8-19-80

Date Out EFB:

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To: Product Manager LaRocca (PM 15) AUG 19 1980
TS-767

From: Dr. Willa Garner
Chief, Review Section No. 1
Environmental Fate Branch

Attached please find the environmental fate review of:

118401

Reg./File No.: 241 - EAR, EAN

Chemical:

Type Product: I

Product Name: AMDRO

Company Name: American Cyanamid

Submission Purpose: Condl on Fire Ants

ZBB Code: 3(c)(7) ACTION CODE: 110

Date in: 7/2/80 EFB # 5

Date Completed: AUG 19 1980

Deferrals To:

_____ Ecological Effects Branch

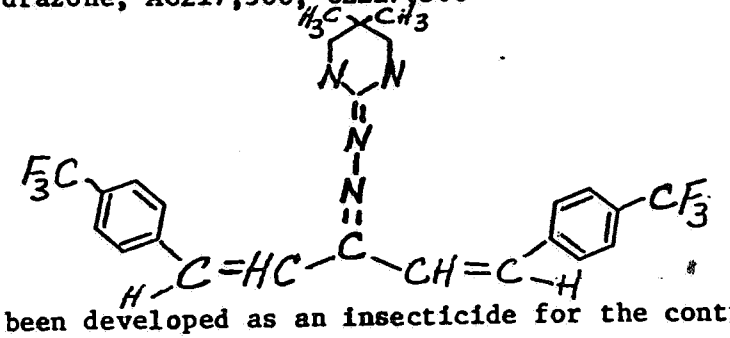
_____ Residue Chemistry Branch

_____ Toxicology Branch

1. Introduction

American Cyanamid has submitted environmental fate data in support of a conditional registration.

1.1 AMDRO = tetrahydro-5,5-dimethyl-2(1H)-pyrimidione(3-4(triflouromethyl) phenyl)-1-(2-(4-(trifluoromethyl)phenyl)ethenyl-2-propenylidene) hydrazone, AC217,300, CL217,300



1.2 AMDRO has been developed as an insecticide for the control of imported fire ants.

1.3 Active ingredient: tetrahydro-5,5-dimethyl-2(1H)-pyrimidone (3-(4-(trifluoromethyl)phenyl)-1-(2-(4-trifluoromethyl)phenyl) ethenyl-2-propenylidene)hydrazone = 0.88%

Inert ingredients = 99.12%

2.0 Directions for use

2.1 Environmental Hazards

This product is toxic to fish. Avoid direction application to lakes, streams, or ponds. Do not apply when weather conditions favor drift from target areas.

2.2 Storage and Disposal

Do not contaminate water, food, or feed. Open dumping is prohibited. Dispose of in an approved landfill for pesticide or buried in a safe place away from water supplies. Dispose of container in an incinerator or approved landfill or burry in a safe place.

2.3 Apply when ants are active (typically when soil temperature is greater than 60°F). Apply with properly calibrated ground equipment to pasture and range grass, grass hay, lawns, turf, and non-agricultural land. Application rate is 1.0 to 1.5 16 (0.14 to 0.21 oz ai)/acre. To treat individual mounds, use one tablespoon of bait for small mounds less than 12" diameter, or two tablespoons for large mounds (greater than 12" diameter).

The AMDRO bait is [redacted]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

3.0 Discussion of Data

3.1 AMDRO Fire Ant Insecticide (CL 217,300): Identification and Characterization of CL 217,30 and its Metabolites in Bluegill Sunfish, B. Reichert, Report PD-M, Volume 17-4, 6/23/80, American Cyanimid Company, Agricultural Research Division, Princeton, N. J., Accession No. 241-260, 241-261.

Experimental Procedures

This study attempted to characterize residues in bluegills exposed to AMDRO in a continuous-flow system. The exposure system and experiment were previously reviewed and evaluated in EFB review of 6/17/80. This study was deemed invalid from the point of view of deriving a bioconcentration factor, due to use of AMDRO concentration in excess of water solubility. This would not, however, necessarily invalid the data from the viewpoint of determining the nature of the residues to be found in fish after AMDRO exposure. Tissues of bluegills receiving exposure to ^{14}C-AMDRO for 14,22 and 30 days and in depuration for 14 days were homogenized with acetone, and the acetone extract partitioned between acetonitrile and hexane. The acetonitrile fraction was taken for two-dimensional TLC analysis with autoradiographic detection. The edible and non-edible tissues were analyzed separately. Chromatographic behaviour was compared with standard metabolites.

