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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

PC 128831

DATA EVALUATION RECORD

CYFLUTHRIN

Study Type: §83-2(b) Oncogenicity Study in Mice

Work Assignment No. 2-01-73B (MRID 44589701)

Prepared for
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CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

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DATA EVALUATION RECORD

STUDY TYPE: Oncogenicity Study in Mice
OPPTS Number: 870.4200 OPP Guideline Number: §83-2b

DP BARCODE: D243160 SUBMISSION CODE: S528018
P.C. CODE: 128831 TOX. CHEM. NO.: 266E

TEST MATERIAL (PURITY): Cyfluthrin technical (≥93.9% a.i.)

SYNONYMS: Cyano(4-fluoro-3-phenoxyphenyl)methyl-3-(2,2-dichloroethenyl)-2,2-dimethyl-cyclopropanecarboxylate

CITATION: Wahle, B.S. and Christenson, W.R., (1998). Technical Grade Cyfluthrin: An Oncogenicity Testing Study in the Mouse. Bayer Corporation Agricultural Division Toxicology, Stilwell, KS. Laboratory Report No. 95-271-DR, May 28, 1998. MRID 44589701. Unpublished.

Wahle, B.S. and Christenson, W.R. (2000) Supplemental Submission to Bayer Report No. 108041 (EPA MRID No. 44589701) Study Title: Technical Grade Cyfluthrin An Oncogenicity Testing Study in the Mouse.Bayer Corporation Agricultural Division Toxicology, Stilwell, KS. Laboratory Report No. 108041-1, September 6, 2000. MRID 45228101. Unpublished.

SPONSOR: Bayer Corporation Agricultural Division, Kansas City, MO

EXECUTIVE SUMMARY: In a mouse oncogenicity study (MRID 44589701), cyfluthrin (≥93.9% a.i., Lot/Batch # 4030059/BF9340-71) was administered in the diet to CD-1 mice (50/sex/group) for up to 80 weeks at 0, 200, 750, or 1400/1600 ppm (equivalent to 0/0, 31.9/38.4, 114.8/140.6, and 232.7/309.7 mg/kg/day [M/F], respectively). The high-doses were chosen based on the results of a 6-week range-finding study, and are the estimated maximum tolerated doses for each sex for a lifetime study in the mouse. Mortality, food efficiency, hematology, and organ weights for both sexes at all doses were unaffected by treatment with cyfluthrin. There were no observations of toxicological concern in either sex at 200 ppm or in the females at 750 ppm.

At 750 ppm, a toxic effect on the ears was observed and considered to be treatment-related based on macroscopic and microscopic pathology findings. Macroscopic findings included crusty zone

of the skin of the ear in the males (11/50 treated vs 5/50 controls). Microscopic findings involving the skin of the ear in the males included: acanthosis (16/50 treated vs 9/50 controls); chronic active inflammation (11/50 treated vs 4/50 controls); inflammation, all types (13/50 treated vs 6/50 controls); ulcer (12/50 treated vs 5/50 controls); and debris (13/50 treated vs 4/50 controls, $p \leq 0.05$). Monthly body weight gain was reduced ($p \leq 0.05$) at the first month in the males (↓21%), but not for the overall study.

At 1400/1600 ppm [M/F], a toxic effect on the ears was also observed and considered to be treatment-related based on clinical signs and macroscopic and microscopic findings. The following were increased ($p \leq 0.05$) in the females at clinical examination: ear lesion redness (5/50 treated vs 0/50 controls) and ear lesion scab (22/50 treated vs 2/50 controls). Related gross necropsy findings included crusty zone of the skin of the ear in the males (12/50 treated vs 5/50 controls) and females (13/50 treated vs 1/50 controls, $p \leq 0.05$). Related microscopic findings ($p \leq 0.05$ or not significant) observed in the skin of the ear both sexes, including: acanthosis (16-17/50 treated vs 2-9/50 controls); chronic active inflammation (8-10/50 treated vs 1-4/50 controls); inflammation, all types (9-16/50 treated vs 1-6/50 controls); ulcer (5-11/50 treated vs 1-5/50 controls); and debris (8-11/50 treated vs 2-4/50 controls).

In addition, at clinical examination, an increased ($p \leq 0.05$) incidence of rough coat was observed in the males (30/50 treated vs 9/50 controls) and females (20/50 treated vs 9/50 controls) and hunched back was observed in the females (5/50 treated vs 0/50 controls). Additional gross necropsy findings included rough coat in the males (22/50 treated vs 7/50 controls, $p \leq 0.05$) and females (16/50 treated vs 8/50 controls, p=not significant) and wet/stained ventrum in the males (7/50 treated vs 0/50 controls). Reductions ($p \leq 0.05$) in mean body weight were observed in the males and females (↓7-20%) throughout the study. Monthly body weight gain was reduced ($p \leq 0.05$) for the first month in the males and females (↓60-69%) as compared to controls. Overall body weight gain, as calculated by the reviewers, was decreased in the males (↓25%) and females (↓54%). Mean absolute food consumption was decreased in the females (↓6-25%) throughout the study.

The LOAEL is 750 ppm for males (equivalent to 114.8 mg/kg/day) based on macroscopic and microscopic ear skin lesions and reduced body weight gains, and 1600 ppm in the females (equivalent to 309.7 mg/kg/day) based on clinical signs, macroscopic and microscopic pathology findings, and reduced body weights, body weight gains, and food consumption. The NOAEL for males is 200 ppm (equivalent to 31.9 mg/kg/day). The NOAEL for females is 750 ppm (equivalent to 140.6 mg/kg/day).

Under the conditions of this study, there was no evidence of carcinogenic potential.

