3/5/75 3/1975

Environmental Chemistry Review for [CGA-24705] 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide

PP #5G-1553
100-EXP-X
CIBA-Geigy
9/11/74

I. INTRODUCTION

A. This is a new herbicide for use on corn. Proposed temporary tolerance:
0.75 ppm corn fodder and forage
0.05 ppm fresh corn
0.02 ppm eggs, milk, and meat
Tolerance covers CGA-24705 and its metabolites converted to 2-([2-ethyl-6-methylphenyl] amino) propanol calculated as CGA-24705.

B. Other chemical names are:

DUAL 2-chloro-6'ethyl-N-(2-methoxy-1-methylethyl)-o-acetotluidine

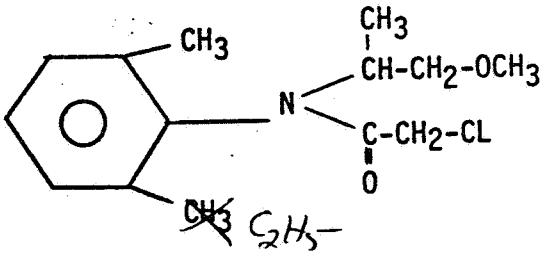
and

N - (2' methoxy-1'-methyl ethyl)-2-ethyl-6-methyl-chloro-acetanilide

There are no common names.

C. Product name is CGA-24705 6 EC.

D. Chemical and Physical Properties:



Empirical Formula: $C_{15}H_{22}NO_2CL$

Molecular Weight: 283.80

Form: liquid

Color: white to tan

Boiling point: 100°/0.001 mm Hg

Vapor pressure: ca 10^{-5} mm Hg

Solubilities:
Water - 530 ppm @ 20°C
Organic solvents - miscible with xylene, toluene, dimethyl formamide, methyl cellusolve, butyl cellusolve, ethylene dichloride, and cyclohexanone
Insoluble in ethylene glycol and propylene glycol

Specific gravity: 1.117

Stability:
a. Halflife of 0.25% solution at 100°C:
acid - 30 hours at pH 3
base - 1.5 hours at pH 10
neutral - 18 hours at pH 7
b. Shelflife of the 6E formulation is estimated to be five years minimum based on no significant decomposition at 70°C for 7 weeks or at 50°C for 24 weeks.

II DIRECTIONS FOR USE

A. CGA-24705 applied alone:

Apply in minimum 15 gallon (ground) or 5 gallon (aerial) of water per acre at planting or before emergence of weeds and corn.

Application rates: (lb ai/A)

Soil texture	Less than 3% O.M.	3% O.M. or greater
Sand, loamy sand, sandy loam	1-2 lb	1-2 lb
Loam, silt loam, silt	1.5-2.5 lbs	2-2.5 lbs
Silty clay loam, sandy clay loam, silty clay, sandy clay, clay loam, clay	2-3 lbs	2-3 lbs

Rotation crops:

If the original application was banded and the second crop is replanted in the untreated row middles, a second banded treatment may be applied.

Any rotation crop may be planted 12 months after the CGA-24705 treatment.

B. CGA-24705 plus Atrazine tank mixture:

Apply in minimum 15 gallon water (ground) or 5 gallon water (air/acre) at planting or before emergence of weeds and corn.

Application rates: lbs ai/A.

Soil texture	CGA-24705	Atrazine
Sand, loamy sand, sandy loam	1.0-1.5	0.8-1.2
Loam, silt loam, silt	1.5-2.0	1.2-1.6
Silty clay loam, sandy clay loam, silty clay, sandy clay, clay loam, clay	2.0-2.5	Less than 3% O.M. 1.2-2.0 3% O.M. or greater 1.6-2.0

C. Rotational crops:

1. Corn, sorghum, or soybeans may be planted 12 months after treatment. On calcareous soils in northcentral Iowa and southcentral Minnesota, soybeans may not be planted until 2 years after treatment.

2. Small grains may not be planted until 15 months after application.

3. Any crop may be planted 2 years after application.

III. DISCUSSION OF DATA

A. Analytical Methods

1. Extraction of radioactive metabolites from treated biological material (Method #AG-214).

Chloroform-methanol, chloroform and water are successivly added to sample, with shaking in between. Sample filtered through sintered glass. Filter cake is washed with

methanol, water, and chloroform. Layers are separated and analyzed by LSC.

2. Extraction of CGA-10832 residues in soil (Method #AG-219).

   Soil sample is extracted with methanol/water (9/1). Soil residue determined by combustion-LSC. Methanol extract is partitioned with chloroform and both organic and aqueous phases are counted by LSC.

3. G.C. determination of CGA-24705 (Method #AG-265).

   CGA-24705 residues in corn, grain, and forage are converted to CGA-37913 by refluxing with HCL. It is made basic with NaOH, partitioned into hexane, injected into a gas chromatogrpah equipped with a Coulson electrolytic conductivity indicator, specific for nitrogen.