Results

Extraction of ^{14}C into acetone was 90% efficient. Of this material, 90% partitioned into acetonitrile. Since the hexane phase was not analyzed, only 81% of the ^{14}C present was actually analyzed. At all times but one, AMDRO accounted for the majority of ^{14}C in the fish which was subjected to analysis.

		% ^{14}C on TLC Plate as AMDRO	
		Edible Tissue	Non-Edible Tissue
Uptake day	14	82.8	85.5
	22	78.6	82.8
	30	74.0	78.4
Depuration day	14	48.2	70.3

The remainder of the ^{14}C was divided among 14 other radioactive spots of varying size. Only one spot was tentatively identified, based on its similar chromatographic properties with CL 98,724 (See Appendix). This metabolite was relatively important only in the edible flesh after 14 days of depuration where it accounted for 12.7% of the ^{14}C during exposure, and 25.9% during depuration in edible tissue.

Conclusions

The only conclusion the data allows is that AMDRO comprises the majority materials accumulated by bluegills under the conditions of this continuous-flow study. Because no data on the composition of the ^{14}C in the exposure water is given, it cannot be assumed that the fish were responsible the

2.2 AMDRO Fire Ant Insecticide (CL 217,300): Metabolism in Soil Under Aerobic Conditions, B. Reichert and P. Gatterdam, Report PD-M, Volume 17-5, 6/23/80, American Cyanamid Compency Agricultural Research Division, Princeton, N. J. Accession No. 241-260, 241-261.

This was a laboratory/field soil metabolism study designed to minimize effects from photodegradation.

Experimental Procedures

A. Laboratory Study

^{14}C-(benzylic carbon-labelled) AMDRO was used (>99% pure). A Princeton sandy loam soil was used with the following characteristics; 70.4% sand, 24.0% silt, 5.6% clay, bulk density 2.08, 2.2 %·organic matter, pH=6.5. AMDRO was mixed with soil at a rate of 5 ppm. The exaggerated rate was justified as necessary to provide sufficient metabolite to characterize. Amended soil was added to flasks, water content of soil made to 75% of field capacity and flasks were connected to gas trains permitting the trapping of evolved CO_2 and organic volatiles. Sample flasks were protected from light and held at 23+2°C. Sampling intervals were 1,2,3,6,8,10, and 12 months. The soil samples were repeatedly shaken with acidified methanol, acetone, and alkaline methanol. Only 1.2 - 3.4% of the ^{14}C remained in the soil after these vigorous procedures. The extracts were pooled for TLC analysis in one or more solvent systems including two-dimensional systems, using known AMDRO degradates for comparative purposes.

B. Field Study

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Open-ended metal cans, 3" in diameter and 4" in depth were pushed into the above Princeton sandy loam soil. Granules of AMDRO [redacted] formulation were placed one inch below the surface of the soil within the cylinders at a rate of 60 g a.i./acre ^{14}C-AMDRO. Soil samples were made at 48 hours, 1,2,5,8,12 and 16 weeks after treatment. Zero to two, and two to four inch sub-samples were taken and portions measured directly for ^{14}C- AMDRO from fortified untreated soil was about 96%.

Results

A. Laboratory Study

Recovery of ^{14}C at 12 months declined only to 89.1% - down from 94.1% at zero-time. Extractable material was 82.5%, 3.4% was soil-bound, and 3.2% was recovered in the gas traps by that time. The chemical composition of the extracts from the TLC analysis is given below. AMDRO dissipates through one half-life in the first 3 months (very approximately) with no degradation after that. It was suggested the microbial populations declined after this time.

B. Field Study

degradation. The study serves no useful purpose for registration.
assumed that degradation. The study serves no useful purpose for registration.

Laboratory Study

% Dose

Compound

Time	1	2	3	4	5	6	7[a]
(Months)	AMDRO CL 98,724						
1	76.2	3.9	-	-	-	2.1	5.8
2	60.8	9.6	-	0.3	1.1	6.0	1.1
3	47.4	25.9	-	-	0.3	5.2	1.0
6	68.1	0.3	1.2	-	2.4	1.0	9.5
8	66.6	0.7	-	-	6.4	0.5	7.8
10	69.8	-	-	-	-	-	11.7
12	58.9	-	-	-	4.2	-	12.5

a material at TLC plate origin

The recovery and identity of ^{14}C in soil in the field study is given below.

