1-21-75

Environmental Chemistry Review for Difenzoquat methyl sulphate (1,2-dimethyl-3,5-diphenyl-1H-pyrazolium methyl sulphate) (Avenge)

Permit No. 241-EXP
PP No. 5G-1576
American Cyanamid
Submitted 11/27/74

1/21/75

I. RECOMMENDATIONS

RL Temporary permit on wheat.

A. The following comments are made on the data submitted:

1. The environmental chemistry studies support only one application per growing season. This limitation must be clearly expressed in the directions for use on the label.

2. The soil metabolism and dissipation study: Fate on Soil under Field Conditions (Report C-540) is incomplete in that the loss of activity from the treated soil is not adequately explained. Additional studies including material balance and chemical identification or characterization of soil degradation products are needed. If volatile products are suspected, a study is needed to trap volatile products and identify them.

3. Concerning the Study: Fate on soil under field conditions (C-540). The summary of this report states that the rapid initial loss is consistent with known routes of photo-degradation. According to the photodegradation studies submitted, the routes of photodegradation would not involve any loss of radioactivity. Please elucidate how this loss was consistent with the photodegradation studies (Notebook numbers AC-2191, 2306, and 2392).

4. Soil characteristics (C. E. C., pH, % O. M., Sand, Silt and Clay) will be needed for the study "Determination of CL 84, 777 Residues in Wheat and Barley in Soil Treated the Previous Year with Avenge" (Report C0574).

5. For the reports: "Avenge Determination of CL 84777 Residues in Soil," reports # C-555 (California), C556 (California), C-557 (Oregon), C-560 (Minnesota), and C-561 (Minnesota) we need the following soil data:

a. Organic content

b. cation exchange capacity

c. pH

d. Field Moisture capacity

e. Percent: sand, silt, clay

f. Nitrate - nitrite level.

6. Concerning the report: "Soil Leaching Studies of CL 84,777" (section H-5, notebook number AC-2266) we must know the position of the radiolabel and the rate of application of Avenge.

7. The following information concerning the report: "Avenge, The Gas Chromatographic Determination of 1,2 dimethyl 3,5 diphenyl pyrazolium methyl sulfate in soil (Report C-462) is needed:

a. position of the Carbon - 14 label

b. Soil characteristics of soil used (i.e., C.E.C., pH, % O. M., Sand, Silt, Clay).

B. Completion of the following studies will be needed before final registration can be considered.

1. An anaerobic metabolism test. See enclosure. (Send out V-22 of second draft guidelines).

ROTATIONAL AND/OR SUBSEQUENT CROP RESIDUE STUDIES

(Radiolabeled study)

1. For crops rotated immediately after harvest of a crop in the treated area, the pesticide is to be aged in a sandy loam soil under aerobic conditions for about 120 days, then the soil planted to a root crop, small grain, and a vegetable. The root crop is required; however, crops in two other crop groupings may be substituted for the small grain and vegetable.

2. For crops rotated the following year after treatment, the pesticide is to be aged in the soil for one year prior to planting. Crops should be as above.

3. If significant residues are found, then actual field studies using non-labeled pesticide will be required. Such data must be obtained under actual agricultural practice.

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4. If residues are found in rotational and/or subsequent crops in the field, then a labeling restriction will be needed. This restriction will take the form of a time interval from application to planting of rotational crops such that illegal residues will not occur in the rotational crop. A restriction longer than 18 months is not acceptable.

5. Cover crops can be rotated if label restrictions are such that the cover crop is plowed under and not grazed.

6. If the agricultural practice is such that a treated crop area is rotated with another crop that will result in another treatment of the pesticide to the same area, residue data will be required on the second crop. The rotational crop is to be grown under actual use conditions.

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NOTE: All radiolabeled studies should be supported with the following information.

a. Sample calculations;

b. Counting efficiency;

c. Counting time;

d. Background levels;

e. Probable error with scintillation techniques.

C. Data will be needed to support each tank mixture combination. The time allowed to complete these studies may extend beyond registration if necessary. Studies should be carried out according to the following outlines.

1. Laboratory study using cold chemicals applied to two soils as recommended in the proposed use. A light and heavy soil will be adequate.

2. Analysis through two halflives of each pesticide applied as a mixture and separately. The same soil types are to be used for the comparison of the mixture vs. individually applied chemicals. Sampling depth should be to bottom of container (pot) or 6 inches.

Even if all the required studies are completed, this would not guarantee registration. Only after all data have been reviewed can this be determined. If other uses are proposed, additional environmental chemistry data may be required.