4. CGA-24705; Gas chromatographic determination of total residues in material of animal origin (Report: REM 5/74).

   This is a total residue method for parent and all metabolites yielding CGA-37913 after acid hydrolysis.

   Sample is subjected to acid hydrolysis with 6N HCL. Solution is then alkalyzed, and steam distilled and extracted into iso-octane. The CGA-37913 is cleaned up on alumina column and by TLC if necessary. Detection is by GLC/mass fragmentmetry.

   Detection limit is .006 ppm in milk, .015 in chicken tissues, and .02 ppm in cow tissues.

5. Modification of REM 12/73 for analysis of residues in soil (Part of Reports #AGA-A-2929, 2969, 2973, 3105, 3133).

   Soil is refluxed with methanol and filtered. NaCL is added to aqueous solution and it is extracted with hexane. Hexane phase is filtered through Na_2SO_4, cleaned up on alumina column and analyzed by GLC equipped with Dohrmann microcoulmetric detection system operating in the chloride sensitive mode.

6. Blending of Soils and Homogenization of Biological Material for Radioassay and Extraction (Method #AG-223).

with dry ice. Dry ice and samples are
sample is put in refrigerator for dry
ıfter which sample is stored frozen.

:ine Residues from Soil (Method #AG-255).

l (Method #AG-223) and refluxed 1 hour
ıater (90/10). Extract is assayed by

ıd AG-265 for the determination of CGA-
ıhich are converted to the CGA-37913
iAAC-74043.)

:e samples treated with ^{14}C-ring
and harvested at different periods
residues in the range of 12-27% of
and about 25% of the extractable
ıd AG-265."

ıic metabolism of ^{14}C-CGA-24705 in silt
:enhouse conditions (Report: Biodynamics

!4705 was added to Hastings silt loam
ıas incubated 30 days aerobically.
:ubated an additional 60 days aerobically
under nitrogen). Soil was extracted with
this was re-extracted with water or
:ts were counted by LSC. Total soil ^{14}C
:ombusion.

ıaracteristics

2.9%
19.2%
61.2%
19.6%
5.7%
20.6 meq/100 g.

% of ^{14}C Activity

System	Interval (days after treatment)	Polar extractable	Non-polar extractable	Bound
Aerobic	30	8	53	40
Aerobic	60	13	46	40
Anaerobic	60	11	49	39
Aerobic	90	7	39	54
Anaerobic	90	6	42	53

Volatile ^{14}C was less than 0.3%

Results:

0.3% or less of ^{14}C recovered as volatile ^{14}C or $^{14}CO_2$

Conclusions:

1. No significant differences in distribution of ^{14}C activity were found between aerobic and anaerobic conditions.

2. Rate of degradation slower in anaerobic soil.

C. Field persistance studies and field leaching (Report nos. AG-A-2929, 2969, 2973, 3105, 3133).

Soil Characteristics

Location	Type	% Sand	% Silt	% Clay	pH	% O.M.	C.E.C.
MississippI	Loam	48.4	37.2	14.4	6.1	1.4	9.0
Nebraska	Silt loam	19.6	56.8	23.6	6.1	1.7	14.8

Characteristics of 3 other soils (New York, California, and Illinois) not submitted.

250 E.C. formulation was applied at 2.0 and 4.0 lb ai/A. Soil samples were analyzed by: "Modification of REM 12/73," involving methanol extraction, hexane partition, clearnup on alumina column and GLC with Dohrmann microcoulmetric detection.

Location	Application (lb ai/A)	Interval (days)	PPM residue 0-6"	PPM residue 6-12"
Mississippi	2	0	0.92	-----
		60	0.11	1/ND
		126	ND	ND
		363	ND	ND
	4	0	2.1	------
		60	0.23	ND
		126	0.14	ND
		363	ND	ND
Nebraska	2	0	0.81	-----
		64	0.55	0.22
		107	0.27	0.10
		162	0.17	ND
	4	0	2.0	-----
		64	1.5	0.25
		107	0.37	0.07
		162	0.33	0.05
New York	2	0	0.58	-----
		60	0.12	ND
		111	0.47	ND
	4	0	1.36	-----
		60	0.12	ND
		111	0.11	ND
California	2	0	0.96	-----
		129	0.12	0.09
	4	0	3.4	-----
		129	0.11	0.09
Illinois	2	0	0.34	-----
		61	0.09	ND
		151	0.13	ND
	4	0	1.1	-----
		61	0.15	ND
		151	0.07	ND

1/ ND = No data.