Field Study

% applied dose at specified time

Time (weeks)

	2 days	1	2	5	8	12	16
AMDRO	45.4	40.0	2.13	17.2	18.4	13.7	17.8
CL 71,640/243,236	2.5	2.0	1.7	2.2	0.9	0.8	-
CL 98,724	1.7	0.45	3.1	2.9	3.1	5.0	5.1
Unidentified [1]	7.1	10.69	5.0	10.0	9.8	9.9	10.2
Unextracted	7.1	8.6	2.3	12.0	10.3	5.6	12.2
Recovery	63.8	61.7	34.2	44.3	43.5	35.0	45.3

1 Comprised of several materials

A half-life of 6.3 weeks for AMDRO was calculated from this data. None of the unidentified materials would occur at 0.01 ppm or more under normal application rates. The low recovery of ^{14}C was attributed to possible removal of bait by ants.

Conclusions

These are well-performed studies which satisfy data requirments under section 163.62-8(b) for aerobic soil metabolism. The data indicates that AMDRO will gradually degrade under aerobic soil conditions in the absence of light. CL 98,724 is the principal identified degradate, although numerous lesser degradates were found.

2.3 CL 217,000: Determination of Mobility in Soil, B. L. Reichert, Report PD-M, Volume 16-25, 2/1/79, American Cyanamid, Agricultural Research Division, Princeton, N. J., Accession No. 241-260.

Experimental Proced e

Four soils were used in these evaluations with the following characteristics:

Soil	Texture	% Sand	% Silt	% Clay	% OM	CEC	pH
Delaware	Sand	89.6	7.2	3.2	0.9	5.91	5.8
Princeton	Sandy loam	61.2	29.6	9.2	2.1	7.81	6.5
Wisconsin	Silt loam	33.2	53.6	13.2	4.6	30.71	6.3
North Dakota	Clay loam	27.2	35.2	37.6	5.6	57.2	6.3

For soil TLC, the Delaware and Princeton soils were sieved to less than 500 microns, and the Wisconsin and North Dakota soils to less than 250 microns. For the soil column, the Princeton soil was sieved to 2mm before drying. ^{14}C-AMDRO, labelled in the benzylic carbons and 99+% pure was used. Soil thin-layer plate were prepared by conventional methods. Between 0.5 and 0.1 microgram of ^{14}C-AMDRO was spotted on each soil plate and the plates immediately developed for 10cm with water. The position of ^{14}C labelled materials was measured with autoradiography.

For the soil column, ^{14}C-AMDRO was added to the Princeton soil at 5ppm, and aged aerobically in the dark for one month. After aging, half the soil was analyzed directly and the remainder of the treated soil was placed on top of a 2 inch diameter X 12 inch tall column of untreated Princeton soil which was eluted with 0.5 inches of water per day for 45 days in the light at 30-40°C. The aged soil samples (pre- or post column) were successively extracted with organic solvents with the solvent extracts analyzed by TLC and the extracted soils checked for ^{14}C content by combustion.

Results

The R_f value of AMDRO on all of the four soils was 0.00 - classifying AMDRO as immobile.

The distribution of applied radioactivity in the soil column after 45 days is given below:

Sample	% of Applied Dose [1]
Treated layer	72.1
0-2 inch soil	3.4
2-4 inch soil	1.1
4-6 inch soil	0.8
6-9 inch soil	0.7
9-12 inch soil	1.4
Combined leachate	0.1
Plant matter	1.0

1 Amount of radioactivity placed on top of the column

The results show that AMDRO and/or is degradates do not leach, although nearly 20% of the applied ^{14}C was not accounted for. Presumably, this missing material may have volatized.

TLC analysis was performed on the extractable portion of material in the pre-column material in the pre-column aged soil, and in the treated layer and 0-2 inch layer after running the column. Results are given below:

	% Extractable Radioactivity		
Metabolite	1 Month Aerobic[1]	Treated Layer	0-2 Inch Layer
AMDRO	86.7	48.6	-
CL 98,724	4.4	20.8	45.7
Polar unknown(s)	2.4	25.2	44.4
Origin	6.6	5.4	9.9

1 Soil analyzed before column application

Conclusions

This study satisfies guideline requirements under 163.62-9(b) and demonstrates that AMDRO and its aerobic soil degradates are immobile in soil.