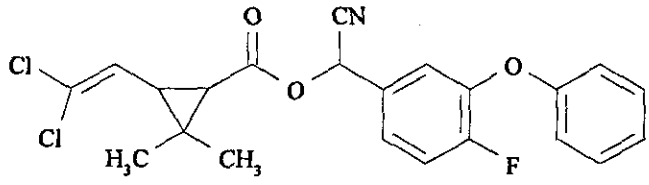
The submitted study is classified as **acceptable (§83-2b)** and does satisfy the guideline requirements for a carcinogenicity study in mice.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Cyfluthrin
   Description: brown viscous liquid
   Lot/Batch #: 4030059/BF9340-71
   Purity (w/w): ≥93.9% a.i.
   Stability of compound: The test substance was stable in the diet for up to 14 days stored at room temperature and up to 28 days frozen.
   CAS #: 68359-37-5
   Structure:



2. Vehicle: Corn oil

3. Test animals: Species: Mouse
   Strain: CD-1
   Age and mean weight at start of dosing: Approximately 8 weeks old; 28.2-29.2 g (males), 23.9-24.6 g (females)
   Source: Charles River Research Laboratories, Inc., Portage, MI
   Housing: Individually in stainless steel wire mesh cages
   Diet: Rodent Lab Chow 5001-4 in "etts" form (Purina Mills), ad libitum
   Water: Tap water, ad libitum
   Environmental conditions:
   Temperature: 18-26°C
   Humidity: 40-70%
   Air changes: Not provided
   Photoperiod: 12 hours light/12 hours dark
   Acclimation period: Approximately 1 week

B. STUDY DESIGN:

1. In life dates: start: 11/15/95 end: 05/23/97

2. Animal assignment: The mice were randomly assigned (stratified by weight) to the test groups shown in Table 1.

Table 1. Study design [a]

Test Group	Dietary Concentration (ppm)	Mean Achieved Dose (mg/kg/day) [M/F][c]	Number of Animals	
			Males	Females
Control	0	0/0	50	50
Low	200	31.9/38.4	50	50
Mid	750	114.8/140.6	50	50
High	1400/1600 [b]	232.7/309.7	50	50

a Data obtained from the study report, page 15.
b High-dose males/females
c Achieved doses obtained from the study report, page 20.

3. Dose selection rationale - The doses chosen for the current study were based on the results of a 2-year oncogenicity study and a 6 week range-finding study in the CD-1 mouse. In the oncogenicity study, no endpoints were clearly affected by cyfluthrin at any dose tested. No doses were reported for the oncogenicity study. In the 6 week range-finding study, body weight was reduced (↓3.4-9.3%) at 1200, 1600, and 2000 ppm in the males and females. Additionally, increased mortality was observed at 2000 ppm. Based on the results of these studies, the doses presented in Table 1 were selected for the subsequent oncogenicity study. The high-doses are the estimated maximum tolerated doses for each sex for a lifetime study in the mouse.

4. Dose preparation, administration, and analysis - All test diets were prepared weekly using an acetone/corn oil mixture to dissolve the test substance prior to mixing with the diet and stored at freezer conditions; no further information was provided. Homogeneity (top, middle, bottom) was determined for 25 and 2000 ppm samples (3 samples each). Stability was determined for 25 and 2000 ppm dose formulations after storage at room and freezer temperatures for 14 and 28 days, respectively. Concentration analyses were performed on samples collected during weeks 1, 14, 27, 40, 53, 66, and 79 from each dose level.

   Results:
   Homogeneity (coefficient of variation): 3-8%
   Stability (range as mean % of nominal):
   111.7-112%; stored at room temperature for up to 14 days
   123.2-125.5%; stored frozen for up to 28 days
   Concentration (range as mean % of nominal): 95.8-115%
   The analytical data indicated that the mixing procedure was adequate and that the variation between nominal and actual dosage to the study animals was acceptable.

5. Statistics - All data were analyzed for homogeneity of variance using Bartlett's test. Data with homogeneous variances were further analyzed using analysis of variance followed by

a Dunnett's test if a significant F-value was observed. In the event of unequal variances, data were analyzed using the Kruskal-Wallis ANOVA followed by the Mann-Whitney U test. Additionally, necropsy and micropathology data were evaluated using a Chi-Square test followed by a one-tailed Fisher's Exact Test.

C. METHODS:

1. Observations - Observations for moribundity and mortality were performed twice daily (once daily on weekends and holidays). Detailed clinical observations were recorded weekly.

2. Body weight - All animals were weighed weekly and at scheduled termination.

3. Food consumption and efficiency - Food consumption (g/mouse/day) was determined weekly. No formula for the calculation of food efficiency was reported.

4. Water consumption - Water consumption was not measured.

5. Ophthalmoscopic examination - Ophthalmoscopic examinations were not performed.

6. Blood analyses - At approximately 12 and 18 months, blood was collected via the orbital sinus from 10 non-fasted animals/sex/dose and a blood smear was prepared. In addition, the checked (X) parameters below were examined at both intervals:

   a. Hematology:

X	Hematocrit (HCT)	X	Leukocyte differential count
X	Hemoglobin (HGB)	X	Mean corpuscular HGB (MCH)
X	Leukocyte count (WBC)	X	Mean corpusc. HGB conc.(MCHC)
	Corrected leukocyte count (Cor WBC)	X	Mean corpusc. volume (MCV)
X	Erythrocyte count (RBC)	X	Reticulocyte count
X	Platelet count	X	Cell morphology
	Blood clotting measurements		
	(Prothrombin time)		
	(Activated partial thromboplastin time)		

7. Sacrifice and Pathology - At study termination, all surviving animals were sacrificed by CO_2 asphyxiation and subjected to a gross pathological examination. The following checked (X) tissues were collected from all animals sacrificed at scheduled termination, animals that died prematurely, and animals sacrificed in extremis. All tissues (except the vagina, and the Zymbal, exorbital/lacrimal, clitoral, and preputial glands) were examined microscopically. Additionally, the (XX) organs were weighed.

	DIGESTIVE SYSTEM		CARDIOVASC./HEMAT.		NEUROLOGIC
	Tongue	X	Aorta	XX	Brain
X	Salivary glands	XX	Heart	X	Periph. nerve
X	Esophagus	X	Bone marrow	X	Spinal cord (3 levels)
X	Stomach	X	Lymph nodes	X	Pituitary
X	Duodenum	XX	Spleen	X	Eyes with optic nerve
X	Jejunum	X	Thymus		
X	Ileum				GLANDULAR
X	Cecum		UROGENITAL	XX	Adrenal gland
X	Colon	XX	Kidneys	X	Lacrimal gland
X	Rectum	X	Urinary bladder	X	Mammary gland
XX	Liver	XX	Testes	X	Parathyroids
X	Pancreas	X	Epididymides	X	Thyroids
X	Gall bladder	X	Prostate		
		X	Seminal vesicle		OTHER
	RESPIRATORY	XX	Ovaries	X	Bone with joint
X	Trachea	X	Uterus	X	Skeletal muscle
XX	Lung	X	Vagina	X	Skin
	Nose	X	Cervix	X	All gross lesions and masses
	Pharynx	X	Clitoral gland	X	Preputial gland
X	Larynx			X	Harderian gland
				X	Zymbal gland