Results:

1. Less than 0.05 ppm residue was found in the 6-12" layer of 3 out of 5 soils.

2. On Nebraska silt loam, 0.22-0.25 ppm had leached to 6-12" layer after 64 days.

Conclusions:

1. Halflives of extractable residues were less than 60 days, except for Nebraska soil which was about 30 days.

2. Soil characteristics for New York, California, and Illinois soils are needed.

D. Metabolism in Plants and Soil.

1. Distribution of ring labelled CGA-24705 in soil and greenhouse corn (GAAC-74015). Corn was treated with 2 lb ai ring labelled CGA-24705. Plant materials were extracted with a biphasic mixture of chloroform, methanol, water (Method #AG-214). Soil was extracted with methanol, water and the extract was partitioned with chloroform (Method #AG-219). Soil was also extracted with acetonitrile/water. Extracts were quantitated by LSC. Non-extractable materials were determined by combustion with LSC. Methanol soluble plant metabolites were chromatographed on a DEAE cellulose anion exchange column. Ionic character of metabolites was determined by an ion exchange technique using Dowex 1 and 50 columns. TLC and LSC were also utilized. Nicotine, kelthane, and chlorobenzilate were used for insect control.

Soil Characteristics

Type	Silt Loam
pH	5.7
CEC	8.4
% O.M.	3.6
% Sand	28.8
% Silt	66.4
% Clay	14.8

Concentration of Radioactive Metabolites in Corn

Interval (weeks)	4	8	12	16 (stalks)	16 (grain)
Total ppm - equivalent to ^{14}C	1.45	.46	.37	.72	.05

Concentration of Radioactive Metabolites in Soil

Interval	1 Day	4 Weeks	8 Weeks	12 Weeks	16 Weeks
Total ppm:					
0-3"	3.02	1.92	0.50	0.69	0.65
3-6"	0.03	0.73	0.20	0.43	0.24
6-9"	-----	0.43	0.25	0.30	0.14

Distribution of ^{14}C in Soil (Percent Present)

	4 Weeks	8 Weeks	16 Weeks
Methanol Extraction			
Organic	43.8	6.0	10.8
Polar	5.7	6.0	3.1
Non-extractable	50.5	86.0	78.5
CGA-24705	39.4	-------	3.6
Unknown Extractables	10.1	-------	10.3
Acetonitrile Extraction			
Organic		18.0	19.8
Polar		6.0	10.8
Non-extractable		70.0	60.0

Results:

1. 81% and 84% of ^{14}C in corn at 4 and 12 weeks is water soluble.

2. Four-week corn extract produced 4 spots on TLC.

3. Concentration of ^{14}C in soil ~~went~~ declined from 3.02 ppm at one day to 0.65 ppm at 16 weeks.

4. Non-extractable residues in soil increased from 51% of ^{14}C present at 4 weeks to 79% of ^{14}C present at 16 weeks.

5. Organic phase of methanol extractable ^{14}C in soil changed from 43.8% of total at 4 weeks to 10.8% at 16 weeks. 89% of this organic phase at 16 weeks was parent compound.

Conclusions:

1. Halflife of ^{14}C soil is approximately 6 weeks.

2. An increasingly greater percentage of the ^{14}C present was bound with time.

3. The compound is very mobile by leaching.

2. Distribution of ring labelled CGA-24705 in soil and field-grown corn (Report GAAC-74022). Corn in the field was treated with 2 lbs ai/A ring labelled CGA-24705. Plant or soil samples were extracted by Methods #AG-219 or AG-255. Non-extractable ^{14}C was determined by combustion. Methanol soluble metabolites were chromatographed on a DEAE cellulose column. Ionic character of metabolites was determined by an ion exchange technique using Dowex 1 and 50.

Soil characteristics: silt loam; pH 5.6; CEC 9.6; % O.M. 0.9; % sand 26.0; % silt 62.0; % clay 12.0.

Concentration of ^{14}C in Field Soil

PPM

Interval	1 Day	4 Weeks	8 Weeks	12 Weeks	16 Weeks
0-3"	1.79	0.73	0.75	0.56	0.31
3-6"	0.04	0.14	0.31	0.26	0.10
6-9"	-----	0.01	0.08	0.11	0.06

% Distribution of Radioactivity in Soil

Balance (MeOH extraction)	4 Weeks	8 Weeks	16 Weeks
Organic	41.2	34.7	*d
H_2O/MeOH	19.2	13.3	d
Non-extracted	31.5	45.3	80.5
TLC Data			
CGA-24705	35.0		
Unknown Extracted	28.1		
Balance (CH_3CN Extraction)			
Organic	46.6	41.3	d
Polar	17.8	14.7	d
Non-extracted	31.5	41.3	74.5

* d - too low for reliable quantitation

Results:

1. Chromatography of corn extract on DEAE cellulose indicated one major metabolite present.

2. TLC of methanolic corn extract showed up to 12 radioactive metabolites.

3. Total ^{14}C in 0-9" soil decreased from 1.83 ppm initially to .47 ppm at 16 weeks.

4. Non-extractable, by methanol, soil residues were 31.5% at 4 weeks and 80.5% at 16 weeks for methanol. Values ranged from 31.5 to 74.5 at 4 and 16 weeks for acetonitrile.