3.4 CL 217,300: the effect of Soil Microorganisms on Carbon-14 Labeled CL 217,300. S. H. Cabella, Report PD-M, Volume 16-21, 9/7/79, American Cyanamid Company, Agricultural Research Division, Princeton, N. J., Accession No. 214-260.

Experimental Procedures

Princeton sandy loam soil (see 2.2 for properties) was fortified with benzylic label ^{14}C- AMDRO (99+% pure) at a rate of 0.9977 mg per 200 g soil (with 12.9% moisture). Two flasks contained sterile soil; another two were non-sterile. The flasks were connected to gas traps for scrubbing CO_2 and volatile organics. The flasks were incubated in darkness at unspecified temperature. At 15 days, one sterile and one non-sterile flask was taken for analysis and the others at 30 days. The soil was extracted for analysis by TLC as described in 2.2.

A second study examined the ability of soil microbes to utilize AMDRO as a sole carbon source. Two flasks were inoculated with 1.5 g soil which had been incubated with AMDRO for 30 days; and 100 ml mineral salt solution was added. One of the flasks received 100 mg of AMDRO and the other 1 ml of 10% glucose solution. Two weekly transfers to fresh medium were made. The third transfer was to flask holding 1 ml 10% glucose and 100 mg AMDRO. Another flask received AMDRO alone. No quantitative methods or further incubation details were provided.

Results

No volatile organic materials were trapped over the 30 day incubation; and only 3% was recovered in the CO_2 traps of the non-sterile samples (none from the sterile samples). The steady but slow release of CO_2 in the non-sterile samples indicated that AMDRO did not stimulate rapid microbial growth. Recoveries of ^{14}C at 30 days from soil were 91.5% extractable and 3.4% non-extractable for non-sterile samples, and 95.7% extractable and 0.5% non-extractable for the sterile samples. Parent AMDRO accounted for 77.5% of extractable ^{14}C in non-sterile samples at 15 days, and 61.7% at 30 days. Unidentified polar material accounted for 77.5% and 61.7% of non-sterile sample recoverable ^{14}C at 15 and 30 days, while comparable figures for sterile samples were 6.6% and 5.9%. CL 98,724 constituted 1.0% of ^{14}C at 30 days in non-sterile samples, and 3.1% in the sterile soil.

It was stated that there was no evidence that AMDRO alone could support microbial growth. Also, a level of 0.1% in the medium did not inhibit growth. No data were provided for either conclusion.

Conclusions

The study is sufficient to demonstrate that soil microbes are capable of degrading AMDRO. No attempt was made to identify the types of organisms responsible for the degradation. Because microbial degradation will be a minor pathway (relative to photolyis) under the proposed use pattern, guideline data requirement 163.62-8(f)(2) is satified.

However, because no quantitative data are given, the study on the effects of AMDRO on microbes cannot be evaluated.

2.5 AMDRO (CL 217,300) Fire Ant Insecticide: Uptake and Residues of Radioactivity in Follow-Crops Grown in Soil containing Aged Residues of Carbon-14 CL 217,300. P. E. Gatterdam, report PD-M, Volume 17-3, 5/22/80, American Cyanamid Company, Agricultural Research Division, Princeton, N. J., Accession No. 240-260.

Experimental Procedure

^{14}C- AMDRO, benzylic label with purity of 99% was used. The study field soil had the following characteristics; Princeton sandy loam - pH 5.5, 1.9% organix matter, 53.6% sandy, 37.6% silt, 8.8% clay, bulk density = 1.034. The labelled AMDRO was formulated or a [redacted] bait and applied to field plots at rates of 6 g ai/A after treatment, the plots were planted with radish, snapbeans, or barley. At maturity (66 days), the plants were harvested. Radish was separated into foliage and root; snapbean and barley were separated into foliage and seedpod. The tissues were extracted three times with methanol/acetone, and the extracts and residual tissue combusted for ^{14}C determination.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Results

The validated limit of sensitivity of the analytical method for AMDRO in pasture grass is 0.05 ppm. At the 6 g/A rate foliage had total residues of

0.004 ppm. All other tissues were less than 0.001 ppm. At the exaggerated rate of 30 g/acre, barley foliage had 0.01 ppm or below. The possibility of dehydration at maturity causing the higher barley levels was raised.

