

CASWELL FILE



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

005584

MAR 10 1986

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Applications for Pesticide Registrations for the
Nonselective Foliar Systemic Herbicides, SC-0224 4-LC
and SC-0224 Concentrate, for Weed Control in Non Food
Crop Areas. Trimethylsulfonium carboxymethylamino-
methylphosphonate. R-50224. CASWELL #893C.
Accession Nos. 250544, 250545, 250547, 250548, 260508.

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

FROM: Brian Dementi, Ph.D.
Review Section #1
Toxicology Branch/HED (TS-769)

Brian Dementi 3/7/86

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

RTJ 3/7/86
W. A. 3/10/86

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

Stauffer Chemical Company requests pesticide registration for
SC-0224 and SC-0224 4-LC, non-selective foliar systemic herbicides,
for weed control in non-crop areas.

Recommendations:

Pesticide registrations for weed control in non food crop areas
for the herbicides SC-0224 and SC-0224 4-LC are supported by available
toxicity data. See the February 8, 1984 review by Dr. R. A. Gessert
and Dr. John Chen on experimental use permits for SC-0224 LC, CASWELL
#893C.

Deficiencies identified in the above review have been satisfied.
Specifically, these include: 1) Information regarding eight mutagenicity
studies (identified in Section 2, A-F of the Review Recommendations).
Supplementary information submitted by Stauffer in response to the
indicated mutagenicity deficiencies has been reviewed and appraised
acceptable by Dr. John Chen (3/4/86 review of Dr. Chen); 2) Individual

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animal data requested in support of the acute dermal toxicity study. Review of this information supports the classification of core minimum as indicated; and 3) Information requested as to dosage used in the the teratology study. Stauffer has affirmed that the dosages contained in the original report were based on, or expressed in terms of, the actual amount of active ingredient. It is recommended that the core rating for this study be upgraded from supplementary to guideline.

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Review of the Registrant's Response to the Previous TB Review Comments Concerning the Following Mutagenicity Studies with SC-0224 (TB Memo 2/8/84 Roland A. Gessert)

1. Mutagenicity Evaluation of R-50224 in Sex-Linked Recessive Lethal Test in *Drosophila melanogaster*
Litton Bionetics Inc. Project No. 22169, June 13, 1982

Registrant's Response:

- 1) In both of these studies males were collected from the strain Oregon-R which is maintained in our laboratory and examined visually for any signs of spontaneous phenotypic mutations.
- 2) Standard procedure in this laboratory is to complete the scoring of the F₂ generation within 20 days of the date of the F₁ cross. In the fruit fly, the elapsed time for a new generation is 15 days at 20°C and no less than 10 days at 25°C, the normal temperature range of our laboratory (Demerec, M; B.F. Kaufmann. Drosophila Guide, Academic Press, 1978.).

Reviewer's Comments:

Registrant has provided the information previously requested.

Recommendation:

This study is upgraded to acceptable.

2. Mutagenicity Evaluation of SC-0224 in Bone Marrow Cytogenetic Analysis in Rats
Stauffer Chemical Co. Report No. T-10884, September, 1982

Registrant's Response:

Bone marrow was aspirated to Hank's Balanced Salt Solution, centrifuged at approximately 700 rpm for 10 minutes to pellet the cells which were then resuspended in the drop of remaining medium to break up the clumps. Three to five milliliters of 0.75 M KCl prewarmed to 37°C was slowly added to the cells. The cells were centrifuged for 10 minutes at 700 rpm, the supernatant discarded, and the pellet resuspended in a drop of residual KCl. Carnoy's fixative (3-5 ml) was added to the cells while they were kept suspended by continuous gentle agitation. After 30 minutes at room temperature the fixative was replaced by 3-5 ml of fresh Carnoy's. Cells in fixative were stored in the refrigerator at 4°C overnight. In the morning, cells were resuspended in 0.05 ml of fresh Carnoy's. This suspension was dropped onto clean, dry microscope slides; the cells were spread by blowing on the slide and allowed to air dry overnight. In our experience this procedure yields preparations superior to those made by dropping swollen cells onto chilled wet slides and "fixing" them by flaming.

Reviewer's Comments:

The provided procedures for the preparation of chromosome slides in this study are considered adequate and acceptable.

Recommendation:

This study is upgraded to acceptable.

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3. Mutagenicity Evaluation of SC-0224 in Salmonella tychimurium. Ames Salmonella/
Microsomal Mutagenesis Assay
Stauffer Chemical Co. Report No. T-10847, January 19, 1982

Registrant's Response:

- 1) The nutrient broth used in this study was Oxoid Nutrient Broth No. 2. The selective plates consisted of Vogel-Bonner medium E with 2% glucose and 1.5% Bacto-difco agar. Bacteria were added to this in overlay agar containing 0.5% NaCl, 0.05 mM L-Histidine and 0.05 mM Biotin.
- 2) The reviewer is correct. The fact that the slight increase was not repeated by additional trials led to the conclusion reported on Page 3 of the report: "R-50224 is not mutagenic in the Ames Salmonella/Microsomal assay when tested directly or in the presence of an Aroclor 1254 or phenobarbital induced rat or mouse liver S-9 metabolic activation system". The criteria by which this conclusion was reached are stated on pages 12 and 13 of the reports.