5. At 16 weeks there was only a trace of residue that was either methanol or acetonitrile extractable in soil.

6. Leaching resulted in 0.31 ppm in the 3-6" at 8 weeks and .11 ppm in 6-9" layer at 12 weeks.

Conclusions:

1. Halflife of total ^{14}C in soil was about 8 weeks.

2. Increasingly larger percentages of the ^{14}C present were bound with lime.

3. The amount of ^{14}C that leached increased with time.

3. Metabolism of CGA-24705 in corn (Report #GAAC-74050).

This study was undertaken to determine whether the major pathways of metabolism include conjugation. A ^{14}C-ring label CGA-24705 solution was utilized.

Corn leaves were incubated with pesticide solution, treated per-emergence with the solution or it was injected into the leaves.

Analysis was by column chromatography utilizing DEAE cellulose, silica gel, and sephadex LH-20, TLC, solvent extraction, and GC-Mass Spec.

Results:

1. 10 Ethyl acetate soluble metabolites were found.

2. CGA-40172 and CGA-37913 were identified.

3. Glutathione conjugate of CGA-24705 was produced by leaf incubation, but not by crop treatment.

Conclusions:

1. Registrant believed that conjuation was probably a major metabolic pathway.

4. A comparison of ^{14}C-CGA-24705 corn biosynthesized metabolites with those in excreta of goats fed with ^{14}C corn (Report #GAAC-74055).

^{14}C ring labelled CGA-24705 containing corn plants were fed to goats. Feces (7 days) and urine (6 days) and corn were subjected to acid hydrolysis, followed by analysis by solvent extraction and TLC.

Results:

1. Of 8 metabolites separated on TLC, CGA-40172 and CGA-37913 were identified.

2. Registrant concluded that the same pesticide moieties were present in feces, urine, and corn, though they may be conjuaged to different conjugating groups.

5. Uptake, translocation, and degradation of ^{14}C-ring-CGA-24705 in corn grown under controlled conditions (Report: Basle project #8/74).

Corn plants were grown in 2 ppm ^{14}C-CGA-24705 for one week and in nutrient solution for the subsequent 5 weeks.

Plant parts were subjected to solvent extraction, and column chromatography, followed by TLC, GLC, and GC-Mass spec. analysis.

The reduction of a postulated C-S bond between glutathione and pesticide moiety by Rainey Nickel was carried out.

Conclusions:

1. Metabolites CGA-41507 and CGA-42446 were present as conjugates which were released by Rainey Nickel reduction.

2. Registrant concluded parent compound is rapidly metabolized since very little ^{14}C could be extracted with hexane.

3. I conclude that polarity of parent compound may be altered, by conjugation, this possibly being the reason it was not extracted with hexane.

E. Photolysis of CGA-2470 in aqueous solution under natural and artificial sunlight conditions (Reports #GAAC-7404 and AG-208).

A 265 ppm aqueous solution of ring labelled CGA-24705 was exposed to natural and artifical (sun lamp at 18") sunlight. Solution was in quartz bottles on turntable.

Aqueous solution was quantitated by LSC at intervals. Aliquots were extracted with chloroform at intervals and analyzed by TLC, GLC, and GC-Mass Spec.

A covered control was used.

Photolysis in Aqueous Solution

Exposure (days)	% Photolysis
Artificial sunlight	
0	0
1	7
4	25
9	33
15	69
Natural sunlight	
0	0
14	4
30	8

Results:

1. Artificial sunlight resulted in 69% photolysis after 15 days, while natural sunlight resulted in 8% at 30 days.

2. 45.5% and 93.5% of recovered radioactivity were parent compound after 15 days artificial and 30 days natural sunlight respectively.

3. After 15 days exposure to artificial sunlight, 70.8% of ^{14}C was extracted by chloroform and 23.0% remained in water (compared to 95.8% and 0.2% respectively for control).

4. Photolysis under artificial sunlight produced 5 chloroform extractable photoproducts, containing 13% of ^{14}C activity. Of these, CGA-13656, CGA-40919 and CGA-40172 were identified. An additional 23% of ^{14}C activity was in the form of water extractable product(s).

5. There was no degradation or loss of ^{14}C in the control.

Conclusions:

- Photolysis takes place rather slowly under natural sunlight, and is greatly accellerated by U.V. light.

F. Effects of CGA-24705 on microbial population in two soils (University of Missouri Report No. 2).

Louisiana commerce loam and Indiana loam soils were treated with 50 and 250 ppm CGA-24705 and incubated at 28°C for 56 days. At intervals, 1g soil was removed, mixed well with 99 ml sterile water, and after serial dilutions the solution was plated on Martins media (fungi), Thorntons media (bacteria), and glycerol asparaginate agar (actinomycetes). Parallel sterile control soils were used and plate counts were made.

Conclusions:

1. On the basis of plate counts, there was no apparent killing or reduction in numbers of fungi, bacteria, or actinomycetes.

