Toxicity of SC-0224 Technical Chemical in Male and Female Sprague-Dawley Rats. Conducted by T. Billow and D. Crume; Stauffer Chemical Co.; Richmond Toxicology Laboratory; Richmond, California. Report T-11185. October-November, 1982. Accession No. 249802. Caswell No. 893C.

Material Tested:

Trimethylsulfonium carboxymethylaminoethyl-phosphonate. SC-0224 Technical Chemical. Lot #7981-12-01. An herbicide of 62% purity.

Male Rats: After 16-18 hours fasting ten male rats per dose level were treated by oral gavage at the rate of 500, 550, 700, 800, or 900 mg/kg. Twenty rats were dosed with 600 mg/kg. Mortality was 10/10, 6/10, 3/10, and 5/20 for doses of 900 mg/kg, 800 mg/kg, 700 mg/kg, and 600 mg/kg, respectively. The oral LD₅₀ for male rats was 748 mg/kg, with 95% confidence limits of 667-840 mg/kg.

Female Rats: After 16-18 hours fasting ten female rats per dose level were treated by oral gavage at the rate of 550, 700, 800, and 900 mg technical chemical per kg body weight. Mortality was 1/10, 5/10, 4/10, and 9/10 for doses of 550, 700, 800, and 900 mg/kg, respectively. The oral LD₅₀ for female rats was 755 mg/kg with 95% confidence limits of 677-841 mg/kg.

Clinical Signs:

A single dose of 900 mg/kg killed 9 male rats within 4 hours and 9 female rats within 24 hours. Adverse clinical signs included mild to severe depression, prostration, ptosis, slow and shallow respiration, and tremors.

Necropsy findings in rats dying on test were dark red spotted lungs, distended bladder filled with dark fluid, darkened livers, and dark spleens. Survivors necropsied on day 14 appeared normal.

Controls: Forty males and 40 females dosed with water appeared normal throughout the 14-day observation period and on necropsy at day 14.

The data meet Core-Minimum standards.

Toxicity Category - III.

Acute Dermal Toxicity of SC-0224 Technical Chemical in Stauffland Albino Rabbits - Abraded Skin. Conducted by A. Howell, B. Jones, and S. Sorenson; Stauffer Chemical Co.; Richmond Toxicology Laboratory; Richmond, California. Report T-11185. October-November, 1982. Accession No. 249802. Caswell No. 893C.

Material Tested:

Trimethylsulfonium carboxymethylaminoethylphosphonate. SC-0224 Technical Chemical. Lot #79810-12-01. An herbicide of 62% purity.

Four male and female Stauffland albino rabbits per dose level had the test material applied to the clipped abraded abdominal skin under a protective binder. Dose levels were 2200, 1900, 1600, 1200, 1000, 900, and 800 mg/kg body weight. Three male and three female rabbits served as zero dose controls. After 24 hours the binder and the test material were removed, the treatment sites were inspected for irritation, and the abdomens were rewrapped in a gauze binder. Three days later the gauze binder was removed, and the rabbits were observed for 14 days following initial treatment. Necropsies were performed on all rabbits that died during the study and on all survivors at 14 days.

Results:

Three of 8 rabbits died at 2200 mg/kg; 2/8 at 1900 mg/kg; 3/8 at 1600 mg/kg; 2/8 at 1200 mg/kg; 1/8 at 1000 mg/kg; and 1/8 at 900 mg/kg. There was no mortality at 800 mg/kg or in the controls.

Necropsy Effects seen in rabbits which died on test included red and purple areas below the right kidney in one rabbit at 2200, 1900, and 1600 mg/kg and also pale lungs in 1 rabbit at each of these doses.

Rabbits which survived to 14 days all appeared normal on necropsy.

Clinical Signs were mild to severe depression in some rabbits at all treatment levels.

Local Dermal Effects was a mild to moderate erythema after 24 hour exposure.

Clinical signs and local dermal effects did not appear to be related to dose.

30

Acute Dermal Toxicity of SC-0224 Technical Chemical in Stauffland Albino Rabbits - Intact Skin.

This portion of the study was conducted in the same manner as for the abraded skin. A single dose level of 2000 mg/kg body weight was used. There was no mortality. The only clinical sign observed was mild depression, all rabbits appearing normal by day 2.

The only local dermal effect was mild erythema after 24 hour exposure.

Necropsy on day 14 revealed no abnormal findings.

However, "data" were provided in a summary form. Individual animal data and observations were not provided. Individual necropsy reports were not provided. The data therefore are classified Core supplementary. Upon submission of complete individual animal data the core classification possibly may be upgraded. ✓

Conclusions:

1. Acute dermal LD₅₀ in male and female rabbits (intact and abraded skin) was greater than 2000 mg/kg.
2. Toxicity Category III.
3. Data are Core Supplementary. ✓

Primary Skin Irritation of SC-0224 Technical Chemical in Stauffland Albino Rabbits. Conducted by T. Billow and D. Crume. Stauffer Chemical Company. Richmond Toxicology Laboratory; Richmond California. Report T-11185. October-November, 1982. Accession No. 249,802. Caswell No. 893C.