II. RESULTS

A. Observations:

1. Clinical signs - An increased ($p \leq 0.05$) incidence of rough coat was observed in the high-dose males (30/50 treated vs 9/50 controls) and females (20/50 treated vs 9/50 controls) (Table 2). An increased ($p \leq 0.05$) incidence of rough coat was also observed in 200 ppm males (18/50 treated), but the effect was not dose-dependent and therefore considered to be not of toxicological concern. In addition, the clinical signs were increased ($p \leq 0.05$) in the high-dose females: hunched back (5/50 treated vs 0/50 controls); ear lesion redness (5/50 treated vs 0/50 controls); and ear lesion scab (22/50 treated vs 2/50 controls). A decreased ($p \leq 0.05$) incidence of neuromuscular seizures was observed in the high-dose males (11/50 treated vs 24/50 controls), 750 ppm males (13/50 treated), and high-dose females (1/50 treated vs 11/50 controls). This observation is considered to be not of toxicological concern. No treatment-related clinical signs were observed at the 750 or 200 ppm dose levels.

Table 2. Selected clinical signs in mice fed cyfluthrin for up to 80 weeks.[a]

Clinical sign	Dietary levels (ppm)			
	0	200	750	1400/1600
Males				
Rough coat	9	18*	16	30*
Neuromuscular seizures	24	21	13*	11*
Females				
Rough coat	9	5	7	20*
Hunched back	0	3	0	5*
Red ear lesion	0	2	1	5*
Ear lesion scab	2	7	7	22*
Neuromuscular seizures	11	9	5	1*

a. These data were obtained from page 20 of the study report. N=50.
* Significantly different from controls at $p \leq 0.05$.

2. Mortality - No differences in survival relative to concurrent controls were observed in either sex of any treated group at any time during the study. Percentage survival in all dose groups of mice at 80 weeks was approximately 78-90%.

B. Body weight - Reductions ($p \leq 0.05$) in mean body weight were observed in the high-dose males (↓7-12%) and females (↓8-20%) throughout the study (Table 3). Minor decreases ($p \leq 0.05$) in body weights that were considered to be not of toxicological concern were also observed in the 750 ppm males (↓4-6%) and females (↓4-9%), and 200 ppm females (↓4-7%).

Monthly body weight gain was reduced ($p \leq 0.05$) during the first month in the mid- and high-dose males (↓21 and 60%, respectively) and high-dose females (↓69%) compared to controls. Differences were observed in subsequent periods, but these were considered to be minor and not of toxicological concern. Overall (weeks 1-77) body weight gain, as calculated by the reviewers, was decreased in the high-dose males (↓25%) and females (↓54%) and mid-dose females (↓20%).

Table 3. Mean body weights (g) and body weight gains (g) at selected intervals in mice fed cyfluthrin for up to 80 weeks.[a]

Week	Dietary levels (ppm)			
	0	200	750	1400/1600
Males				
1	29.2	29.1	28.4	28.2
2	30.7	30.6	29.0*(↓6)	26.9*(↓12)
26	39.2	38.8	37.3*(↓5)	36.1*(↓8)
52	41.1	40.5	38.7*(↓6)	37.4*(↓9)
68	41.0	40.5	39.6	38.0*(↓7)
77	40.5	40.0	38.8*(↓4)	36.7*(↓9)
Month 1 body weight gain (g/month)	4.8	4.4	3.8*(↓21)	1.9*(↓60)
Overall (weeks 1-77) body weight gain	11.3	10.9	10.4	8.5(↓25)
Females				
1	24.6	23.9	24.4	24.3
4	27.7	27.2	26.6*(↓4)	24.4*(↓12)
8	28.9	29.0	28.4	26.5*(↓8)
21	33.3	31.9*(↓4)	31.7*(↓5)	28.9*(↓13)
50	37.7	35.1*(↓7)	34.5*(↓8)	31.3*(↓17)
65	37.6	35.0*(↓7)	34.2*(↓9)	30.6*(↓19)
77	37.8	35.7*(↓6)	34.9*(↓8)	30.4*(↓20)
Month 1 body weight gain (g/month)	3.5	3.8	2.9	1.1*(↓69)
Overall (weeks 1-77) body weight gain	13.2	11.8	10.5(↓20)	6.1(↓54)

a. Data were obtained from the study report, Table BW-MEAN, pages 45 through 80. Numbers listed parenthetically represent the percent difference from controls. Overall body weight gain data were calculated by the reviewers from data contained in this table.

* Significantly different from controls at $p \leq 0.05$.

C. Food consumption and efficiency: Mean absolute food consumption was decreased in the mid- and high-dose females (↓7-10% and ↓6-25%, respectively; $p \leq 0.05$) compared to controls throughout the study (Table 4). Relative (to body weight) food consumption was decreased ($p \leq 0.05$) at weeks 2, 4, 10, and/or 11 in the mid- (↓9-10%) and high-dose (↓9-24%) females, then increased (↑9-15% and 8-19%, respectively; $p \leq 0.05$) at sporadic intervals thereafter. The decrease in food consumption at 750 ppm is minor and not of toxicological concern. There were no differences of toxicological concern in food consumption in the

males. Mean absolute food consumption was decreased in the mid-dose males (↓5-11%, p≤0.05), but was variable in the high-dose males (↓15-↑9%) at sporadic intervals throughout the study. Relative food consumption was increased throughout the study in the high-dose males (↑7-20%).

No food efficiency data were provided. It was stated that food efficiency was unaffected by treatment.

Table 4. Mean food consumption (g/mouse/day) at selected intervals in female mice fed cyfluthrin for up to 80 weeks.[a]

Week	Dietary levels (ppm)			
	0	200	750	1600
2	7.80	7.38	7.16*(↓8)	5.87*(↓25)
37	6.21	5.86	5.85	5.81*(↓9)
61	6.00	5.70	5.57*(↓7)	5.23*(↓13)
78	6.28	5.73*(↓9)	5.65*(↓10)	5.61*(↓11)

a Numbers listed parenthetically represent the percent difference from controls. Data were obtained from the study report, Table FC-MEAN, pages 108 through 126.