2. Changes in species composition, or non-lethal (bacteriostatic) effects were not investigated.

G. Hydrolysis of CGA-24705 (Report #SPR 2/74).

CGA-24705 was added to aqueous media at 100 ppm with pH values ranging from 1-13, and incubated at 30, 50, or 70°C. Aliquots were extracted with hexane and the amount of CGA-24705 was determined by GLC at various hourly intervals during the first day and at various daily intervals over a 28-day period.

Separation and identification of hydrolysis products: ^{14}-C-ring labelled CGA-24705 was incubated in 0.1 N HCL or NaOH. Solution was extracted with hexane, subjected to TLC, spots were detected by autoradiography, scraped, and characterization of metabolites was by GLC and mass spec.

Results:

1. At 20°C halflives were greater than 200 days at pH 5, 7, and 9, and 97 days at pH 13.

2. At 50°C halflife ranged from 79 days (pH 5) to 138 days (pH 9); at 70°C halflife ranged from 10 days (pH 5) to 17 days (pH 9).

3. Hydrolysis with 0.1 N NaOH at 30°C resulted in 78% parent and 5% CGA-40172 at 5 days and 51% parent and 37% CGA-40172 at 28 days.

4. Hydrolysis in 0.1 N HCL at 70°C results in 70% parent and 19% CGA-40191 at 5 days and 27% parent and 57% CGA-40919 at 28 days.

5. Acid hydrolysis yielded CGA-41638 which was rapidly converted to CGA-40919.

Conclusions:

Hydrolysis proceeds rapidly at temperatures above 50°C or at pH 13. It proceeds much more slowly at lower temperatures of pH values.

H. Report on parent leaching for CGA-24705 (University of Missour Report No. 1).

1.9 mg of ^{14}C-CGA-24705 was added to 12" columns containing 5 soil types. Columns subjected to 20" rain at a maximum rate of 1 inch/hour. Soil from each inch and leachate were counted by LSC.

Soil Analysis

Soil	Source	Organic matter	pHw	CEC	Sand	Silt	Clay
Muck	New York	77.0	5.1	22.6	76.8	17.2	6.0
Silt loam	Indiana	3.9	5.7	11.7	22.4	66.0	11.6
Sandy loam	Texas	0.6	8.0	12.5	65.2	21.2	13.6
Loam	Louisiana	0.7	6.1	10.9	42.8	49.6	7.6
Sand	Florida	1.6	7.0	2.9	93.6	2.8	3.6

Distribution of ^{14}C in Columns (% of initial ^{14}C)

Inches	Sandy loam	Sand	Loam	Silt loam	Muck
0-3	4.7	26.4	10.7	57.9	100
3-6	10.5	16.1	18.4	22	0
6-9	16.8	18.2	35.5	19.1	0
9-12	31.6	18	37.3	0.4	0
Leachate	36.4	20.9	4.0	0.4	0.0

Results:

1. 36.4%, 20.9%, and 4.0% of ^{14}C applied was found in leachate for sandy loam, sand, and loam soils respectively.
2. 100% of ^{14}C was retained in 0-3" layer on muck soil.
3. 18-37% of ^{14}C had leached to 9-12" in sandy loam, sand, and loam soils. 0.4% leached to 9-12" in silt loam.

Conclusions:

1. Position of ^{14}C label not given.
2. Compound leaches considerably in sandy soils. It leaches only very slightly in silt loam and not at all in muck.
3. The lower the % O.M., the greater the leaching.

I. Leaching of metabolites (aged leaching) (Report 73021-6).

4 lb ai/A ^{14}C-ring CGA-24705 was applied to top of 12" column packed with sandy loam. Water was added to 60% field capacity and column incubated 30 days. Then column was subjected to 0.5 acre-inch rain per day for next 45 days. Column was divided into twelve 1" segments, and soil and leachate were counted by LSC.

Soil characteristics: O.M. - 1.5%; sand - 82.8%; silt - 13.6%; clay - 3.6%; pH - 6.9; CEC - 2.6 meq/100 g.

Distribution of ^{14}C

Soil Depth	% of Applied ^{14}C
0-3"	61.2
3-6"	13.7
6-9"	8.8
9-12"	3.0
Leachate	26.6

Results:

1. 26.6% of ^{14}C activity was in leachate.
2. 11.8% of ^{14}C was found in soil between 6-12".

Conclusions:

1. A large portion of applied ^{14}C is found in the leachate.
2. Metabolites definitely leach in sandy loam.

J. Runoff-lab study (Report: Biodynamics 73022-1).

1 lb ai/A of ^{14}C-ring CGA-24705 were applied to upper third of a 2' x 3' sandy loam slab soil runoff apparatus with an 8° slope. Runoff water, sediment, and leachate was counted by LSC. Area was subjected to artificial rainfall at 1, 3, and 7 days after treatment.

Soil characteristics: O.M. - 1.5%; sand - 82.8%; silt - 13.6%; clay - 3.6%; pH - 6.9; CEC - 2.6.