Material Tested:

Trimethylsulfonium carboxymethylaminoethylphosphonate. SC-0224 Technical Chemical. Lot #7981-12-01. An herbicide of 62% purity. pH 5.65.

Twenty-four Hour Exposure:

Six Stauffland albino rabbits were used in the study. One-half ml of SC-0224 technical chemical was placed on an abraded site and an intact site and covered with a one-inch square gauze patch. This was secured by adhesive tape and wrapped with rubberized damming for 24 hours. After 24 hours the coverings and test material were removed and the reactions scored. The site reactions were also scored after 72 hours.

Results:

At 24 hours mild erythema was observed in all 6 rabbits in intact and abraded skin. Mild edema was seen in abraded sites in 3 rabbits and in the intact site in one additional rabbit. At 72 hours the irritation had subsided, with mild edema being seen in 1 intact site of only 1 rabbit. The Primary Irritation Score (Draize) was 0.67.

Four-Hour Exposure:

The above procedure was also conducted with an exposure time of 4 hours and observations and scoring being made after 4 hours, 24 hours, and 72 hours.

After 4 hours mild erythema was seen at the abraded sites in 4 rabbits. In 2 of these rabbits the erythema persisted for 24 hours. In one of the rabbits mild edema was also seen at 4 hours, but not subsequently. No reactions were seen at 72 hours. The Primary Irritant Score was 0.19.

Conclusions:

1. SC-0224 technical chemical is a mild dermal irritant.
2. Toxicity Category - IV.
3. Data are Core-Minimum.

Primary Eye Irritation of SC-0224 Technical Chemical in Stauffland Albino Rabbits. Conducted by T. Billow and D. Crume. Stauffer Chemical Company. Richmond Toxicology Laboratory; Richmond California. Report T-11185. October-November, 1982. Accession No. 249802. Caswell No. 893C.

Material Tested:

Trimethylsulfonium carboxymethylaminoethylphosphonate.
SC-0224 Technical Chemical. Lot #7981-12-01. 62% purity.
pH 5.65.

Nine rabbits were treated by placing 0.1 ml of the chemical inside the lower lid of one eye of each rabbit. In 3 of the rabbits the eye was washed with water 20-30 seconds after exposure, and in the remaining 6 rabbits the eye was not washed. Untreated eyes served as negative controls. The cornea, iris, and conjunctivae were observed at 24, 48, and 72 hours, and at 4, 7, 10, 11, and 14 days after treatment. Scoring was according to the method of Draize.

Results:

There was no corneal involvement in any of the eyes. In the unwashed eyes, mild iritis was seen in 1 rabbit and mild conjunctivitis in all 6 rabbits at 24 hours. All unwashed eyes were cleared by 7 days.

In the 3 washed eyes mild conjunctivitis was seen in 2 of the rabbits. This had cleared by day 3.

Conclusions:

1. SC-0224 is mildly irritating to the conjunctivae. The irritation is reduced by washing.

2. Toxicity Category - III.

3. The data are Core-Minimum.

Acute Inhalation Toxicity of SC-0224 Technical Chemical in Sprague-Dawley Rats. Conducted by Stephen MacAskill, M. R. Chaffee, et al., Stauffer Chemical Company, Environmental Health Center Inhalation Facility, 400 Farmington Ave., Farmington, Connecticut 06032. September 1982. Accession No. 249802. Study No. T-11084. Caswell #893C.

Material Tested:

Trimethylsulfonium carboxymethylaminoethylphosphonate. SC-0224 Technical Chemical. Lot #7981-12-01. 62% purity. pH 5.65.

Procedure:

Before exposing the rats to inhalation exposure of the test chemical, the equipment was adjusted and tested to produce the highest attainable concentration, about 5 mg/L (aerosol plus vapor). This was done by regulating chamber airflow, generator airflow, and generator "dilution airflow."

Ten male and 10 female Sprague-Dawley rats, 8-10 weeks old were then exposed to this regulator atmosphere. They were caged individually within the chamber, having first been weighed and ear-tagged.

The rats were exposed to the test atmosphere for 4 hours with a chamber flow of 17.4 air changes per hour, and then remained in the chamber for an additional hour with air only in order to air flush the chemical from their pelts.

Ten male and 10 female rats were then similarly treated in a clean chamber, but using air only instead of the test atmosphere.

The rats were observed during exposure and then twice daily for 14 days. They were weighed on the day of exposure, on days 2 and 7 after exposure and on day 14 at the end of the experiment. On day 14 the rats were anesthetized by sodium pentobarbital injection, killed by exsanguination, and necropsied. The following tissues were collected, fixed in 10% neutral buffered formalin and held for future histopathological examination, if needed: trachea, larynx, bronchi, nasal passages, lungs, liver, spleen, kidneys, adrenals, heart, and any tissues which appeared abnormal.