Reviewer's Comments:

The registrant's response to the two deficiencies cited in the previous TB review of this study is acceptable.

Recommendation:

This study is upgraded to acceptable.

4. Mutagenicity Evaluation of SC-0224 in Salmonella typhimurium. Ames Salmonella/
Microsomal Mutagenesis Assay
Stauffer Chemical Co. Report No. T-11070

Registrant's Response:

See the response indicated in the previous study (Report No. T-10847).

Reviewer's Comments:

See the comments indicated in the previous study (Report No. T-10847).

Recommendation:

This study is upgraded to acceptable.

5. SC-0224 Mutagenicity Evaluation in the Chinese Hamster Ovary Cytogenetic Assay
(Lot #6841-48-3). Stauffer Chemical Co. Report No. T-10875. July 6, 1982

Registrant's Response:

- 1) The conditions required to obtain well-spread, high-quality metaphases vary from cell type to cell type in our experience and are best determined empirically for the cell type being used. Cells used in these experiments

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were in hypotonic medium (0.075 M KCl at ambient room temperature (approximately 21° C) for ten minutes and then collected by centrifugation for 5 minutes at 500 rpm. Therefore, total time in hypotonic was about 15 minutes (5 minutes for the centrifuge to decelerate and stop). This procedure provides adequate numbers of well-spread chromosomes. Cells were fixed with three changes of 3:1 methanol:glacial acetic acid (the last refrigerated at 4° C overnight), and the swollen, fixed cells dropped onto clean, dry slides at ambient room temperature and air dried. We find this procedure to yield preparations as good as those obtained by dropping cells onto chilled, wet slides with subsequent "fixing" by flaming.

- 2) The exposure without S-9 activation was for 10 hours; that with an S-9 system included was 2 hours.

Reviewer's Comments:

The provided information concerning the preparation of chromosome slides and the exposure time for this study are adequate and acceptable.

Recommendation:

This study is upgraded to acceptable.

6. SC-0224 Mutagenicity Evaluation in the Chinese Hamster Ovary Cytogenetic Assay (Lot #7466-18-01). Stauffer Chemical Co. Report No. T-10875. July 22, 1982

Registrant's Response:

See the response indicated in the previous study (Report No. T-10875; Lot #6841-48-3).

Reviewer's Comments:

See the comments indicated in the previous study (Report No. T-10875; Lot #6841-48-3).

Recommendation:

This study is upgraded to acceptable.

7. SC-0224 Mutagenicity Evaluation in Mouse Lymphoma Multiple Endpoint Test - Forward Mutation Assay (Lot #7269-10 and #6841-48-3). Stauffer Chemical Co. Study No. T-10348. February 8, 1982

Registrant's Response:

Table 4 is labeled correctly. It presents data gathered from an activation study in which a second sample of R-50224 was tested for comparison with result from 2 other trials (Tables: 2, activation; 3, activation) using a different sample. Non-activation tests were also conducted. These data are also presented in Table 2 (non-activation) and 3 (non-activation).

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Reviewer's Comments:

The provided explanation for the data presented in Table 4 is justified.

Recommendation:

This study is upgraded to acceptable.

8. SC-0224 Morphological Transformation of Balb/3T Cells (Lot #7269-10)
Stauffer Chemical Co. Report No. T-10849. January 4, 1982

Registrant's Response:

Dishes (Petri plates) were used in toxicity assay and T-25 flasks for the transformation assay. T-25 flasks were used for all studies. These culture vessels are incubated at 37°C in a humidified 5% CO₂ in air atmosphere. CO₂ is automatically injected into the incubator when levels fall below 5%. Checks are made daily with a Fyrite CO₂ monitoring device to confirm that the CO₂ sensors are working accurately. Caps on T-25 flasks were open slightly during incubation to permit free gas exchange. Transformation assays are all incubated in a designated incubator.

Reviewer's Comments:

The provided information concerning the specific culture flasks and the humidified 5% CO₂ incubator for this Balb/3T cells transformation study are adequate.

Recommendation:

This study is upgraded to acceptable.

John H. Chen
John Chen
Reviewer
Section #1
TB/HED
3/4/86

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John, These are
the 8 Muta
Studies for Sulfisate
since suggested for
your Review. Brian D.

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3/7/86

Memorandum To Caswell File # 893C, Re: SC-0224 and SC-0224 4-LC

Review of the registrant's information submitted in response to the previous toxicology review concerning the acute dermal toxicity of SC-0224 technical in Staufferland albino rabbits/T-11185 (see February 8, 1984 review by Drs. Gessert and Chen)

Stauffer Chemical Company has submitted individual animal necropsy data (accession no. 260508) for review as the means of satisfying the requirements for upgrading the core rating, as suggested in the Branch review. Inspection of this necropsy data does not disclose any finding that would preclude updating the study to core minimum.

Recommendation: Change study rating to Core Minimum

With respect to the previous Toxicology review concerning the teratology study in CD rats with SC-0224/T-11050, Stauffer has affirmed that the dosages contained in the original report were expressed in terms of the actual amount of active ingredient used.

Recommendation: Upgrade core rating from Supplementary to Guideline

Brian Dementi

Brian Dementi, Ph.D.
Review Section 1

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