## II. INTRODUCTION

1. Avenge - 2A-5 Wild Oat Herbicide CL-84,777.

2. Proposing residues of Avenge in Wheat straw at 20 ppm and in wheat grain, meat, fat and meat by-products of poultry at 0.05 ppm (negligible residue).

3. See environmental reviews dated 12/6/74 and 2/15/74.

4. Applicant wishes to ship 785 gallons (1,570 lb. ai.) Avenge 2-A5 for experimental purposes.

5. Degradation Products:

   a. 1,2-diphenylcyclopropene
      photodegradation (major route)

   b. azomethane
      photodegradation (major route)

   c. CL-84,760; N-methyl-3,5-diphenyl pyrazole
      photodegradation (minor route)

   d. 1,2-diphenyl-3-methyl cyclopropene
      (photodegradation)

   e. $CH_3$-N = NH
      postulated photodegradation intermediate resulting from photodegradation of CL-84760.

## III. DIRECTIONS FOR USE

A. Types of wheat and geogrphical locations.

May be used on fall seeded wheat throughout the U.S.

May be used on all varieties of spring seeded wheat grown only in Arizona, New Mexico, California, Utah, Nevada, Idaho, Oregon and Washington.

May be used on specified varieties of spring seeded or Durum wheat grown in Montana, North Dakota, South Dakota and Minnesota.

B. Ground or aerial application when wild oats are in 3-5 leaf stage of growth. At this time fall seeded wheat will be in the four leaft to tillered stage and spring wheat will be in the 3-6 leaf stage.

Application rate is 0.625-1.0 lb. ai/A, dependent on degree of wild oat infestation.

C. Tank Mix Data

1. Tank mix with Broadleaf herbicides.

Avenge may be tank mixed with MCPA, bromoxynil, or MCPA plus bromoxynil. Broadleaf herbicide should be applied in accordance with label recommendations.

2. Tank mix of Avenge 2A-5 plus MCPA amine or esters.

Use avenge at recommended rates based on wildoat infestation. Use MCPA formulation at 0.25 - 1.0 lb/A MCPA acid equivalent in accordance with the MCPA label recommendations.

3. Tank mix of Avenge 2A-5 plus bromoxynil.

Use Avenge at recommended rates based on wildoat infestation. Apply bromoxynil at 0.375 - 0.5 lb ai/A in accordance with bromoxynil label recommendations.

4. Tank mix of Avenge 2A-5 plus MCPA plus bromoxynil.

Use Avenge at recommended rates based on wild oat infestation. MCPA at 0.25 - 0.5 lb ai/A plus bromoxynil at 0.25 - 0.5 lb ai/A; select proper rate in accordance with the label recommendation for the specific formulation.

D. Do not plant subsequent crops for 18 months, except wheat and barley.

## IV. DISCUSSION OF DATA

1. Analytical Methods

a. $^{14}C$ validation of the method: The Gas Chromatographic Determination of Avenge in Soil (Section H-1) Procedure M-471; soil is mixed with sea sand, packed in a column, and eluted with 4% HA-methanol. Eluate is extracted with methylene chloride followed by clean-up on an Alumina column. Measurement of Avenge is by GLC with alkalai flame ionization detector.

$^{14}C$ Avenge was applied to soil to obtain data to validate procedure M-471.

3/

Extractability of $^{14}C$ from Soil After Surface Applicator of $^{14}C$ Avenge

| Soil Type | Interval (months) | % of Radioactivity Present Extracted |
|---|---|---|
| Delaware - Silt loam | 6 | 84 |
| | 12 | 75.5 |
| Wisconsin - Sandy Loam | 1 | 84.5 |
| | 12 | 80.9 |
| North Dakota - Fargo Clay | 1 | 91.3 |
| | 12 | 73.3 |

Conclusions:

1) Position of $^{14}C$ label not given.

2) Soil characteristics not given.

3) At 12 months from 73-81% of $^{14}C$ present was extracted from soils ranging from sandy loan to clay.

b. The GLC Determination of Avenge in Fortified Wheat, Foliage, Grain and Straw (Section H-1) Procedure M-411.

Green foliage is extracted with methanol; straw and grain is extracted with 20% methanol in methylene chloride. Extracts are cleaned up by utilizing 2 solvent partitioning systems followed by Alumina column chromatography. Avenge is determined by GLC equipped with a nitrogen sensitive detector.

Conclusions:

1) Recoveries from fortified samples ranged from 64-101% for grain, 70-102% for foliage and 60-117% for straw.

