(005100 EXCERPT)

EPA: 68-02-4225
DYNAMAC No. 1-029-C
January 13, 1986

DATA EVALUATION RECORD

CYHALOTHRIN

Three-Generation Reproduction Study in Rats

STUDY IDENTIFICATION: Milburn, G. M., Banham, P., Godley, M. J., Pigott, G., and Robinson, M. Cyhalothrin: Three generation reproduction study in the rat. (Unpublished study for project CTL/P/906 7/HD/007119 prepared by Imperial Chemical Industries PLC; dated May 13, 1984.) Accession Nos. 073207-073209.

APPROVED BY:

I. Cecil Felkner, Ph.D.
Department Manager
Dynamac Corporation

Signature: I. Cecil Felkner

Date: 1-13-86

1. CHEMICAL: Cyhalothrin; (RS) α-cyano-3-phenoxybenzyl (Z)-(1RS, 3RS)-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate.

2. TEST MATERIAL: Cyhalothrin technical from batch No. ADM/46156/80 (CTL Reference number Y00102/010/007) had a purity of 89.2% (w/w).

3. STUDY/ACTION TYPE: Three-generation reproduction study in rats.

4. STUDY IDENTIFICATION: Milburn, G. M., Banham, P., Godley, M. J., Pigott, G., and Robinson, M. Cyhalothrin: Three generation reproduction study in the rat. (Unpublished study for project CTL/P/906 7/HD/007119 prepared by Imperial Chemical Industries PLC; dated May 13, 1984.) Accession Nos. 073207-073209.

5. REVIEWED BY:

Michael J. Norvell, Ph.D., D.A.B.T.
Principal Reviewer
Dynamac Corporation

Signature: G Millicovsky FOR
Date: 13 Jan 86

Michael A. Gallo, Ph.D., D.A.B.T.
Independent Reviewer
Dynamac Corporation

Signature: G Millicovsky FOR
Date: 13 Jan 86

6. APPROVED BY:

Guillermo Millicovsky, Ph.D.
Teratogenicity and Reproductive Effects
Technical Quality Control
Dynamac Corporation

Signature: G Millicovsky FOR
Date: 13 Jan 86

Pamela Hurley, Ph.D.
EPA Reviewer

Signature: Pamela Hurley
Date: 4/23/86

Edwin Budd, M.S.
EPA Section Head

Signature: John Rheij
Date: 5/5/86

7. CONCLUSIONS:

A. We assess that the NOEL and LOEL for parental toxicity are 10 ppm and 30 ppm, respectively. The NOEL for offspring toxicity could not be determined because of compound-related effects even at the lowest dose level tested. Therefore, 10 ppm is assessed as the LOEL for offspring toxicity, based on statistically significant reductions in parental and offspring body weights. In addition, a statistically significant reduction in offspring viability was observed at 100 ppm.

B. This study had two major deficiencies:

- Compound-related toxicity occurred at all doses; hence, the NOEL for offspring toxicity could not be established.

- There were discrepancies between the summary tables and individual animal data.

Due to these deficiencies, this study is classified Core Supplementary until the discrepancies between the summary tables and individual animal data are corrected, at which time it may be reclassified as Core Minimum.

8. RECOMMENDATIONS:

1. The toxicity of the test material in the offspring of rats should be assessed at lower dose levels.

2. The data submitted for the present study should be revised by the study authors to remove possible errors in the summary tables and/or individual animal data.

Items 8 through 10--see footnote 1.

11. MATERIALS AND METHODS (PROTOCOLS): (See Appendix A for details.)

Cyhalothrin technical (89.2% pure) was mixed into one of two cereal-based open formula diets at doses of 0, 10, 30, and 100 ppm throughout the duration of the study.

Male and female weanling SPF Wistar-derived rats were subjected to a quarantine/acclimatization period, individually identified, and randomly assigned to one of the dose groups. Prior to mating, each of the four dose groups consisted of 30 females (housed two per cage) and 15 males (housed one per cage). Male and female rats were housed in adjacent stainless steel cages in a temperature-, humidity-, and light-controlled room with a minimum of 15 air changes per hour. Feed and water were provided ad libitum.

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[1] Only items appropriate to this DER have been included.

Microbiological sentinels were included in the study design.

During the study, all rats were observed once daily for abnormalities in clinical condition and behavior; a detailed examination of each rat was made once each week.

At 7-8 weeks of age (maturity), each female rat was examined for imperforate vagina.

The premating periods were 12 weeks for the F_0 animals and 11 weeks for the F_1 and F_2 animals. During these periods, body weight and food consumption values were recorded weekly. Following mating, the males were weighed approximately every 4 weeks until termination, and the females were weighed on days 1, 8, 15, and 22 of pregnancy.