* Significantly different from controls at p≤0.05.

E. Hematology - No treatment-related differences from concurrent controls were observed in the blood smears obtained at day 348 or 537. Decreases (↓40-42%; p≤0.05) in white cell counts were observed in the 200 and 750 ppm females at day 537; these findings were not dose-dependent and therefore considered to be not of toxicological concern. Differences (↓3-9%, p≤0.05) in other parameters, including MCH, MCHC, and Heinz bodies, were observed in the males and females, but were minor and/or not dose-dependent.

G. Sacrifice and pathology:

1. Organ weights - No treatment-related differences were observed in organ weights. The observed differences (p≤0.05) from controls were attributed to reduced body weights and were considered to be not of toxicological concern because they were minor, not dose-dependent, and/or lacked corroborating microscopic or macroscopic pathology data as evidence of toxicity. The following decreases in absolute weights were noted: in the 200 ppm females - absolute liver (↓9%) and spleen (↓26%) weights; in the 1600 ppm females, absolute brain (↓3%), heart (↓15%), liver (↓11%), and spleen (↓38%) weights; in the 1400 ppm males, absolute spleen weights (↓27%). Relative (to body) organ weights were increased as follows: in the 200 ppm females, relative brain weights (↑7%); in the 750 ppm females, relative brain (↑10%), kidney (↑3%), and lung (↑8%) weights; in the 1600

ppm females, relative brain (↑19%), kidney (↑7%), liver (↑10%), lung (↑8%) and ovaries (↓16%) weights; in the 750 ppm males, relative heart (↑8%) and testes (↑11) weights; and in the 1400 ppm males, relative brain (↑8%), heart (↑10%), kidneys (↑7%), liver (↑4%), and testes (↑11%) weights.

2. Gross pathology - Treatment-related gross pathology findings included the following: rough coat in the high-dose males (22/50 treated vs 7/50 controls, p≤0.05) and females (16/50 treated vs 8/50 controls, p=not significant); crusty zone of the skin of the ear in the 750 ppm males (11/50 treated vs 5/50 controls) and high-dose males (12/50 treated) and females (13/50 treated vs 1/50 controls, p≤0.05); and wet/stained ventrum in the high-dose males (7/50 treated vs 0/50 controls) (Table 5).

Table 5. Incidence (# of animals) of selected macroscopic lesions in mice dosed with cyfluthrin for up to 80 weeks. [a]

Observation	Dietary Level (ppm)			
	0	200	750	1400/1600
Males				
Rough coat	7	12	13	22*
Ear skin, crusty	5	8	11	12
Ventrum, wet/stained	0	1	2	7*
Females				
Rough coat	8	6	7	16
Ear skin, crusty	1	6	2	13*

a Data were obtained from Table GP1-SUM of the study report, pages 201, 211, 228, and 238; n=50
* Significantly different from controls at p≤0.05.

3. Microscopic pathology:

a) Non-neoplastic: Treatment-related findings were limited to lesions involving the skin of the ear (Table 6). These lesions (p = not significant unless stated) included the following: acanthosis in the 750 ppm males (16/50 treated vs 9/50 controls) and high-dose males (17/50 treated) and females (16/50 treated vs 2/50 controls, p≤0.05); chronic active inflammation in the 750 ppm males (11/50 treated vs 4/50 controls) and high-dose males (10/50 treated) and females (8/50 treated vs 1/50 controls, p≤0.05); inflammation, all types in the 750 ppm males (13/50 treated vs 6/50 controls) and high-dose males (16/50 treated, p≤0.05) and females (9/50 treated vs 1/50 controls, p≤0.05); ulcer in the 750 ppm males (12/50 treated vs 5/50 controls) and high-dose males (11/50 treated) and females (5/50 treated vs 1/50 controls); and debris in the 750 ppm males (13/50 treated vs 4/50 controls, p≤0.05) and high-dose males (11/50

treated) and females (8/50 treated vs 2/50 controls).

Table 6. Incidence (# of animals) of selected microscopic ear skin lesions in mice dosed with cyfluthrin for up to 80 weeks. [a]

Observation	Dietary Level (ppm)			
	0	200	750	1400/1600
	Males			
Acanthosis	9	13	16	17
Inflammation, chronic active	4	5	11	10
Inflammation, all types	6	6	13	16*
Ulcer	5	4	12	11
Debris	4	3	13*	11
	Females			
Acanthosis	2	5	4	16*
Inflammation, chronic active	1	2	2	8
Inflammation, all types	1	2	3	9*
Ulcer	1	2	2	5
Debris	2	3	2	8

a Data were obtained from Table MP1-SUM of study report, pages 303 and 304; n=50
* Significantly different from controls at $p \leq 0.05$.

b) Neoplastic: No treatment-related neoplastic changes were observed.

III. DISCUSSION

A. Investigators conclusions - Treatment with cyfluthrin for approximately 18 months at dose levels of up to 1400/1600 [M/F] ppm produced no evidence of carcinogenicity in mice of either sex.

B. Reviewer's discussion/conclusions - In a mouse oncogenicity study (MRID 44589701), cyfluthrin (≥93.9% a.i., Lot/Batch # 4030059/BF9340-71) was administered in the diet to CD-1 mice (50/sex/group) for up to 80 weeks at 0, 200, 750, or 1400/1600 ppm (equivalent to 0/0, 31.9/38.4, 114.8/140.6, and 232.7/309.7 mg/kg/day [M/F], respectively). The high-doses were chosen based on the results of a 6-week range-finding study, and are the estimated maximum tolerated dose for each sex for a lifetime study in the mouse. Dietary analyses at selected study intervals confirmed that nominal diet concentrations of cyfluthrin were

achieved.

Mortality, food efficiency, hematology, and organ weights for both sexes at all doses were unaffected by treatment with cyfluthrin at any tested dose.

At 750 ppm, the following observations were made:

A toxic effect on the ears was observed and considered to be treatment-related based on macroscopic and microscopic pathology findings. Macroscopic findings included crusty zone of the skin of the ear in the males (11/50 treated vs 5/50 controls). Microscopic findings involving the skin of the ear in the males included the following: acanthosis (16/50 treated vs 9/50 controls); chronic active inflammation (11/50 treated vs 4/50 controls); inflammation, all types (13/50 treated vs 6/50 controls); ulcer (12/50 treated vs 5/50 controls); and debris (13/50 treated vs 4/50 controls, $p \leq 0.05$).