2. Field Soil Studies

a. Avenge - difenzoquat: Fate on Soil under Field Conditions (radiolabelled study)
(Report #C-540; Section H-3)

A mixture of $^{14}C$ and $^{2}H$ labelled Avenge was applied to a 600 square inch field plot at 1 lb. ai/A. $^{14}C$ label was on 3-carbon (pyrrole ring) and $^{2}H$ label was at the meta positions of both phenyl groups.

0-1" and 0-3" soil samples were taken. Total radioactivity was by combustion. Soils were mixed with celite in a column, and eluted with HCl-methanol. Eluates were cleaned up by TLC, bands were scraped, and were analyzed by 2-dimensional TLC - co-chromatography, and GLC.

Soil characteristics: Sandy loam; Sand 51%; Silt 26%; Clay 23%; O. M. 1.8%; pH 7-8; CEC 14.1 meg/100g.

Recovery of Radioactive Residues 0-3"
% of Applied Radioactivity

| Time Interval (weeks) | Accumulated Rainfall (inches) | 0-1" / 0-3" | 0-3" / 0-3" |
|---|---|---|---|
| 0 | 0.00 | 94.2% | 104.8% |
| 1 | 0.03 | 45.1 | 51.7 |
| 2 | 0.53 | 53.2 | 54.2 |
| 4 | 3.94 | 62.1 | 63.1 |
| 8 | 4.44 | 41.9 | 43.8 |
| 16 | 6.57 | 51.7 | 55.5 |

Results:

1) Total $^{14}C$ (by combustion) declined to about 50% after 1 week and then did not decline during subsequent 15 weeks.

2) 95-98% of $^{14}C$ present (0-16 weeks) was extractable with organic solvents.

3) 93% of radioactivity present at 16 weeks was in top inch.

4) Only parent compound was found by both TLC and GLC at all time intervals.

Conclusions:

1) Study showed 50% decline of $^{14}C$ during first weeks and no further decline during subsequent 15 weeks. Registrant concludes rapid decline was due to photodegradation followed by voltilization of photoproducts. Registrant

concludes that after initial photodegradation avenge particles were leached into the soil where light is not able to reach them. Reviewer concludes that initial loss of 50% of applied radioactivity was not adequately explained because:

a) Other studies show no photodegradation on soil.

b) Photodegradation does take place on thin film and in water, but in both cases it involves no loss in total radioactivity.

c) Volatilization of parent compound is unlikely: vapor pressure is $10^{-7}$mm Hg. Leaching would not be responsible for loss since Avenge does not leach and there was only 0.03" rainfall (artificial or natural) until after the second week.

2) After the initial decline no further decline in 16 weeks.

3) Avenge neither leaches nor binds to the soil.

4) All recovered radioactivity from soild was parent.

5) A soil degradation study with a means of trapping and counting volatile radioactive fragments is needed to adequately explain the degradation of Avenge in the soil environment.

6) Soil metabolism study utilizing $^{14}C$ - N-methyl Avenge (review of 3/26/74) resulted in 93% of applied $^{14}C$ present at 10 weeks. Only parent compound was identified.

b. Determination of CL 84,777 (Avenge) Residues in Soil at Various Locations (Sections H-4a-4g; Reports C-555-C-561)

Avenge was applied post emergence to barley or wheat planted fields or to bare soil. 0-3" and 3-6" soil samples were taken at intervals and analyzed by GLC method M-471.

| Location | Soil Type | % Sand | % Silt | % Clay | % O.M. | C.E.C. | pH |
|---|---|---|---|---|---|---|---|
| Montana | Clay loam | 28 | 37 | 35 | 2 | -- | -- |
| S. Dakota | Silty Clay Loam | 17 | 55 | 28 | 4.3 | -- | -- |

Interval between planting and treatment ranged from 12-90 days.

Samples were taken with a 1" core sampler (or spade if soil too wet or dry). 20 cores were taken per plot, and frozen immediately.