Two females were housed with one male during the mating period, and daily vaginal examinations were performed to confirm mating. In cases of suspected male infertility, the first male was replaced with a male of proven fertility. Females with a positive vaginal smear were individually housed during the gestation and lactation periods.

Females from each generation were mated to males from the same dose group and allowed to produce the A litter; 10 days after the last A litter was weaned, females were remated with a different male to produce a second (B) litter. The interval between mating for the A and B litters was approximately 2.5 to 3 months; brother-sister matings were avoided.

The F_1B and F_2B litters were weaned at day 29 but remained housed as litters until day 36. Thirty females and 15 males were selected from each dose group of the F_1B and F_2B litters to produce the subsequent generations.

All parental animals that died or were sacrificed were subjected to a full postmortem examination, and the reproductive organs and other selected tissues were taken for histopathological examination.

All live and stillborn pups were counted, checked for clinical abnormalities, and their sex and individual body weights were recorded within 24 hours of parturition and at days 5, 11, 22, and 29 postpartum. Litters were examined once daily; dead or grossly abnormal pups were removed for soft tissue examination. All grossly abnormal pups and those found dead within the first 18 days were examined teratologically by the methods described by Wilson.

Moribund or dead pups older than 18 days of age were subjected to a full postmortem examination.

At approximately 36 days postpartum, all offspring from the A litters and those from the B litters not selected to produce the subsequent generation were sacrificed. Approximately half of the A litter offspring (including those with externally visible abnormalities) were subjected to a gross autopsy and abnormal tissues were examined histologically. The remaining half were discarded after gross external

examination. Approximately five male and five female pups per group from the F_1B and F_2B litters and 10 male and 10 female pups per group from the F_3B litters were subjected to a full postmortem examination, and selected tissues were examined histologically. The remaining pups from B litters were subjected to a gross postmortem examination with only abnormal tissues submitted for examination. Normally distributed parametric data such as body weight, weight gain, and food consumption were subjected to analysis of variance and/or analysis of covariance and Student's t-test. Parametric data such as litter sizes and proportional data were analyzed by analysis of variance on transformed data or by one-tailed Fisher's exact test.

12. REPORTED RESULTS:

A. Dietary Analyses: Twenty-three batches of feed were analyzed for concentrations of cyhalothrin at each dose level, including the control feed. No test material was detected (at a level of sensitivity of less than 0.1 ppm) in any of the control diets. The maximum deviation of the doses from nominal concentration was 16.7%, and in all but four instances, the mean concentrations were within 10% of nominal value. In five different batches of feed the test material was found to be stable when stored for up to 2 months at levels between 10 and 100 ppm.

The homogeneity of the test material was found to be satisfactory in three batches of diet containing 10, 30, or 100 ppm cyhalothrin.

B. Parents:

1. Mortality: One F_1 male from the 10-ppm dose group was found dead. Unscheduled sacrifices were performed on two females (one F_0 control and one F_2 from the 30-ppm dose group) because of parturition difficulties.

2. Clinical Observations: None of the parental animals exhibited clinical signs related to administration of the test material.

3. Body Weight Gain: During the first week of study, F_0 males in the high-dose group showed small (but statistically significant) reductions in weight gain. For the remainder of the study, the weight gain of F_0 males was comparable to that of controls. There was a statistically significant reduction in the mean body weight gain of F_1 and F_2 males in the high-dose group. According to the text of the study report, the low-dose F_1 males showed a slight, but not statistically significant, reduction in body weight gain. However, the study authors' analyses of the tabulated data (p. 36 of the report) indicated that this reduction was statistically significant. These data are presented in Table 1.

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TABLE 1. Effects of Cyhalothrin on Mean Body Weight Gain (g) During the Premating Period in Rats

End of Week	Dose Level (ppm) 0	10	30	100
		F_0 Males		
1	54.7	53.8	53.7	50.5*
6	302.3	297.0	301.7	295.8
12	422.7	414.1	418.8	415.0
		F_1 Males		
1	59.3	56.6	57.6	54.9*
6	276.8	271.8	283.5	266.4
11	382.7	351.7*	363.5	349.0*
		F_2 Males		
1	61.2	60.3	58.5	56.7
6	287.0	291.7	280.7	264.7
11	385.7	391.5	373.1	352.8*
		F_0 Females		
1	40.0	41.0	42.6*	38.3
6	161.2	160.2	165.9	160.3
12	211.5	209.9	219.0*	208.4
		F_1 Females		
1	40.6	39.9	40.4	40.4
6	142.7	137.4	134.2*	131.4**
11	182.3	173.2	168.9**	165.1**
		F_2 Females		
1	37.6	41.7*	37.6	37.7
6	131.4	135.9	129.0	122.3*
11	166.0	169.0	160.6	156.0*

*Statistically different from control value ($p \leq 0.05$).