Distribution of ^{14}C Activity

Interval days	Rainfall acre-inches	^{14}C-Activity, %, in Leachate	Runoff Water	Runoff Sediment
1	0.37	0.24	0.76	0.51
3	0.46	0.02	1.06	0.46
7	0.69	0.02	1.33	0.44
Totals	1.52	0.28	3.15	1.41

Results:

1. Total of 3.15% of ^{14}C activity was in runoff water.

2. Total of 1.41% of applied ^{14}C activity was found in runoff sediment.

Conclusions:

The amount of compound found in runoff water and sediment compresises less than 5% of applied ^{14}C.

K. Animal metabolism studies.

1. Metabolism and Balance Study of ^{14}C (ring) CGA-24705 in a lactating goat (Report #GAAC-74020).

Goats were administered ^{14}C-CGA-24705 capsules containing 4.7 ppm ai for 10 consecutive days.

Recovery of Radioactivity from Goats

	% of Total Dose Ingested
Urine	82.5
Feces	18.3
Milk	0.1
Blood	0.3
Tissue*	1.8
Rumen + Intest. wash	2.6
CO_2 + volatiles	0.0

Radioactive Residues in Goat Tissues

Tissue	ppm
Omental Fat	<0.006
Peripheral Fat	<0.006
Tenderloin	<0.004
Leg Muscle	<0.004
Heart	<0.004
Brain	<0.004
Kidney	0.033
Liver	0.073

Results:

1. 82.5%, 18.3%, and 1.8% of ^{14}C dose was found in urine, feces, and tissue; 0.3% and 0.1% found in blood and milk.

2. .033 ppm and .073 ppm ^{14}C-CGA-24705 were found in kidney and liver. All other tissues had less than .006 ppm

3. The aromatic ring was not cleaved, as shown by the fact no radioactivity was released in CO_2 or volatiles.

5. One unstable acidic major metabolite was found in urine. It was not identified.

2. Goat metabolism study with Δ ^{14}C-CGA-24705 and Δ ^{14}C-CGA-17020 (Report titled: September 17, 1974).

Results:

1. Exhaled $^{14}CO_2$ comprised .001-.002% of daily dose (measured over a 5-day period).

2. Exhaled volatile ^{14}C, measured over a 5-day period, was less than 0.01% of dose.

Conclusions:

1. Protocol by which data were obtained was not submitted. Registrant referred to "attached" protocols number 13001 and 199003 which were neither attached to this report nor found in other part of section D.

2. Meaning of the Δ (delta) as to position of label is unclear.

3. Metabolism and balance study of ^{14}C (ring) CGA-24705 corn biosynthesized metabolism in a goat (Report # GAAC-74046).

Greenhouse corn treated preemergence with 2 lb ai/A and grown 12 weeks was fed to goats at a rate of 0.033 ppm ^{14}C-CGA-24705 per day for 10 consecutive days.

Recovery of Radioactivity from Goats

	% of Total Dose Injected
Urine	36.6
Feces	44.2
Milk	0.1
Blood	0.0
Tissues	0.0
Rumen + Intestinal Wash	2.7
CO_2	<0.1
Volatile	0.0

Results:

1. 36.6% and 42.2% of total dose injected was found in urine and feces.
2. There was no volatile ^{14}C and less than 0.1% $^{14}CO_2$.
3. No detectable ^{14}C was found in fat, leg muscle, heart, brain, kidney, and liver.
4. TLC shows 11 metabolites.
5. Goat excreta metabolites were less polar than plant metabolites.

4. Distribution, degradation, and extretion of CGA-24705 in the rat (Report: Basle Project 1/74).

Rats were fed 3 mg/Kg randomly ring labelled ^{14}C-CGA-24705 by stomach tube for 9 days and then killed.

Excretion of Radioactivity by Rats

	% of Dose	
	Male	Female
Urine 0-216 hours	35	44
Feces 0-216 hours	63	51
Expired Air 0-96 hours	<0.01	<0.01
Tissue Residues	3.41	3.46

Tissue Residues

PPM

	Male	Female
Liver	0.126	0.181
Fat	0.014	0.021
Kidney	0.076	0.094
Muscle	0.013	0.013
Blood	0.111	1.504
Brain	0.032	0.042

Results:

1. 23-25% and 23-37% of ^{14}C were excreted in urine and feces respectively during first 24 hours.

2. TLC showed no detectable parent (CGA-24705) in urine or feces.

5. Metabolism of CGA-24705 in the rat (Basle project report # 7/74).

Rats were fed random ring labelled ^{14}C-CGA-24705 at a rate of 52 mg/kg. Length of feeding study was not specified.

Results:

1. Half of the radioactivity in the excreta was organic extractable.

2. Enzyme method indicated absence of glucuronide and sulfate esters.

3. CGA-24705 was not found in the urine or feces.

4. 36.6% and 47.1% of ^{14}C does were found in urine and feces.