Average Residues in 0-3" Soil

| Soil Type (and crop) | Location | 180 day rain (inches) | lb ai/A | Apparent Residue (PPM) Days 0 | 7 | 30 | 90 | 180 | 360 |
|---|---|---|---|---|---|---|---|---|---|
| Sandy Loam (wheat) | Calif. | 1.87 | 0.62 | 1.04 | 0.55 | 0.22 | 0.22 | NDR | -- |
| | | | 1.0 | 1.47 | 0.82 | 0.54 | 0.15 | 0.47 | -- |
| Clay (barley) | Calif. | 20.3 | 0.62 | 0.23 | 0.20 | 0.49 | 0.24 | NDR | -- |
| | | | 1.0 | 0.36 | 0.51 | 0.40 | 0.56 | NDR | -- |
| Sandy Clay Loam (wheat) | Oreg. | 8.2 | 1.0 | 0.45 | 0.45 | 0.30 | 0.20 | 0.18 | 0.18 |
| | | | 2.0 | 0.85 | 0.85 | -- | 0.47 | 0.40 | 0.26 |
| Clay Loam (barley | Mont. | 8.6 | 0.5 | 0.68 | 0.40 | 0.30 | 0.25 | 0.13 | NDR |
| | | | 1.0 | 1.00 | 0.48 | 0.50 | 0.36 | 0.30 | NDR |
| Silty Clay Loam (wheat) | S. D. | 12.3 | 0.5 | 0.99 | 1.1 | 0.40 | 0.11 | 0.17 | -- |
| | | | 1.0 | 1.31 | 1.44 | 0.56 | 0.13 | 0.13 | -- |
| Silt Loam (bare soil) | Minn. | 9.62 | 0.5 | 0.21 | 0.24 | 0.12 | 0.13 | NDR | NDR |
| | | | 1.0 | 0.64 | 0.37 | 0.22 | 0.11 | NDR | NDR |
| Silt Loam (wheat) | Minn. | 16.11 | 0.5 | NDR | 0.17 | 0.12 | 0.12 | NDR | NDR |
| | | | 1.0 | 0.19 | 0.26 | 0.28 | 0.17 | NDR | NDR |

Results:

1) 3-6" soil cores contained no detectable residues (less than 0.1 ppm) except South Dakota soil which had 0.33 and 0.17 ppm at 0 and 30 days after 1 lb application.

2) For 1.0 lb ai application 0 day recoveries ranged from 0.19 - 1.47 ppm.

3) Half lives ranged from 30-180 or more days.

4) Minnesota silt loam showed no residue at 0 days for 0.5 lb ai application.

5) Half of soils tested had residues at 180 days ranging from 0.12 - 0.47 for 1.0 lb application.

Conclusions:

1) Avenge does not leach.

2) Soil characteristics were not submitted for four soils.

3) It was almost impossible to calculate half lives because of erratic nature of some of the data.

4) Avenge is resistent and did not degrade rapidly.

3. Microorganism Studies

a. Effects of Avenge on microorganisms (Section H-7) (See previous review dated 3/11/74).

b. The Degradative Effects of Soil Microorganisms on the Metabolism of Avenge (Report #C-554, Section H-8)

Attempts were made to isolate fungi or bacteria that could metabolize Avenge by providing $^{14}C$ Avenge as a source of carbon in bacterial and a fungal media, with and without glucose, and innoculating the media with Princeton sandy loam or Wisconsin silt loam soil. Aerobic and anaerobic $^{14}C2$ formation was studies by incubating silt loam under aerobic and anaerobic conditions with 5.1 and 1.0 lb ai/A Avenge respectively, and trapping $^{14}CO2$.

Cells from culture media were washed with 0.85% NaCl. Saline wash was subjected to TLC-autoradiography. Cells were then lysed with 10% NaCl, and lysate was extracted with methylene chloride, and the organic extract was subjected to TLC-autoradiography.

Results:

1) Attempts to isolate bacteria or fungi that could use Avenge as a source of carbon were negative.

2) Aerobic and anaerobic CO2 trapping procedure resulted in very little $^{14}CO2$ being formed and 95% recovery of $^{14}C$ in soil in 66 and 33 days for aerobic and anaerobic studies.

3) TLC autoradiography of culture media and cell lysates revealed avenge as the only labelled compound.

4) Avenge did enter the cells but was not metabolized by the cells.

Conclusions:

1) Avenge is not metabolized by soil microorganisms and had not effect on the microbes in this study.

4. Metabolic Studies of Avenge in Hydrolytic and Photolytic Environments (Section H-9, Notebook numbers AC-2191, 2306 and 2392)

Three labels were used. Methyl labelled Avenge was labelled in the N-methyl group of the cation and in the methyl sulfate onion. Ring labelled Avenge was labelled in the number 3 carbon of the pyrazolium ring. Deuterium ($^{2}H$) Avenge was labelled on the meta position of 1-oth phenyl groups.

This report was broken up into seven studies. In all photolysis studies dark control plates were used.

a. Hydrolysis in sterile water.

A 2.17 ppm mixture of deuterium and ring $^{14}C$ labelled Avenge was incubated in sterile buffers (pH 5,7 and 9) in the dark.