**Statistically different from control value ($p \leq 0.01$).

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CYHALOTHRIN

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Female F_0 rats in the mid-dose group showed a statistically significant increase in body weight during the premating period.

Female F_1 rats in the mid- and high-dose groups showed statistically significant reductions in body weight gain during the premating period. The F_2 females in the high-dose group showed statistically significant reductions in body weight gain during the premating period (Table 1).

During pregnancy, there was no consistent evidence of decreased body weight gain for the F_0 animals. The mean body weights of F_1 and F_2 females at the initiation of pregnancy were significantly reduced for all of the 100-ppm and most of the 30-ppm groups. There were significant reductions in body weight gain during pregnancy for the F_2 animals in the high-dose groups (Table 2).

4. Food Consumption: Variations in food consumption measurements during the premating period precluded interpretation of any results on food consumption or calculations of dosage rates. However, the study authors noted that no consistent differences were evident between dosage groups. Food consumption was not measured during pregnancy or lactation.

5. Fertility: Male fertility was comparable among all groups (Table 3).

   No effects on female fertility were noted except for a statistically significant reduction in the fertility of F_2 females from the mid-dose group producing the F_3B generation when compared to controls (Table 3). However, the study authors did not consider this reduction compound related.

6. Precoital Interval: The test article did not affect the length of the precoital interval during this study.

7. Gestation Period: The test article did not affect the length of gestation during this study.

8. Maternal Neglect: The test article did not affect maternal neglect during this study (Table 4).

C. Offspring:

1. Litter Size: There was a statistically significant reduction in litter size for the F_2A and F_3B litters of high-dose females (Table 5).

TABLE 2. Effects of Cyhalothrin on Mean Maternal Body Weight (g) and Weight Gain (g) During Gestation in Rats

	Dose Level (ppm)			
	0	10	30	100
		F_0, Litter A		
Initial weight	289.0	288.5	298.6	286.1
Wt. gain at day				
8	23.7	27.5*	26.6	23.0
15	55.7	60.6	58.4	56.0
22	127.2	129.6	132.7	127.6
		F_0, Litter B		
Initial weight	328.3	326.5	330.2	323.5
Wt. gain at day				
8	21.6	26.0	25.1	25.2
15	55.2	59.3	60.3	54.5
22	125.4	129.4	143.9**	132.8
		F_1, Litter A		
Initial weight	306.3	298.3	282.7**	287.0*
Wt. gain at day				
8	23.4	24.7	23.4	24.0
15	55.3	55.9	53.0	55.4
22	134.5	132.1	130.1	133.2
		F_1, Litter B		
Initial weight	348.3	344.6	321.7**	323.0**
Wt. gain at day				
8	23.9	25.3	20.8	22.0
15	56.1	58.0	51.1	56.7
22	131.3	132.3	120.8	128.2

(Continued)

*Statistically different from control value ($p \leq 0.05$).

**Statistically different from control value ($p \leq 0.01$).

TABLE 2. Effects of Cyhalothrin on Mean Maternal Body Weight (g) and Weight Gain (g) During Gestation in Rats (Continued)

	Dose Level (ppm)			
	0	10	30	100
		F_2, Litter A		
Initial weight	297.1	296.9	284.6	278.7*
Wt. gain at day				
8	26.3	26.0	26.1	22.4*
15	54.2	56.8	54.1	50.8
22	123.7	124.4	128.5	119.4
		F_2, Litter B		
Initial weight	331.1	330.9	315.5*	312.4**
Wt. gain at day				
8	23.4	25.5	21.8	20.8
15	53.6	55.5	54.4	50.3
22	142.2	137.0	136.7	127.2*

(Concluded)

*Statistically different from control value ($p \leq 0.05$).

**Statistically different from control value ($p \leq 0.01$).

TABLE 3. Effects of Cyhalothrin on Group Mean Percentage Parental Fertility in Rats

	Dose Level (ppm)			
	0	10	30	100
		Males		
F_0, Litter A	100%[a]	93%	92%	87%
F_0, Litter B	100%	93%	100%	100%
F_1, Litter A	93%	93%	86%	100%
F_1, Litter B	93%	85%	93%	100%
F_2, Litter A	93%	93%	100%	100%
F_2, Litter B	100%	93%	80%	93%
		Females		
F_0, Litter A	77%[b]	87%	88%	96%
F_0, Litter B	73%	86%	77%	89%
F_1, Litter A	89%	80%	78%	87%
F_1, Litter B	83%	75%	87%	90%
F_2, Litter A	90%	90%	86%	79%
F_2, Litter B	97%	83%	77%*	83%

[a]Based on approximately 15 males per group.

[b]Based on approximately 30 females per group.

*Statistically different from control value ($p \leq 0.05$).