5. Feces contained 6-10 metabolites. 13% of ^{14}C present was CGA-41632.

6. CGA-46129 and CGA-37735, 5% and 5.3% of urinary ^{14}C were only metabolites isolated from urine.

L. Residues in milk, meat, eggs, and poultry.

1. CGA-24705; Residues in milk, meat, eggs, and chickens - three-level studies (Report GAAC-74064).

Cows were fed 0, 0.2, 1.0, and 5.0 ppm ai incorporated into feed. Milk was analyzed at 7 time intervals between 0 and 28 days. Cows were sacrificed and tissue samples were taken at 14, 21, and 28 days.

Chickens were fed 0, 0.1, 0.5, and 2.0 ppm. Egg samples were analyzed, whites and yolks separately, at 6 time intervals. Animals were sacrificed at 7, 14, and 21 days and meat, liver, and fat tissues were analyzed.

Analysis was by total residue GLC/Mass Spec. method # REM 5/74.

Results:

1. Cows fed 5 ppm in all cases had less than 0.02 ppm residue in blood, kidney, liver, fat, and muscle. Milk contained less than 0.006 ppm.

2. Chickens fed 2.0 ppm had less than 0.015 ppm in eggs, meat and fat. Liver contained 0.003 ppm.

2. GCA-24705; Total residues in chicken tissues and eggs, 1974. (Report: Basle RVA 88/74.)

Chickens were fed 0.5 ppm and 2.0 ppm ai in feed. Tissue, egg white, and egg yolk samples were analyzed at intervals over a 28-day period.

Analysis was by GLC/MS total residue method REM 5/74.

Results:

1. There were no detectable residues (less than 0.015 ppm) in meat, fat, egg yolks, and egg whites of chickens fed 0.5 ppm and 2.0 ppm CGA 24705.

2. Chickens fed 0.5 ppm and 2.0 ppm CGA-24705 had 0.02 ppm and 0.03 ppm residue respectively in the liver.

M. Degradation Products.

1. CGA-37913
2[(2-ethyl-6-methylphenyl)amino] propanal

Corn

2. CGA-40172
N-(2-Hydroxyacetyl)-N-(1-Methoxypropane-2-YL)-2 Ethyl-6-Methylaniline

Corn
Photolysis
Basic Hydrolysis

3. CGA-37735
N-(2-Hydroxyacetyl)-2-Ethyl-6-Methylaniline

Rat Urine

4. CGA-41638

N-(2'-hydroxy-1'-methyl-ethyl)-2-ethyl-6-methyl-chloroacetanilide

Acid Hydrolysis
Rat Feces

5. CGA-24705 - Glutathione Conjugate.

   Leaf incubation of corn leaves in CGA-24705 solution.

6. CGA-41507
   N-(2-acetyl)-N-(1-methoxypropane-2 YL)-2 ethyl-6-methylaniline

   Corn, as a conjugate.

7. CGA-42446
   N-(2-acetyl)-N-(1-hydroxypropane-2 YL)-2 ethyl-6-methylanline

   Corn as a conjugate.

8. CGA-46129
   N-(1'-carboxyethyl)-2-ethyl-6-methyl-hydroxy acetanilide

   Rate Urine

9. CGA-13656
   N-choroacetyl 2-ethyl-6-methylanline

   Photolysis

10. CGA-40919
    4-(2-methyl-6-ethylphenyl)-5-methyl morphalin-3-ONE

    Photolysis
    Acid Hydrolysis

IV. CONCLUSIONS

1. Soil metabolism

   There were no significant differences in ^{14}C activity found under aerobic and anaerobic conditions at 90 days.

   Percentage of total ^{14}C that is extractable decreased with time, while percentage that is bound increased over 120 days.

2. Field persistence

Halflife of extractable residues ranged from 60-80 days.

3. Leaching - Parent compound

Compound leaches to considerable extent in sand, sandy loam, and loam. Leaches very little in silt loam and not at all in muck.

4. Leaching - Metabolites

Aged ^{14}C metabolites leached into lower layers of soil and were found in high concentrations in the leached water.

5. Photolysis

Photodegradation proceeded slowly in natural sunlight.

6. Microbial studies

CGA-24705 caused no reduction in number of type of fungi, bacteria, and actinomycetes found in soil.

7. Hydrolysis

Hydrolysis proceeds quickly at higher temperatures or very basic pH values. At 20°C, at pH 5, 7, 9, halflife is over 200 days. CGA would be stable to hydrolysis under normal environmental conditions.

8. Animal metabolism

Majority of compound is excreted through urine or feces. Trace amounts were found in expired air, milk, blood, fat, or tissues.

9. Plant metabolism

CGA-24705 is taken up and conjugated by plants. Pesticide residues are bound in corn plants after 16 weeks.