Aliquots were analyzed at four intervals up to two months. Analysis was by LSC and U. V. spectrophotometry at 253 nm for parent compound.

Results:

1) Total radioactivity ranged from 93-104% of applied over two months.

2) U. V. spectrophotometry showed 97.3-100% of radioactivity present to be parent compound.

Conclusions:

Avenge is stable at pH 5,7 and 9.

b. Photolysis in Pond Water under Natural Sunlight.

Methyl and ring labelled Avenge were added to pH 5.7 pond water to 5.02 ppm in vycor tubes and was exposed to natural sunlight for two months.

Aliquots were assayed by LSC, and TLC with scraping-LSC. Compounds isolated by TLC were subjected to mass spec. analysis.

Results:

1) There was no loss of total radioactivity by the end of two months.

2) TLC of ring labelled compound showed 18 products, five of which accounted for more than 5% of the radiation present. None of the products were identified.

3) The degradation products could not be partitioned into methylene chloride under acidic, basic or neutral pH.

4) Parent compound had a photolytic half life of less than three days.

5) TLC of the methyl labelled compound showed one degradation product designated as product #21.

6) Mass spectral data gave an indication that polymers may be formed.

7) Compound #21 was identified as a metal complex of azomethane by mass-spec. NMR and Ir.

Conclusions:

1) Difenzoquat photodegrades very quickly as shwon by the breakdown of both N-methyl groups and both pyrazolium nitrogens.

2) The degradation product 1,2 diphenylcyclopropene, resulting from the evolution of azomethane, may undergo polymerization.

3) Degradation products were very polar or ionic.

c. Photolysis in Pond Water under Artificial Light

Ring and methyl labelled Avenge were added to pH 5.7 pond water and exposed to a 1000 watt metal halide lamp at 2 feet in vycor tubes for 2 months. Samples were taken at four intervals.

Samples were counted by LSC. Degradation products were isolated on TLC and scraped and counted by LSC.

Results:

1) Ring labelled Avenge gave 8 degradation products.

2) Methyl labelled Avenge produced one radioactive product, compound #21.

3) Mass spec, Ir and NMR data indicate compound #21 is a complex of azomethane.

4) Synthesized Cu C12 complex of azomethane had the same retention time as compound #21 on two GLC columns.

Conclusions:

1) Avenge undergoes photodegradation, losing both N-methyl groups and both pyrazolium nitrogens to form azomethane.

d. Photolysis - Thin Film on Glass Under Natural Sunlight.

Thin film of methyl or ring labelled Avenge on Vycor test tubes was exposed to natural sunlight for 2 months.

At four intervals, residue was dissolved in methanol and counted by LSC.

Results:

1) After 2 months irradiation, 98% of applied ring Carbon-14 was recovered.

2) Two months irradiation resulted in 40% loss of methyl label from treated surface.

3) Azomethane was the only degradation product found by TLC of both labels.

Conclusions:

1) Avenge undergoes photodegradation resulting in possible formation of azomethane as shown by ring and methyl labels. Azomethane is either volatilized or further photodegraded.

e. Photolysis - Silica Gel Plates under Natural Sunlight.

Pyrazolium ring carbon labelled Avenge was spotted on silica gel plates and with and without anthraquinone. Plates were covered with a vycor shield and exposed 4 months to sunlight.

Results and Conclusions:

1) 100% of applied radioactivity was found on all the plates.

2) Small amounts of CL 84,760 were found.

f. Photolysis - Soil Plates under Natural Sunlight.

Pyrazolium ring labelled or N-methyl labelled were spotted on 500-700 nm thick Wisconsin silt loam soil plates. Plates were placed in a box covered with a vycor window and exposed to natural sunlight for two months.

Results:

1) After two months there was no loss of Carbon-14 from either label study.

2) TLC of plate extracts showed only parent compound.

Conclusions:

1) Avenge does not readily photodegrade on soil surfaces.

2) Registrant concludes that results indicate that compound was bound to clays in soil matrix and not exposed to sunlight at the surface. There is no proof to support this.

g. Conclusions to Hydrolysis/Photolysis studies.

1) Avenge does not hydrolyze at pH 5, 7 or 9.

2) Avenge is very quickly photolyzed on glass plates and in water, but may not be photolyzed readily in soil.

3) Photolysis involves a splitting of azomethane from the pynole ring and polymerization of the remaining fragment. Photoproducts have not been identified.

4) Registrant concludes azomethane rapidly photodegrades to nitrogen and ethane, but shows no evidence. To the contrary the azomethane was persistent enough to be identifiable by TLC, GLC, I.r. and NMR.