Conclusions

The study us adequately performed, satifies requirement 163.62-11(b) and supports the conclusion that AMDRO aged residues will not accumulate in typical root, small grain, and vine vegetable crops. Leafy vegetables were not examined.

3.6 CL 217,300: Anaerobic Soil Metabolism, B. L. Reichert, Report PD-M, Volume 16-26, 11/2/79, American Cyanamid Company, Agricultural Research Division, Princeton, N. J., Accession No. 241-2600, 241-261.

Benzylic-Labelled ^{14}C-AMDRO, 99+% pure, was used. Princeton sandy loam soil (described in Section 2.2) was used. The labelled AMDRO was mixed with soil at 5 ppm (after adjusting soil moisture to 75% of field capacity, and soil placed in flasks. The flasks were continuously flushed with air and effluent trap and passed through an organic volatiles trap and a CO_2 trap. The samples were kept in the dark at 23°C. This aerobic phase was run for 30 days, at which time the flasks were flooded with water to 2-3 cm depth and purged with N_2 for up to 60 days.

Soil samples were analyzed by combustion and soil extracts were analyzed also by TLC. Gastraps were periodically monitored.

Results

The recoveries of ^{14}C are as follows:

	% Applied ^{14}C		
Time	Extractable	Bound	Total
Zero-time	96.3	0.2	96.7
1 Month Aerobic	93.7	0.9	94.6
1 Month Anaerobic	98.0	0.7	98.7
2 Month Anaerobic	86.0	1.3	87.3

Very little (<0.5%) of ^{14}C was recovered in gastraps.

The percentage distribution of extractable ^{14}C was:

	Aerobic 30 Day	Anaerobic 30 Day	Anaerobic 60 Day
AMDRO	86.7	81.8	69.8
CL 98,724	4.4	12.0	20.7
Polar & Origin	9.0	6.7	9.6

Conclusions

The results show that AMDRO degrades slowly under anaerobic conditions, principally to CL 98,724. Anaerobic metabolism data is not required for non-crop terrestrial use. However, the data suggest that should treated fields become flooded, AMDRO degradation would proceed, and novel degradates would not be informed.

3.7 AMDRO Fire Ant Insecticide (CL 217,300): Metabolism of Surface Applied Compound under Field Conditions, P. Gatterdam, Report No. C-1743. American Cyanamid Company, Product Development, Princeton, N. J., Accession No. 241-260, 241-261.

The Experimental Procedure section was skipped.

The recovery of AMDRO and degradates is listed in the table below.

Percentage of applied Dose at Indicated Time (hr.)

Depth (in.)	1	2	4	8	24	48	96
0-2	75.2	85.3	86.6	81.5	54.4	65.8	37.6
2-4	0.1	<0.01	<0.01	<0.01	0.20	0.20	0.80
TOTAL	75.3	85.3	86.6	81.5	54.6	66.0	38.4
ppm	0.324	0.395	0.350	0.356	0.219	0.231	0.159

The possibility that the low recovery of material initially was due to removal of bait by foraging ants.

The recovery of AMDRO and degradates is listed in the table below;

Amount of ^{14}C material as % Dose at Indicating Sampling Intervals (hrs.)

Compound	1	2	4	8	24	48	96
AMDRO	46.7	50.9	49.5	45.7	23.7	24.1	8.7
CL 71,640/ 243,236	5.3	4.0	10.3	10.7	9.6	9.2	5.3
Unidentified	11.8	18.8	18.6	18.1	14.4	19.6	12.6
Unextracted	10.6	11.0	2.7	2.9	2.6	6.1	4.8

The half-life of AMDRO dissipation derived from a graphical plot is approximately 18 hrs. It is obvious that the degraded material is not accounted for. Leaching apparently did not occur, leaving volatilization or translocation by foraging ants as the most likely means of dissipation.

Conclusions

This study can be used to satisfy the field dissipation data requirements (section 163.62-10) for non-crop use. It demonstrates that AMDRO dissipates rapidly (half-life = 18 hours) when exposed to light under actual field conditions. The fate of the dissipated AMDRO is unknown. Until a valid photolysis study on soil is submitted, the most likely possibility is that a photo product is formed which is very volatile. Removal of formulation by ants is another possibility, although some precautions were taken to prevent this.

