

METABOLISM DEPARTMENT
AGRICULTURAL DIVISION
CIBA-GEIGY CORPORATION
VERO BEACH, FLORIDA

CGA 48'988

BIOLOGICAL REPORT FOR THE METABOLISM OF
¹⁴C-METALAXYL IN LAYING HENS

M88-409-001A

Project No.: 409925

Report No.: BIOL-89005

Biological Coordinator:

Title: Senior Group Leader
Biological Studies

Signature:

Date: 1/8/90

Submitted By:

TEST INITIATION: 1/16/89

TEST COMPLETION: 1/19/89

TEST SUBSTANCE: ϕ -¹⁴C-Metalaxyl
GSO Number: CL-XVIII-27
Purity: Radiochemical 97.7% Chemical 96.5%
Specific Activity: 37.7 μ Ci/mg

OBJECTIVES

This study was conducted to support the reregistration of metalaxyl (CGA-48988). Five laying hens each received a daily dose of ϕ -¹⁴C-metalaxyl for four consecutive days and were sacrificed six hours after the final dose. Samples of eggs, excreta, blood and selected tissues were taken for analysis to determine the amount and nature of the metabolism of metalaxyl.

SUMMARY

Five Leghorn hens [#3 Hen (1), #32 Hen (2), #25 Hen (3), #22 Hen (4), and #6 Hen (5)] each received a daily dose of 10.0 mg of ϕ - ^{14}C -metalaxyl orally by gelatin capsule for four consecutive days.

During the test, all hens remained in good health and egg productions were normal (75-100%) except for Hen #6 which dropped 44% in feed consumption and 10% in body weight. All other hens remained relatively stable in feed consumption and body weight. During the necropsy Hen #6 appeared normal but because of her significant drop in feed and body weight, her health status is questionable. Hen #6's drop in feed began during the acclimation period; therefore, her health status does not appear to be compound related.

All requested samples were taken as scheduled and have been shipped and received in acceptable condition at CIBA-GEIGY Corporation in Greensboro, North Carolina. The sample analyses will be covered in a separate analytical report.

This study was conducted according to the January 4, 1989 Protocol 158-88. The original data of this study is contained in the Vero Beach Notebook #3166, pp. 1-96.

EXPERIMENTAL: Treated Hen Data #3 (1), #32 (2), and #25 (3)
Project No. 409925

Compound: ¹⁴ C-Metalaxyl	Chicken(s): Hen 3 (1) Hen 32 (2) Hen 25 (3)	Age(s): 66 wks.	Body Weights (kg): Initial Final Avg. Hen 3 1.72 1.75 1.74 Hen 32 1.53 1.59 1.56 Hen 25 1.57 1.55 1.56	Avg. Egg Production: Accli- Test mation Period Hen 3 86% 100% Hen 32 100% 100% Hen 25 86% 75%
C-G Representative: 5.1.2.e Woo	Location: VBRC Vero Beach, FL	Bioch. Protocol: 158-88 Amendment(s)	Acclimation: 7 days 1/9-16/89	Dosing: 4 days 1/16-19/89
Dose: 10 mg ¹⁴ C-Metalaxyl/ hen/day 377 μ Ci/hen/day	mg/kg Body Wt.: Hen 3 5.75 mg Hen 32 6.41 mg Hen 25 6.41 mg	Avg. Feed Consumption During Test Period: Hen 3 126 g/day Hen 32 118 g/day Hen 25 96 g/day	Feed Level Equivalence: Hen 3 79 ppm ¹⁴ C-Metalaxyl Hen 32 85 ppm ¹⁴ C-Metalaxyl Hen 25 104 ppm ¹⁴ C-Metalaxyl	
Sacrifice: 5.97-6.22 hrs. after the fourth dose Date: 1/19/89	Items Sampled/Shipped Frozen: Excreta Lean Meat Skin + Fat Gizzard	Items Sampled/Shipped Refrigerated: Blood Egg Yolks Egg Whites		

Summary of Results:

	Hen #3 (1)		Hen #32 (2)		Hen #25 (3)	
	Acclimation	Test Period	Acclimation	Test Period	Acclimation	Test Period
Avg. Water Intake	224 ml/day	197 ml/day	211 ml/day	210 ml/day	182 ml/day	163 ml/day
Avg. Feed Intake	127 g/day	126 g/day	121 g/day	118 g/day	117 g/day	96 g/day
Avg. Egg Production	86%	100%	100%	100%	86%	75%
Avg. Excreta Production	171 g/day	142 g/day	121 g/day	121 g/day	128 g/day	111 g/day

Daily values are tabulated on page 7.
Animal(s) Health: All hens remained healthy throughout the study.
Necropsy report given on page 9.
Experimental continued on page 4.

EXPERIMENTAL: Treated Hen Data #22 (4) and #6 (5)
(Continued) Project No. 409925

Compound: ¹⁴ C-Metalaxyl	Chicken(s): Hen 22 (4) Hen 6 (5)	Age(s): 66 wks.	Body Weights (kg): Initial Final Avg. Hen 22 1.63 1.62 1.63 Hen 6 1.47 1.32 1.40	Avg. Egg Production: Acclimation Test Hen 22 86% 100% Hen 6 100% 75%
Specific Activity: 37.7 μ Ci/mg				
C-G Representative: 5.1.2e Woo	Location: VBRC Vero Beach, FL	Bioch. Protocol: 158-88 Amendment(s)	Acclimation: 7 days 1/9-16/89	Dosing: 4 days 1/16-19/89
Dose: 10 mg ¹⁴ C-Metalaxyl/ hen/day 377 μ Ci/hen/day	mg/kg Body Wt.: Hen 22 6.13 mg Hen 6 7.14 mg	Avg. Feed Consumption During Test Period Hen 22 133 g/day Hen 6 63 g/day	Feed Level Equivalence: Hen 22 75 ppm ¹⁴ C-Metalaxyl Hen 6 159 ppm ¹⁴ C-Metalaxyl	
Sacrifice: 6.33-6.45 hrs. after the fourth dose Date: 1/19/89	Items Sampled/Shipped Frozen: Gizzard Excreta Lean Meat Skin + Fat	Items Sampled/Shipped Refrigerated: Blood Egg Yolks Egg Whites		

Summary of Results:

	Hen #22 (4)	Hen #6 (5)
Avg. Water Intake	237 ml/day	200 ml/day
Avg. Feed Intake	139 g/day	63 g/day
Avg. Egg Production	86%	75%
Avg. Excreta Production	163 g/day	98 g/day

Daily values are tabulated on page 8.
Animal(s) Health: Both hens #22 and #6 remained healthy throughout the study.
Necropsy report given on page 9.

COMMENTS

1. The tables in this report include:
 - a. Table 1, "Production of Excreta and Eggs, Daily Water and Feed Consumption, and Body Weights," pps. 7 and 8.
 - b. Chicken Necropsy Report, p. 9.
2. Test Animals
The white Leghorn (H and N) hens used in the study were purchased from Anthony Farms, 2520 Banana Road, Lakeland, Florida 33809 on 8/31/88. The birds were approximately 66 weeks of age when the study began on 1/16/89.
3. Deviations from the protocol include:
 - a. The hens were significantly older than 40 weeks.
 - b. Predose samples were collected earlier than scheduled to avoid collecting on the weekend.
 - c. Commercial bottled drinking water was used, not well water.
 - d. The stability capsule was shipped along with the A shipment, not within two days of the last dose.
4. Temperature ranged from 69-73°F and relative humidity between 54-65% during the test period.
5. The interval between the final treated dose and sacrifice was 5.97-6.45 hours. The birds were sacrificed by cervical dislocation.
6. The birds were maintained on a 24-hour continuous lighting regime for the duration of the study.
7. Hen #6 did not lay a Day 3 egg. Day 4 eggs were excised from Hens #3 and #32. Hen #25 did not have a Day-4 egg. Hen #22 laid her Day-3 egg within the Day-2 dose period.
8. Hens #3, #32, #25, #22, and #6 represent Hens 1, 2, 3, 4, and 5, respectively, as described in the protocol.