5. Rotational Crops

Determination of CL 84,777 Residues in Wheat and Barley in soil treated the Previous Year with Avenge (Section H-10) (Report C-574)

Soil was planted to grain and given 1 lb ai/A post emergence application of Avenge. One year later ground was plowed and re-planted to barley and wheat. Some of the newly planted grain was given a 1.0 lb ai post emergence application of Avenge.

Samples were analyzed by residue method #411, utilizing GLC with a nitrogen sensitive alkalai flame detector.

Soil was clay loam.

Residues in Barley and Wheat

| Commodity | Last treatment to Sampling (Days) | Treatment (lb ai/A) | Apparent Residue (ppm) |
|---|---|---|---|
| Barley grain | 459 | 1.0 | < 0.05 * |
| | 67 | 1.0 + 1.0 | < 0.05 |
| Barley straw | 459 | 1.0 | < 0.10 |
| | 67 | 1.0 + 1.0 | 0.825 |
| Wheat grain | 459 | 1.0 | < 0.05 |
| | 67 | 1.0 + 1.0 | < 0.05 |
| Wheat straw | 459 | 1.0 | < 0.10 |
| | 67 | 1.0 + 1.0 | 0.154 |

*Sensitivity is 0.05 for grain and 0.10 for straw.

Conclusions:

1) Residues at 67 days as well as at 459 days are below proposed tolerances for grain and straw of barley and wheat.

2) Soil characteristics were not submitted.

3) This was a cold study.

4) This method would not detect the photodegradation product, 1, 2-diphenyl cyclopropene if it were present.

5) A labelled study using a root crop is needed.

6. Plant Metabolism

a. The Persistence and Metabolism of Avenge in Barley and Wheat
(Report #PD-M10:344-422, Section H-11)

$^{14}C$ (labelled on 3-carbon of pyrazolium ring) was applied to barley and wheat foliage at 0.5 and 1.0 lb ai/A. Application was by spray to barley and wheat and also by direct application to barley leaves.

Plants were extracted 3 times with methanol and then with 0.25 N HCl-methanol. Both extracts were assayed by LSC. Solid residue was assayed by combustion.

Methanol extracts of sprayed barley were evaporated to dryness. Residue was taken up in HCl, and extracted 3X with diethyl ether. Both phases were assayed by LSC. Aqueous phase was treated with sodium perchlorate, and extracted 3 times with methylene chloride. This extract was subjected to TLC with co-chromatography with parent, autoradiography and scraping with LSC assay of all spots.

Methanol extracts of direct treated barley were subjected directly to TLC without cleanup.

Bound residues were recovered by acid digestion, piperidine digestion and benzene and toluene extractions.

Soil characteristics: Type - Silty Clay; pH 6.5; Moisture capacity - 83.9% C.E.C. 41.6 meg/100 g; O.M. 6.03%; Sand 8%; Silt 40%; Clay 52%.

Results:

1) 100 and 89% of radioactivity present in barley at 0 and 16 weeks respectively was methanol extractable.

2) TLC showed 98% of recovered Carbon-14 to be parent compound.

3) Bound plant residues were parent compound.

Conclusions:

1) Avenge is not metabolized by barley but it is probably translocated to soil and roots.

(A) Photo degradation is only method of degradation (but not in soil). It is not metabolized by plants but it is rapidly translocated to roots and soil. Label restriction on root crop rotation will be needed until we can get root crop data.

7. Animal Metabolism

a. Rat Metabolism of Avenge
(Section ~~H-12~~)

Rats were given a single dose of 150 mg/Kg of a mixture of 3-c pyrazolium ring $^{14}C$, methyl - $^{14}C$ and meta $^{2}H$ labelled applied into the stomach. Some rats were given a single dose of 14.1 kg/mg ring labelled Avenge in the stomach. To study metabolite formation 0.2 and 0.5 mg of a mixture of labelled Avenge as above was injected intraperitoneally. Some of 150 mg/kg treated rats above were placed in metabolism cages and $CO_2$ was trapped with ethanolamine.

Solid wastes and tissues were analyzed by combustion while liquids were analyzed by LSC.

Some urine, fecal and tissue samples were extracted and subjected to TLC.

An in-vitro study with rat liver homogenate was carried out.