V. RECOMMENDATIONS

A. Object to experimental permit.

1. We cannot accept the two-year restriction for the tank mixture with atrqzine for the following reason.

Pesticide products and their metabolites whose phyto-toxicity or plant residue data indicate the necessity

6 month added Label SR 2/26/75

for rotational restrictions in excess of more than 2 normal potential plantings (18 months) should be considered prohibitatively persistent.

Environmental persistence of pesticide products frequently presents complex registration considerations because (1) the product must remain effective long enough to mitigate the target pest, while (2) soil residuals of the product, or its metabolites, must not produce phytotoxic effects on rotational plantings, and (3) soil persistence must not result in illegal residues in rotational food and fiber crops.

An important part of good agricultural practice is the maintenance of options for land use. Versatility of land use is optimal when there are no post-harvest restrictions, for this allows maximal flexibility in the timing of land preparation and choice of planting. When the effects of a pesticide treatment do not appear on any subsequent crop, rotational restrictions are not required. A rotational limitation of 12 months will restrict only a post-harvest fall planting and is considered to be consistent with good farm practices. Extending the rotational limitation to 18 months will restrict both a post-harvest fall planting and a following spring planting. This is considered to be the maximum planting restriction that is feasible.

The following criteria are required to assess soil persistence of pesticide products. They form the Standard to be routinely applied for evaluation prior to issuance of experimental use permits.

a. Laboratory soil metabolism studies are required to be carried out through first generation metabolites for a minimum time of 6 months. Major metabolite products must be identified or analytically defined. Laboratory and small plot tests are required to measure phytotoxicity of the product on normal rotational crops.

b. Phytotoxicity and degradation studies in several soil types are required. These should be conducted in small plots over a 12-month period of through three chemical halflives, whichever comes first.

If multiple applications are proposed, these studies should be conducted at maximum application rates and maximum numbers of treatments proposed on the label. Protocols for these studies will be described in the Appendix to the Guidelines for Registering Pesticides in the United States.

c. Pesticide products that degrade rapidly usually do not induce residues or phytotoxicity in crops normally planted in rotation after the harvest of a treated crop. These products usually have a halflife of less than 2 months. Specific rotational restrictions will not be required.

d. Residue and phytotoxicity data on rotational crops will be required for pesticides have halflife values in soil from 2 to 6 months. The rotational crop selected for residue analysis should be grown on the lightest textured soil which, in the degradation studies (See 2 above), is shown to have a halflife greater than 2 months, and wherein the pesticide has been allowed to weather for the normal period between harvest of the crop for which a tolerance is requested and planting time for the rotational crop. Chemical residue determinations must include feed and forage portions of the mature crop. Data concerning germination, stand, vigor, and yield on the rotational crop should be submitted for phytotoxicity assessment.

e. More persistent pesticide products or their metabolites having halflife values greater than 6 months will require plant residue analyses and phytotoxicity assessments on two additional rotational crops.

f. Pesticide products and their metabolites whose phytotoxicity or plant residue data indicate the necessity for rotational restrictions in excess of more than 2 normal potential plantings (18 months) should be considered prohibitatively persistent.

B. The rotational crop restriction for CGA-24705 will have to be changed to 18 months in lieu of rotational crop data supporting the 12-month restriction on the label.

1. The following will be required at the time of permanent registration and/or future permits.

ROTATIONAL AND/OR SUBSEQUENT CROP RESIDUE STUDIES

(Radiolabel study)

a. 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.

b. 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.

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

d. 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.

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

f. If the agricultural practice is such that a treated crops 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.

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

i. Sample calculations;

ii. Counting efficiency;

iii. Counting time;

iv. Background levels;

v. Probable error with scintillation techniques.

C. The following comments are on an R L basis. This data will be needed at the time of permanent registration along with all other environmental chemistry data.

1. Soil characteristics (CEC, pH, % sand, silt, clay, O.M.) are needed for reports AG-2973, AG-3105 and AG-3133.

A fish accumulation study on catfish.

a. A sandy loam is to be treated in a way that catfish would be exposed to 0.01 ppm and 1.0 ppm. The labeled pesticide is to be aged in soil under aerobic conditions for 30 days prior to fish exposure. If a rice use is anticipated then the labeled pesticide should be aged in the soil under water for 30 days prior to fish exposure.

b. Catfish are to be exposed to treated soil for 30 days. If a plateau level has not been reached then exposure should be extended for an additional 30 days.

c. The rate of residue dissipation is to be determined by placing the catfish in a pesticide-free environment at the end of exposure time.

d. Residue determination of edible tissue are needed throughout the study. When a plateau level is reached or at an interval of high residues in the edible tissues, determination for polar and nonpolar extractable residues are needed along with determination of unextractable residues. Determination for residues in viscera should be made at several intervals to correspond with other sampling intervals.

e. Accumulation factors should be recorded.

f. Determination for amounts of residues present in water and in soil should be made and sampled along with catfish samples.

g. In some cases identification of residues in fish tissues will be needed.

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11/27/74

3/5/75

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