Monthly body weight gain was reduced ($p \leq 0.05$) after the first month of treatment in the males (↓21%), but not for the overall study. Overall body weight gain, as calculated by the reviewers, was decreased in the females (↓20%), but mean absolute food consumption was also decreased in the females (↓7-10%; $p \leq 0.05$), whereas food efficiency was unchanged. These observations suggest that decreased body weight gains in the females are the result of decreased food consumption, and therefore are not of toxicological concern.

At the high-dose, the following observations were made:

A toxic effect on the ears was observed at the high-dose and considered to be treatment-related based on clinical signs and macroscopic and microscopic findings. Ear lesion redness (5/50 treated vs 0/50 controls) and ear lesion scab (22/50 treated vs 2/50 controls) were observed ($p \leq 0.05$) in the females at clinical examination. Related gross necropsy findings included crusty zone of the skin of the ear in the males (12/50 treated vs 5/50 controls) and females (13/50 treated vs 1/50 controls, $p \leq 0.05$). Related microscopic findings ($p \leq 0.05$ or not significant) observed in the skin of the ear included the following: acanthosis in the males (17/50 treated vs 9/50 controls) and females (16/50 treated vs 2/50 controls); chronic active inflammation in the males (10/50 treated vs 4/50 controls) and females (8/50 treated vs 1/50 controls); inflammation, all types in the males (16/50 treated vs 6/50 controls) and females (9/50 treated vs 1/50 controls); ulcer in the males (11/50 treated vs 5/50 controls) and females (5/50 treated vs 1/50 controls); and debris in the males (11/50 treated vs 4/50 controls) and females (8/50 treated vs 2/50 controls).

In addition, an increased ($p \leq 0.05$) incidence of rough coat was observed in the males (30/50 treated vs 9/50 controls) and females (20/50 treated vs 9/50 controls) and hunched back was observed in the females (5/50 treated vs 0/50 controls) at clinical examination. Additional gross necropsy findings included the following: rough coat in the males (22/50 treated vs 7/50 controls, $p \leq 0.05$) and females (16/50 treated vs 8/50 controls, p=not significant) and wet/stained ventrum in the males (7/50 treated vs 0/50 controls).

Reductions ($p \leq 0.05$) in mean body weight were observed in the males (↓7-12%) and females (↓8-20%) throughout the study. Monthly body weight gain was reduced ($p \leq 0.05$) at the first month in the males (↓60%) and females (↓69%) compared to controls. Overall body weight gain, as calculated by the reviewers, was decreased in the males (↓25%) and females (↓54%). Mean absolute food consumption was decreased in the females (↓6-25%) compared to controls during the study.

The LOAEL is 750 ppm for males (equivalent to 114.8 mg/kg/day) based on macroscopic and microscopic ear skin lesions and reduced body weight gains and the LOAEL for the females is 1600 ppm (equivalent to 309.7 mg/kg/day) based on clinical signs, macroscopic and microscopic pathology findings, and reduced body weights, body weight gains, and food consumption. The NOAEL for males is 200 ppm (equivalent to 31.9 mg/kg/day). The NOAEL for females is 750 ppm (equivalent to 140.6 mg/kg/day)

Under the conditions of this study, there was no evidence of carcinogenic potential.

The submitted study is classified as **acceptable (§83-2b)** and does satisfy the guideline requirements for a carcinogenicity study in mice.

C. Study deficiencies -None noted.

ATTACHMENT - Neoplastic Incidence Summary
MRID 45228101

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 1

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
ADRENAL				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Hemangiosarcoma	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		
Sarcoma,Histiocytic		1/50 (2%)		
Adenoma,Cortical		1/50 (2%)		
AORTA				
NO. EXAMINED	50			
MISSING/FAULTS	0/50 (0%)			
Leukemia,Granulocytic	1/50 (2%)			
BONE MARROW				
NO. EXAMINED	50	50	50	
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	
Leukemia,Granulocytic	2/50 (4%)	2/50 (4%)	1/50 (2%)	
Malignant Lymphoma		1/50 (2%)		
BONE,FEMUR				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		
BONE,RIB/COSTOCHONDRAL JUNCTION				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

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Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 2

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
BONE,STERNUM				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		
BRAIN				
NO. EXAMINED		50		50
MISSING/FAULTS		0/50 (0%)		1/50 (2%)
Malignant Lymphoma		1/50 (2%)		1/49 (2%)
Neoplasm,Metastatic		1/50 (2%)		
CECUM				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
Malignant Lymphoma		1/50 (2%)		
COLON				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
AUTOLYSIS		1/50 (2%)		
Malignant Lymphoma		1/50 (2%)		
EPIDIDYMIS				
NO. EXAMINED		50	50	
MISSING/FAULTS		0/50 (0%)	0/50 (0%)	
Leukemia,Granulocytic			1/50 (2%)	
Malignant Lymphoma		1/50 (2%)		

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

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Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 3

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC - ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
EYE				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		
GALL BLADDER				
NO. EXAMINED		50		
MISSING/FAULTS		1/50 (2%)		
AUTOLYSIS		1/49 (2%)		
Malignant Lymphoma		1/49 (2%)		
HARDERIAN GLAND				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	1/50 (2%)	0/50 (0%)
Adenoma	4/50 (8%)	1/50 (2%)	2/49 (4%)	1/50 (2%)
Malignant Lymphoma		1/50 (2%)		
HEART				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
Malignant Lymphoma		1/50 (2%)		
KIDNEY				
NO. EXAMINED	50	50	50	
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	
Leukemia,Granulocytic	1/50 (2%)	1/50 (2%)	1/50 (2%)	
Lipoma	1/50 (2%)	1/50 (2%)		
Malignant Lymphoma		2/50 (4%)	1/50 (2%)	
Sarcoma,Histiocytic	1/50 (2%)	1/50 (2%)		

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

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Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 4