% of dosed $^{14}C$

| Sample | Collection Interval (hours) | 162 mg/kg dose ($^{14}C$ and $^{2}H$ labels) | 15 mg/kg dose (ring $^{14}C$ label) |
|---|---|---|---|
| Urine | 0-96 | 3.86 | 2.96 |
| Feces | 0-96 | 90.10 | 86.05 |
| $CO_2$ | 0-115 | 0.04 | ----- |
| Tissues | 96 | 0.16 | 0.07 |

Results:

1) TLC of tissue, urine and feces extracts showed only parent compound.

2) Only parent compound was present after incubation with liver homogenate.

3) In the intraperitonial injection experiment, all excreted $^{14}C$ was in the urine and none was excreted through the feces.

Conclusions:

1) Avenge is not metabolized in or by the rat.

b. Lactating Goat Metabolism of Avenge
(Section H-13)

Avenge, labelled on 3-carbon of pyrazolium ring was fed to goats at a daily dosage rate of 0.63, 1.26 and 3.78 ppm of daily diet.

Samples of milk, feces and urine were taken daily and assayed. Extracts of urine, feces and liver were subjected to 2-dimensional TLC.

Average Total Recovery of Radioactivity from Goats
% of applied

| | |
|---|---|
| Urine | 1.6 |
| Feces | 65.8 |
| Milk | < 0.1 |
| Blood | < 0.1 |
| Rumen Content | 13.0 |
| Intestinal Wash | 5.5 |
| Tissues | 0.14 |

Results:

1) Liver and kidney were only tissues with residues above 0.001 ppm.

2) Radioactivity of urine, feces and liver was parent compound.

Conclusions:

1) The goat does not metabolize Avenge.

c. Avenge Residues in Chicken Tissues and Eggs
(Report #C-447, Section H-14)

Chickens were dosed at 0.05, 0.10 and 0.50 ppm in diet for 28 days. Analysis was by g/c utilizing a flame ionization detector with a rubidium sulfate salt tip.

Results:

1) At a 0.50 ppm daily rate, apparent Avenge residues were less than 0.10 ppm in all tissues and less than 0.05 ppm in eggs at each sampling interval.

(B) Avenge is not metabolized in animals, but it is readily excreted, mostly through feces. Avenge does not accumulate in bluegill fish (see review dated 2/15/74).

8. Soil Leaching Studies of CL 84,777 (Section H-5)

Four soil types were prepared in 14" soil columns. Labelled Avenge was added to top. Columns were subjected to rainfall at a rate of one inch per hour for 20 inches.

An aged leaching study was prepared by aging Avenge for 30 days in sandy loam and then placed on a 14" sandy loam column. Water was passed through this column at 0.5" per day for 45 days.

Leachate was collected and re-dioassayed. Soil was divided into 4 sections and assayed by combustion.

Soil Characteristics

| Type | pH | % Sand | % Silt | % Clay | O.M. | C.E.C. |
|---|---|---|---|---|---|---|
| Sand | 4.9 | 96 | 3 | 1 | 0.26 | 1.6 |
| Sandy Loam | 5.1 | 68 | 24 | 8 | 3.6 | 6.1 |
| Silt Loam | 6.7 | 24 | 56 | 20 | 5.6 | ---- |
| Silty Clay Loam | 6.5 | 8 | 40 | 52 | 6.03 | 41.6 |

A column of soil was eluted with NaCl to determine the break-through volume.

% of Applied $^{14}C$
Soil Type

| Sample | Sand | Sandy Loam | Silt Loam | Silty Clay Loam |
|---|---|---|---|---|
| 0-3.5" | 78.9 | 96.7 | 94.4 | 52.6 |
| 3.5-7" | 0.5 | 1.7 | 0.3 | 0.5 |
| 7-10.5" | 0.3 | 1.6 | 0.3 | 0.7 |
| 10.5-14" | 0.4 | 0.7 | 0.3 | 0.7 |
| Leachate | 0.3 | 1.8 | 0.5 | 0.18 |

Results:

1) 94-98% of recovered $^{14}C$ was in 0-3.5" for the regular leaching study.

2) For aged ~~l~~eaching study, 91% ~~of~~ applied $^{14}C$ was in 0-3.5" layer, 0.3% was in the lower soil and no activity found in the leachate.

Conclusions:

1) Rate of application was not given.

2) Position of $^{14}C$ label was not given.

3) Registrant said low recovery for silty clay loam was due to difficulty in handling sticky soil.

4) Avenge does not leach in soils ranging from a sand to silty clay loam.

5) Registrant concludes Avenge did not leach because it was bound to soil particles.

6) Results of this study agree well with field study, where there was also almost no leaching.

7) Reviewer concludes that non-leachability is due to the non polar nature of the persistent parent compound, since other studies have shown that Avenge is not bound to the soil and is almost totally extractable with organic solvents.