Results:

The nominal concentration of the chemical was 14.93 mg chemical per liter of atmosphere. (Weight of test substance used during exposure/total chamber air flow).

The actual measured chamber concentration of the chemical was 6.92 mg per liter of atmosphere.

The Mass Medium Aerodynamic Diameter of the aerosolized chemical particles was 3.5 um (at 64 minutes) and 2.8 um (at 184 minutes).

The only effects seen during treatment were wet fur (4 rats) and salivation. Most of the rats exposed to the chemical also had stained fur for one day following exposure. 6 male rats and 2 female rats also showed chromorhinorrhea, especially on the day of exposure (day 0).

In body weight after 14 days, the females exposed to the chemical weighed 99% of their pre-exposure weight whereas the exposed males and all the controls showed a net weight gain of 5-12% over the 14 day observation period, the greater weight gains being seen in the controls.

On necropsy there were no findings which could be related to exposure.

Conclusions:

1. The $LC_{50} > 6.9$ mg/liter.
2. Data meet Core-Minimum standards.

January 8, 1990

Tox Chem No. 6930

MEMORANDUM

SUBJECT: EPA ID No. 10182-ETT/10182-ETA
New Chemical Screen: Sulfosate

TO: William Evans
Special Projects & Science Management/EFED

FROM: David G. Van Ormer, Ph.D. *DVO 01-08-90*
Science Administration Section
Science Analysis and Coordination Branch (H7509C)

THRU: Esther Saito *E. Saito 01-09-90*
Acting Head, Science Administration Section
Science Analysis and Coordination Branch, HED (H7509C)

Sulfosate now passess the Toxicology Screen.

The requested organ/body weight ratios (our memo of Oct 11, 1989)
have been submitted.

filed 10/1-8-90

TABLE 6

SUMMARY OF RECHALLENGE RESULTS

EXPERIMENTAL GROUP	SKIN RESPONSE	HOURS AFTER FIRST CHALLENGE APPLICATION					
		24		48		72	
		TMC	VC	TM	V	TM	V
TEST MATERIAL (SC-0224 4LC-E)	ERYTHEMA	SCORE ^a	0	0	0	0	0
		FREQUENCY ^b	0/10	0/10	0/10	0/10	0/10
	EDEMA	SCORE	0	0	0	0	0
		FREQUENCY	0/10	0/10	0/10	0/10	0/10
NEGATIVE CONTROL (0.85% Saline)	ERYTHEMA	SCORE	0	0	0	0	0
		FREQUENCY	0/10	0/10	0/10	0/10	0/10
	EDEMA	SCORE	0	0	0	0	0
		FREQUENCY	0/10	0/10	0/10	0/10	0/10
POSITIVE CONTROL (0.1% DNCB)	ERYTHEMA	SCORE	2.1	0	1.9	1.7	0
		FREQUENCY	10/10	0/10	10/10	10/10	0/10
	EDEMA	SCORE	2.3	0	2.7	1.0	0
		FREQUENCY	3/10	0/10	7/10	1/10	0/10

^a AVERAGE SCORE FOR RESPONSES > 1
^b FREQUENCY OF RESPONSE SCORES > 1
^c TM - TEST MATERIAL OR DNCB SITE
^d V - VEHICLE SITE



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

CASWELL FILE

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

December 26, 1989

MEMORANDUM

SUBJECT: New Chemical Screening Meeting for Sulfosate

TO: Addressees

FROM: William Evans *W.E.*
Special Projects and Science Management Staff/EFED

Attached please find data submitted for the registration of Sulfosate for use on corn. As required by SOP #3003.4 EFED and HED are to screen the chemical to ensure that the data package is acceptable for scientific review. You may recall that Sulfosate previously failed the screen in October, 1989 in the EFWGB and TOX branches due to the inadequate characterization of residues of the two confined rotational crop studies and the 21-day dermal study which required additional data to provide organ/body weight ratios.

A meeting has been arranged for **Wednesday January 10, 1990 at 9:00 in room 1023** for EFED, HED, and RD to discuss the results of this rescreen. If the chemical passes this rescreening it will immediately be put into review and a due date will be assigned. EFGWB and TOX should be prepared bring the data and a pass/fail decision to the meeting. A memo (report) stating the reasons for passage or failure is to be submitted within two days of the meeting.

Please plan to attend this meeting or have someone from your branch attend. If you have any questions please contact me on 557-7634.

ADDRESSEES

Norm Cook, EEB/EFED (cover memo only)
Robert Holst, EFGW/EFED
Bob Coberly, TOX/HED
Charles Frick, TOX/HED (cover memo only)
Micheal Firestone, NDEB/HED (cover memo only)
Cynthia Giles, FHB/RD (cover memo only)
Larry Chloupek, RSEB/RD (cover memo only)
Lynn Bradley, RSEB/RD (cover memo only)
Bob Quick, DEB/HED (cover memo only)
Nancy Schwall, RD (cover memo only)
Stephanie Irene, RD (cover memo only)

40