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
LARYNX				
NO. EXAMINED		50		
MISSING/FAULTS		1/50 (2%)		
Malignant Lymphoma		1/49 (2%)		
LIVER				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
Adenoma,Hepatocellular	4/50 (8%)	3/50 (6%)	1/50 (2%)	1/49 (2%)
Carc.,Hepatocell.	1/50 (2%)	2/50 (4%)		1/49 (2%)
Hemangiosarcoma	1/50 (2%)		1/50 (2%)	1/49 (2%)
Leukemia,Granulocytic	2/50 (4%)	1/50 (2%)		
Malignant Lymphoma		1/50 (2%)	2/50 (4%)	2/49 (4%)
Sarcoma,Histiocytic		1/50 (2%)		
LUNG				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
Adenoma,Alv./Bronch.	8/50 (16%)	4/50 (8%)	2/50 (4%)	6/49 (12%)
Leukemia,Granulocytic	1/50 (2%)	1/50 (2%)		
Malignant Lymphoma		1/50 (2%)		
Neoplasm,Metastatic		1/50 (2%)		
LYMPH NODE, OTHER				
NO. EXAMINED		7		5
MISSING/FAULTS		0/7 (0%)		0/5 (0%)
Leukemia,Granulocytic		1/7 (14%)		
Malignant Lymphoma		2/7 (28%)		1/5 (20%)

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 5

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
LYMPH NODE,CERVICAL				
NO. EXAMINED	50	50	50	
MISSING/FAULTS	0/50 (0%)	1/50 (2%)	0/50 (0%)	
Leukemia,Granulocytic	1/50 (2%)		1/50 (2%)	
Malignant Lymphoma	1/50 (2%)	2/49 (4%)	1/50 (2%)	
LYMPH NODE,MESENTERIC				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	2/50 (4%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
Leukemia,Granulocytic		1/50 (2%)	1/50 (2%)	
Malignant Lymphoma		1/50 (2%)	1/50 (2%)	1/48 (2%)
Sarcoma,Histiocytic	1/48 (2%)	1/50 (2%)		
OPTIC NERVE				
NO. EXAMINED	50	50		
MISSING/FAULTS	1/50 (2%)	2/50 (4%)		
Leukemia,Granulocytic	1/49 (2%)			
Malignant Lymphoma		1/48 (2%)		
PANCREAS				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		
Sarcoma,Histiocytic		1/50 (2%)		
PENIS				
NO. EXAMINED			2	
MISSING/FAULTS			0/2 (0%)	
Leukemia,Granulocytic			1/2 (50%)	

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
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Study : 95-271-DR TABLE MP2-SUM
Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 6

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
PITUITARY				
NO. EXAMINED		50		
MISSING/FAULTS		1/50 (2%)		
Malignant Lymphoma		1/49 (2%)		
PROSTATE				
NO. EXAMINED		50	50	
MISSING/FAULTS		0/50 (0%)	0/50 (0%)	
AUTOLYSIS			1/50 (2%)	
Hemangioma			1/50 (2%)	
Leukemia,Granulocytic		2/50 (4%)	1/50 (2%)	
Malignant Lymphoma		1/50 (2%)		
SALIVARY GLAND				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	1/50 (2%)		
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		2/49 (4%)		
SEMINAL VESICLE				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
Leukemia,Granulocytic		1/50 (2%)		
Malignant Lymphoma		1/50 (2%)		
SKELETAL MUSCLE,PROTOCOL				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
Malignant Lymphoma		1/50 (2%)		

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

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Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 7

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
SKIN,PROTOCOL				
NO. EXAMINED		50	50	
MISSING/FAULTS		0/50 (0%)	0/50 (0%)	
Leukemia,Granulocytic			1/50 (2%)	
Malignant Lymphoma		1/50 (2%)		
SKIN,OTHER				
NO. EXAMINED		9		
MISSING/FAULTS		0/9 (0%)		
Hemangioma		1/9 (11%)		
SKULL				
NO. EXAMINED	50	50	50	
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	
Fibroma		1/50 (2%)		
Leukemia,Granulocytic	1/50 (2%)		1/50 (2%)	
Malignant Lymphoma		1/50 (2%)		
Sarcoma,Osteogenic		1/50 (2%)		
SMALL INTESTINE				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Adenocarcinoma	1/50 (2%)			
Malignant Lymphoma	1/50 (2%)	1/50 (2%)		
SPINAL CORD				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
Malignant Lymphoma		1/50 (2%)		

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 8

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
SPLEEN				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
Hemangioma				1/50 (2%)
Hemangiosarcoma	1/50 (2%)			
Leukemia,Granulocytic	2/50 (4%)	2/50 (4%)	1/50 (2%)	
Malignant Lymphoma		2/50 (4%)	2/50 (4%)	2/50 (4%)
Sarcoma,Histiocytic	1/50 (2%)	1/50 (2%)		
STOMACH				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Adenocarcinoma	1/50 (2%)			
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma		1/50 (2%)		
Sarcoma,Histiocytic		1/50 (2%)		
TESTIS				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
Cystadenoma		1/50 (2%)		
Interst.Cell Tumor		2/50 (4%)		
THYMUS				
NO. EXAMINED	50	50		50
MISSING/FAULTS	0/50 (0%)	5/50 (10%)		3/50 (6%)
Leukemia,Granulocytic	1/50 (2%)	1/45 (2%)		
Malignant Lymphoma		2/45 (4%)		1/47 (2%)

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:48
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Male All sub-sets MALES
Page : 9

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	D
DOSAGE:	CONTROL	200 ppm	750 ppm	1400 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
THYROID				
NO. EXAMINED			50	
MISSING/FAULTS			0/50 (0%)	
Adenoma,Follicular			1/50 (2%)	
URINARY BLADDER				
NO. EXAMINED	50	50		
MISSING/FAULTS	0/50 (0%)	0/50 (0%)		
Leukemia,Granulocytic		1/50 (2%)		
Sarcoma,Histiocytic	1/50 (2%)			
MULTICENTRIC LESIONS				
NO. EXAMINED	15	13	14	7
MISSING/FAULTS	0/15 (0%)	0/13 (0%)	0/14 (0%)	0/7 (0%)
Hemangiosarcoma	2/15 (13%)		1/14 (7%)	1/7 (14%)
Leukemia,Granulocytic	2/15 (13%)	2/13 (15%)	1/14 (7%)	
Malignant Lymphoma	1/15 (6%)	3/13 (23%)	2/14 (14%)	2/7 (28%)
Sarcoma,Histiocytic	1/15 (6%)	1/13 (7%)		
SKIN,EAR				
NO. EXAMINED				18
MISSING/FAULTS				0/18 (0%)
Mast Cell Tumor				1/18 (5%)

NOTE: Report excludes Secondary and Metastatic lesions, unless explicitly requested in key.