COMMENTS (Continued)

9. All hens were housed in plastic coated wire cages.
10. On dose Day 4, the hens were sacrificed approximately six hours after the fourth dose; therefore, Day 4 feed and water consumption and excreta production were excluded from the averaged data.
11. Calculation for feed level equivalency:

$$\frac{\text{mg compound/day} + \text{avg. daily feed consumption (gms)} \times 1000}{1000} = \text{equivalent ppm of feed}$$

Dit document is geen eigendom van het CtgB en wordt beschikbaar gemaakt vallen onder de wetten op grond waarvan auteursrechten en/of auteursrechten in derde rusten, waaronder intellectuele eigendomsrechten, of de inhoud hiervan zonder de toestemming van de rechthebbende. Op dit document worden geen rechten van auteursrechten en/of auteursrechten in derde rusten, waaronder intellectuele eigendomsrechten, of de inhoud hiervan zonder de toestemming van de rechthebbende.

The document is not the property of the CtgB and only provided based on mandatory freedom of information requirements. rights of third parties. Furthermore, this document may be subject to intellectual property and copy regime. Consequently, any publication, distribution, reproduction and/or publishing and any commercial exploitation and use of this document or its contents without the permission of the owner of this document may therefore be prohibited and violate the right of its owner.

TABLE 1 (Continued)
Production of Excreta and Eggs, Daily Water and Feed Consumption, and Body Weights

Project: 409925

Date	Schedule	Water (ml)		Feed (g)		Excreta (g)		Egg Production	
		22 ¹	6 ²	22	6	22	6	22	6
1/9-10	Accl.	310	250	128	128	165	151	+	+
1/10-11	Accl.	240	220	136	137	153	136	+	+
1/11-12	Accl.	220	140	136	129	181	136	+	+
1/12-13	Accl.	230	140	146	109	168	102	o	+
1/13-14	Accl.	220	160	144	94	147	88	+	+
1/14-15	Accl.	220	170	143	111	157	112	+	+
1/15-16	Accl.	220	150	141	74	169	99	+	+
Average		237	176	139	112	163	118	86%	100%
1/16-17	Day	240	150	139	76	159	71	+	+
1/17-18	Day	220	230	134	72	132	104	+	+
1/18-19	Day	210	220	127	41	154	118	+	o
1/19/89	Day	60	40	45	10	53	30	+	+
*Average		223	200	133	63	148	98	100%	75%

Initial Body Weights: 22 = 1.63 kg; 6 = 1.47 kg

Final Body Weights: 22 = 1.62 kg; 6 = 1.32 kg

22¹ = Treated Hen (4); 6² = Treated hen (5)

*Only 3 out of the 4 test days were averaged because of the short time span between Day 4 dosing and sacrifice, except for egg production.

ADDENDUM 1

BIOCHEMISTRY DEPARTMENT
AGRICULTURAL DIVISION
CIBA-GEIGY CORPORATION
VERO BEACH, FLORIDA

CHICKEN NECROPSY REPORT

Biochem. Protocol No.: 158-88
Project No.: 409925
Experiment No.: M88-409-001A
Compound: ¹⁴C-Metalaxyl

<u>Date of Sacrifice</u>	<u>Test Day</u>	<u>Bird No.</u>	<u>Treatment mg/day</u>	<u>Necropsy Findings</u>
1/19/89	4	3	10 mg/day	Normal - 1 inch cyst in right vestigial oviduct..
	4	32	10 mg/day	Normal - 2.5 inch cyst in right vestigial oviduct.
	4	25	10 mg/day	Normal - 1.5 inch cyst in right vestigial oviduct.
	4	22	10 mg/day	Normal - 1.5 inch cyst in right vestigial oviduct.
	4	6	10 mg/day	Normal - 1.5 inch cyst in right vestigial oviduct.

The occurrence of these cysts in older, high egg producing hens are very common.

Necropsy performed by 5.1.2.e Woo.