9. Runoff Characteristics of $^{14}C$ Avenge under Greenhouse Conditions (Report no. 74004-A, Section H-6)

Silt loam soil was packed in an 8°, 3" deep, 12 x 36" runoff apparatus. Avenge was sprayed on upper third at 1.0 lb ai/A. Artificial rainfall was applied at 1, 3 and 7 days for a total of approximately 2 acre inches of simulated rainfall. Soil leachate, runoff water and sediment were assayed radiochemically for $^{14}C$.

Avenge was labelled on number 3-Carbon of pyrazolium ring.

Soil characteristics: Silt loam; O.M. 5.2%; Sand 24%; Silt 56%; Clay 20%; Water retention 30.65%; pH 6.7.

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Distribution of $^{14}C$ in Water and Sediment
% of Applied $^{14}C$

| Interval (days) | Rainfall (acre-inches) | Leachate | Water | Sediment |
|---|---|---|---|---|
| 1 | 1.4 | < 0.01 | 0.01 | 0.02 |
| 3 | 0.5 | < 0.01 | < 0.01 | < 0.01 |
| 7 | 0.7 | < 0.01 | < 0.01 | 0.02 |

Results:

1) Only 3.2% of applied $^{14}C$ had migrated from the area of application.

2) Insignificant amounts of $^{14}C$ were found in runoff sediment, leachate or runoff water.

Conclusions:

Avenge did not runoff in this study.

(C) Avenge is very immobile. It will not leach in soils ranging from silty clay loam to sand. It does not runoff. It is not bound to soil though.

V. CONCLUSIONS

1. Field persistence - label study

Label study showed 50% decline during first week and no further decline during subsequent 15 weeks. Registrant concludes rapid decline is due to photodegradation followed by volatilization of photoproducts. Registrant also concludes that after initial photodegradation Avenge particles are leached into soil where light is not able to reach them.

Reviewer concludes that 50% loss of radioactivity was not adequately explained because photodegradation study showed no photodegradation on soil. Also photodegradation did take place on thin film and in water, but in both cases the product was 1, 2 diphenyl cyclopropene, which involved no loss in total radioactivity.

Leaching and runoff would not be responsible for loss since compound does not leach, does not runoff in water or soil sediment, and only 0.03" of rain fell during the first week when the decline took place.

All radioactivity in the soil was parent compound. Volatilization of parent would seem unlikely since vapor pressure is $10^{-7}$ mm Hg.

Soil degradation studies - using radio labelled Avenge - with a means of trapping volatile radioactive fragments would be needed to adequately explain the fate of Avenge in the soil.

Previous lab study resulted in 93% of $^{14}C$ present at 10 weeks when $^{14}C$-Methyl Avenge was applied to soil (Review: 3/26/74). Only parent compound was identified.

2. Field persistence - cold study

One half of the soils had residues at 180 days ranging from 10-50% of zero day residue level. Results were erratic. Zero day recoveries ranged from <0.10 to 1.47 ppm (on different crops in different locations) for a 1.0 lb ai/A application. In some cases residue levels increased and then decreased. Registrant used careful sampling technique and recovery levels for analytic method with aged soils were good.

Half life on some soils was over 180 days, so Avenge can be considered to be persistent.

3. Microorganisms

Avenge is not metabolized by the microorganisms tested.

4. Photodegradation

Avenge in pond water and thin film underwent photodegradation to form azomethane and 1, 2-diphenyl cyclopropene. 17 other products were produced in pond water; there is some evidence that this is the result of polymerizations. No degradation took place at all on thin layer soil plates. Parent had 3 day half life in pond water.

There was no loss of applied radioactivity in any of the photodegradation studies, which were run for periods of 1-4 months.

Registrant concludes that azomethane rapidly degrades to nitrogen and ethane, but provides no evidence. To the contrary the azomethane was persistent enough to be identified during the test.

5. Rotational Crops

Cold study - wheat and barley, no detectable residues at sampling 459 days from application in grain and straw. Root crop study and study with dicot were not submitted.

6. Plant Metabolism

Avenge was not metabolized by wheat and barley but it was probably translocated to the soil and roots.

7. Animal Metabolism

Avenge was not metabolized by rats and goats. Most of it was excreted by way of feces.

8. Leaching

Avenge did not leach in soils from sand to silty clay loam.

9. Runoff

Avenge does not leave a tendency to run off.

10. Hydrolysis

Avenge is not hydrolyzed at pH 5, 7, and 9.

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Ronald E. Ney, Jr. 1/21/75

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