4.0 Executive Summary and Conclusions

4.1 The majority of residues in bluegill sunfish exposed to AMDRO in a flow-through system are in form of AMDRO.

4.2 Under aerobic soil conditions protected from light, AMDRO is gradually degraded with a half-life of 3 months in the laboratory and 6 weeks in the field. Several degradates including CL 98,724 were formed.

4.3 Neither AMDRO nor its aerobic soil degradates are mobile in soil.

4.4 Soil microbes are capable of slowly degrading AMDRO (38.3% degraded after 30 days).

4.5 AMDRO and its degradates will not accumulate in rotated crops planted 3 months after AMDRO treatment.

4.6 AMDRO degrades slowly under anaerobic soil conditions, principally to CL 98,724.

4.7 AMDRO degrades extremely rapidly (half-life = 18 hours) when applied under field conditions. It is inferred that photodegradation is the dominant degradation mechanism. Numerous degradates, including CL 98,724 were noted.

5.0 Recommendations

As enumerated in EFB review/memo of 7/17/80, the following data gaps exist concerning the use of AMDRO in non-crop terrestrial situations;

1) Hydrolysis - all degradates constituting more than 10% of total must be identified.

2) Photodegradation - data in both aquatic and soil systems must be provided. Dark controlsare to be used, and major degradates identified.

3) Fish accumulation - flow through/bluegill; to be valid, the study must be done with all of the test chemical in solution, either by running below AMDRO water solubility (preferable), or by using carrier solvents seech as used in toxicity determinations.

4) Effect of AMDRO on microbes

5) Soil/water adsoprtion: desorption

Other portions of the submission were less than satisfactory. For instance, the static catfish accumulation requires characterization of fish, soil, and water residues. This was not done for the submitted study. However, EFB recognizes the great difficulty in identifying numerous degradates formed from a low application rate. In view of the unlikelihood that AMDRO degradates will enter aquatic habitats in significant quantities, this data will not be required. Also, identification of soil microbes responsible for for AMDRO degradation is a technical requirement. However, because such metabolism is a relatively minor component of AMDRO degradation, this requirement will be relaxed.

EFB does not contemplate hazardous exposure situations arising from the environmental chemical properties of AMDRO. It is applied in a bait form at a very low rate (4 g ai/A) and has a very fast field dissipation rate. Neither AMDRO nor its degradates leach through soil. The most important degradative pathway is probably photolyis, with soil and microbial degradation, and hydrolysis relatively slower processes. Neither AMDRO nor its degradates accumulate in rotational crops and uptake in catfish is rather low (51-fold in whole fish).

EFB requests that data gaps 1-5 above be listed as conditions for the registration of AMDRO. EFB also notes that certain data deficiencies noted in this review may have to be removed if additional use patterns or formulations are requested in the future.

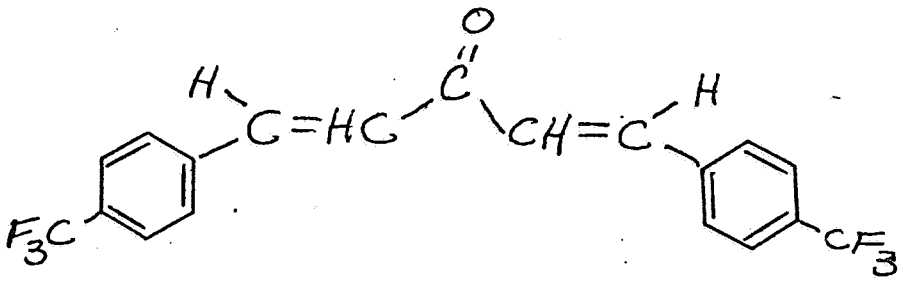
Henry Appleton

Henry Appleton
Review Section No. 1
Environmental Fate Branch
Hazard Evaluation Division

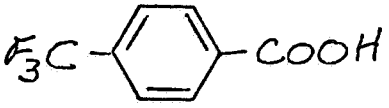
APPENDIX

Principal AMDRO Degradates

A) CL 98,724: 1,5-bis(alpha, alpha, alpha-tri-fluoro-p-tolyl)-1, 4-pentadien-3-one



B) CL 71,640: p-toluic acid alpha, alpha, alpha-trifluoro-



C) CL 234,236: Cinnamic acid, p-tri-fluoromethyl