[END OF REPORT]

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:50
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Female All sub-sets FEMALES
Page : 1

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
ADIPOSE TISSUE				
NO. EXAMINED			1	
MISSING/FAULTS			0/1 (0%)	
Sarcoma,Histiocytic			1/1 (100%)	
ADRENAL				
NO. EXAMINED	50	50		50
MISSING/FAULTS	1/50 (2%)	0/50 (0%)		0/50 (0%)
Adenoma	1/49 (2%)			1/50 (2%)
Malignant Lymphoma	1/49 (2%)			1/50 (2%)
Sarcoma,Histiocytic		1/50 (2%)		1/50 (2%)
AORTA				
NO. EXAMINED	50		50	50
MISSING/FAULTS	0/50 (0%)		0/50 (0%)	0/50 (0%)
Malignant Lymphoma	1/50 (2%)		1/50 (2%)	1/50 (2%)
BONE MARROW				
NO. EXAMINED	50		50	50
MISSING/FAULTS	0/50 (0%)		0/50 (0%)	0/50 (0%)
Leukemia,Granulocytic	1/50 (2%)		1/50 (2%)	1/50 (2%)
Malignant Lymphoma	1/50 (2%)			
BONE,RIB/COSTOCHONDRAL JUNCTION				
NO. EXAMINED	50		50	50
MISSING/FAULTS	0/50 (0%)		0/50 (0%)	0/50 (0%)
Leukemia,Granulocytic				1/50 (2%)
Malignant Lymphoma	2/50 (4%)		1/50 (2%)	

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:50
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Female All sub-sets FEMALES
Page : 2

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
BONE,STERNUM				
NO. EXAMINED	50		50	50
MISSING/FAULTS	0/50 (0%)		0/50 (0%)	0/50 (0%)
Leukemia,Granulocytic				1/50 (2%)
Malignant Lymphoma	3/50 (6%)		1/50 (2%)	
CECUM				
NO. EXAMINED				50
MISSING/FAULTS				0/50 (0%)
Sarcoma,Histiocytic				1/50 (2%)
CERVIX				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	1/50 (2%)	2/50 (4%)
Leiomyoma				1/48 (2%)
Leiomyosarcoma			1/49 (2%)	
Malignant Lymphoma		1/50 (2%)		1/48 (2%)
Sarcoma,Histiocytic	2/50 (4%)	2/50 (4%)	1/49 (2%)	1/48 (2%)
COLON				
NO. EXAMINED				50
MISSING/FAULTS				0/50 (0%)
Sarcoma,Histiocytic				1/50 (2%)
EYE				
NO. EXAMINED				50
MISSING/FAULTS				0/50 (0%)
Leukemia,Granulocytic				1/50 (2%)

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

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Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Female All sub-sets FEMALES
Page : 3

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
HARDERIAN GLAND				
NO. EXAMINED	50			
MISSING/FAULTS	0/50 (0%)			
Adenoma	1/50 (2%)			
HEART				
NO. EXAMINED	50		50	50
MISSING/FAULTS	0/50 (0%)		0/50 (0%)	0/50 (0%)
Leukemia,Granulocytic				1/50 (2%)
Malignant Lymphoma	2/50 (4%)		1/50 (2%)	
KIDNEY				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
AUTOLYSIS	1/50 (2%)			
Malignant Lymphoma	2/50 (4%)	1/50 (2%)	4/50 (8%)	2/50 (4%)
Neoplasm,Metastatic	1/50 (2%)			
Sarcoma,Histiocytic	1/50 (2%)	2/50 (4%)		1/50 (2%)
LARYNX				
NO. EXAMINED				50
MISSING/FAULTS				5/50 (10%)
Leukemia,Granulocytic				1/45 (2%)
LIVER				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
Adenoma,Hepatocellular		1/50 (2%)		
Carc.,Hepatocell.	1/50 (2%)			
Hemangioma				1/50 (2%)

CYFLUTHRIN **Oncogenicity study in mice (§83-2b)**

AN ONCOGENICITY TOXICITY TESTING STUDY IN THE MOUSE
Bayer Corp., Agriculture Division - Toxicology
Date : 25-AUG-00
Study : 95-271-DR TABLE MP2-SUM
Time : 10:50
Species: Mouse MICROPATHOLOGY NEOPLASTIC DATA
Sex : Female All sub-sets FEMALES
Page : 4

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
Hemangiosarcoma			1/50 (2%)	1/50 (2%)
Leukemia,Granulocytic	1/50 (2%)			
Malignant Lymphoma	1/50 (2%)			1/50 (2%)
Sarcoma,Histiocytic	1/50 (2%)	2/50 (4%)	1/50 (2%)	1/50 (2%)
LUNG				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	1/50 (2%)	0/50 (0%)	0/50 (0%)
Adenoma,Alv./Bronch.	2/50 (4%)	4/49 (8%)	6/50 (12%)	4/50 (8%)
Carc.,Alv./Bronch.		1/49 (2%)	1/50 (2%)	
Malignant Lymphoma	4/50 (8%)	2/49 (4%)	2/50 (4%)	2/50 (4%)
Neoplasm,Metastatic	1/50 (2%)			
Sarcoma,Histiocytic	1/50 (2%)	2/49 (4%)	1/50 (2%)	
LYMPH NODE, OTHER				
NO. EXAMINED	2	1	4	
MISSING/FAULTS	0/2 (0%)	0/1 (0%)	0/4 (0%)	
Malignant Lymphoma	1/2 (50%)		2/4 (50%)	
Sarcoma,Histiocytic		1/1 (100%)	1/4 (25%)	
LYMPH NODE,CERVICAL				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
Malignant Lymphoma	3/50 (6%)	1/50 (2%)	2/50 (4%)	1/50 (2%)
Sarcoma,Osteogenic		1/50 (2%)		
LYMPH NODE,MESENTERIC				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	1/50 (2%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
AUTOLYSIS	1/49 (2%)			
Malignant Lymphoma	5/49 (10%)	2/50 (4%)	1/50 (2%)	2/50 (4%)

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Page : 5

Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
Sarcoma,Histiocytic		1/50 (2%)		1/50 (2%)
MAMMARY GLAND				
NO. EXAMINED	50			50
MISSING/FAULTS	0/50 (0%)			0/50 (0%)
Adenocarcinoma	1/50 (2%)			
Malignant Lymphoma	2/50 (4%)			1/50 (2%)
MESENTERY				
NO. EXAMINED				1
MISSING/FAULTS				0/1 (0%)
Sarcoma,Histiocytic				1/1 (100%)
MUSCLE,OTHER				
NO. EXAMINED			3	1
MISSING/FAULTS			0/3 (0%)	0/1 (0%)
Sarcoma,Histiocytic			2/3 (66%)	1/1 (100%)
Schwannoma,Malignant			1/3 (33%)	
OPTIC NERVE				
NO. EXAMINED				50
MISSING/FAULTS				0/50 (0%)
Sarcoma,Histiocytic				1/50 (2%)
OVARY				
NO. EXAMINED	50	50		50
MISSING/FAULTS	1/50 (2%)	0/50 (0%)		0/50 (0%)
AUTOLYSIS	1/49 (2%)			
Malignant Lymphoma	2/49 (4%)	1/50 (2%)		1/50 (2%)
Sarcoma,Histiocytic		1/50 (2%)		1/50 (2%)

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Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
PANCREAS				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
Malignant Lymphoma	2/50 (4%)	1/50 (2%)	1/50 (2%)	1/50 (2%)
Sarcoma,Histiocytic				1/50 (2%)
PITUITARY				
NO. EXAMINED				50
MISSING/FAULTS				5/50 (10%)
Malignant Lymphoma				1/45 (2%)
RECTUM				
NO. EXAMINED	50	50		50
MISSING/FAULTS	3/50 (6%)	1/50 (2%)		1/50 (2%)
Malignant Lymphoma				1/49 (2%)
Polyp (neopl.)	1/47 (2%)			
Sarcoma,Histiocytic		1/49 (2%)		
SALIVARY GLAND				
NO. EXAMINED	50			
MISSING/FAULTS	0/50 (0%)			
Malignant Lymphoma	3/50 (6%)			
SKIN,PROTOCOL				
NO. EXAMINED	50			
MISSING/FAULTS	0/50 (0%)			
Malignant Lymphoma	1/50 (2%)			
SKULL				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)

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Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
Leukemia,Granulocytic			1/50 (2%)	1/50 (2%)
Malignant Lymphoma	1/50 (2%)			1/50 (2%)
Sarcoma,Histiocytic		1/50 (2%)	1/50 (2%)	
SMALL INTESTINE				
NO. EXAMINED		50		
MISSING/FAULTS		0/50 (0%)		
AUTOLYSIS		2/50 (4%)		
Malignant Lymphoma		1/50 (2%)		
SPLEEN				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
Hemangiosarcoma			1/50 (2%)	1/49 (2%)
Malignant Lymphoma	7/50 (14%)	3/50 (6%)	9/50 (18%)	1/49 (2%)
Sarcoma,Histiocytic	1/50 (2%)	1/50 (2%)		1/49 (2%)
STOMACH				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	0/50 (0%)
AUTOLYSIS	1/50 (2%)			
Malignant Lymphoma	3/50 (6%)	1/50 (2%)	1/50 (2%)	2/50 (4%)
Sarcoma,Histiocytic		1/50 (2%)		1/50 (2%)
THYMUS				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	3/50 (6%)	0/50 (0%)	2/50 (4%)	2/50 (4%)
Malignant Lymphoma	5/47 (10%)	4/50 (8%)	8/48 (16%)	3/48 (6%)
Sarcoma,Histiocytic		1/50 (2%)		

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Pathology Incidence Report

INCIDENCE KEY: ,NEOPLASTIC ,

GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
THYROID				
NO. EXAMINED		50		50
MISSING/FAULTS		0/50 (0%)		0/50 (0%)
Adenoma,C-Cell				1/50 (2%)
Adenoma,Follicular		1/50 (2%)		
URETER				
NO. EXAMINED			1	
MISSING/FAULTS			0/1 (0%)	
Malignant Lymphoma			1/1 (100%)	
URINARY BLADDER				
NO. EXAMINED	50			50
MISSING/FAULTS	1/50 (2%)			1/50 (2%)
Malignant Lymphoma	1/49 (2%)			
Sarcoma,Histiocytic				1/49 (2%)
UTERUS				
NO. EXAMINED	50	50	50	50
MISSING/FAULTS	0/50 (0%)	0/50 (0%)	0/50 (0%)	1/50 (2%)
AUTOLYSIS	1/50 (2%)			
Hemangiosarcoma		1/50 (2%)		
Leiomyoma	1/50 (2%)	1/50 (2%)	1/50 (2%)	1/49 (2%)
Malignant Lymphoma	1/50 (2%)			1/49 (2%)
Polyp,Endometr.Stromal	1/50 (2%)	1/50 (2%)	2/50 (4%)	
Sarcoma,Histiocytic	1/50 (2%)	1/50 (2%)		1/49 (2%)
MULTICENTRIC LESIONS				
NO. EXAMINED	19	18	27	13
MISSING/FAULTS	0/19 (0%)	0/18 (0%)	0/27 (0%)	0/13 (0%)

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Pathology Incidence Report

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GROUP:	A	B	C	E
DOSAGE:	CONTROL	200 ppm	750 ppm	1600 ppm
NO. OF ANIMALS EXAMINED:	50	50	50	50
Hemangiosarcoma		1/18 (5%)	2/27 (7%)	1/13 (7%)
Leukemia,Granulocytic	1/19 (5%)		1/27 (3%)	1/13 (7%)
Malignant Lymphoma	8/19 (42%)	8/18 (44%)	11/27 (40%)	3/13 (23%)
Sarcoma,Histiocytic	2/19 (10%)	1/18 (5%)	2/27 (7%)	1/13 (7%)
SKIN,HINDLIMB				
NO. EXAMINED		2		
MISSING/FAULTS		0/2 (0%)		
Osteosarcoma		1/2 (50%)		

NOTE: Report excludes Secondary and Metastatic lesions, unless explicitly requested in key.

[END OF REPORT]

13544

R058382

Chemical:	**Cyfluthrin**
PC Code:	**128831**
HED File Code	**13000 Tox Reviews**
Memo Date:	**10/30/2000 12:00:00 AM**
File ID:	**DPD243160**
Accession Number:	***412-04-0046***

HED Records Reference Center
03/25/2004