TABLE 4. Effects of Cyhalothrin on the Mean Percentage of Viable Litters that Did Not Survive Due to Maternal Neglect in Rats

	Dose Level (ppm)			
Litter	0	10	30	100
F_1A	4%[a]	4%	5%	4%
F_1B	5%	8%	0%	8%
F_2A	8%	0%	0%	12%
F_2B	0%	5%	0%	0%
F_3A	0%	0%	0%	0%
F_3B	0%	0%	0%	4%

[a]Based on 21-29 litters per group.

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TABLE 5. Effect of Cyhalothrin on Mean Litter Size in Rats

Postnatal Day	Dose Level (ppm) 0	10	30	100
		F_1A		
1	12.0	11.8	12.1	10.9
5	10.5	11.0	11.0	10.3
11	10.5	10.8	10.9	10.0
22	10.4	10.8	10.9	9.9
29	10.4	10.8	10.8	9.9
		F_1B		
1	9.8	10.1	11.9	11.5
5	9.2	9.7	11.6	10.3
11	8.7	9.5	11.6	10.1
22	8.6	9.5	11.6	9.9
29	8.6	9.5	11.5	9.9
		F_2A		
1	11.6	11.3	11.3	10.0
5	10.9	10.7	11.3	8.7*
11	10.8	10.6	11.2	8.6*
22	10.7	10.4	11.2	8.6*
29	10.7	10.4	11.2	8.6*
		F_2B		
1	10.2	10.3	9.6	9.9
5	9.7	9.9	9.2	9.5
11	9.5	9.7	9.2	9.5
22	9.5	9.7	9.2	9.5
29	9.5	9.7	9.2	9.4
		F_3A		
1	10.8	10.9	11.2	10.2
5	10.4	10.7	11.1	10.0
11	10.4	10.7	11.1	9.9
22	10.4	10.7	11.1	9.9
29	10.4	10.7	11.1	9.9

(Continued)

*Statistically different from control value ($p \leq 0.05$).

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TABLE 5. Effect of Cyhalothrin on Mean Litter Size in Rats (Continued)

Postnatal Day	Dose Level (ppm) 0	10	30	100
		F_3B		
1	11.3	10.9	11.3	10.0
5	11.0	10.8	10.8	9.6
11	10.9	10.7	10.7	9.5*
22	10.9	10.7	10.7	9.5*
29	10.9	10.7	10.7	9.5*

(Concluded)

*Statistically different from control value ($p \leq 0.05$).

2. Live-Born Index: The only statistically significant decreases in the percentage of live-born pups were noted in the F_1B pups dosed with 10 ppm and in the F_3B groups dosed with 30 and 100 ppm. The study authors considered only the effects in the F_3B generation to be compound related (Table 6).

3. Survival to Day 22: The test article did not affect pup survival to day 22 in this study (Table 7).

4. Clinical Condition: The test article did not affect the clinical condition of pups in this study.

5. Body Weight Gain: Statistically significant reductions in body weight gain were noted in F_1A females from the 10-ppm group, F_1B female pups from the 30- and 100-ppm groups, F_1B males from the 100-ppm group, F_2B males from the 100-ppm group, F_3A females from the 30- and 100-ppm groups, F_3A males from the 10-, 30-, and 100-ppm groups, and F_3B females and males from the 30-ppm groups (Table 8).

6. Soft Tissue Examination: The quality of the soft tissues was adversely affected by autolysis. The hearts of three pups from F_2 dams in the high-dose group were reportedly "apparently" absent. However, the study authors stated that there were no consistent differences in findings between dose groups or between A and B litters.

D. Pathology:

1. Gross Pathology: The test material did not affect the gross pathologic findings reported in the parental animals or pups in this study.

2. Histopathology: No compound-related findings were noted.

13. STUDY AUTHORS' CONCLUSIONS/QUALITY ASSURANCE MEASURES:

A. The study authors concluded that 100 ppm of cyhalothrin in the diet of rats was associated with reductions in body weights in the F_2B, F_3A, and F_3B generations. No other parameter was affected. They assessed 30 ppm as the NOEL.

B. A quality assurance statement was signed and dated May 14, 1984.

14. REVIEWERS' DISCUSSION AND INTERPRETATION OF STUDY RESULTS:

A. Diets containing cyhalothrin at concentrations of 30 and 100 ppm were associated with reductions in parental and offspring body weight in rats. No distinct compound-related effects on body weights were noted in the 10-ppm groups, except for occasional reductions in pup body weights that, at times, had statistical

TABLE 6. Effects of Cyhalothrin on Mean Percentage of Pups Born Alive in Rats

Litter	Dose Level (ppm)			
	0	10	30	100
F_1A	96.2%[a]	99.5%	99.3%	98.7%
F_1B	98.3%	93.2%*	98.9%	99.2%
F_2A	99.5%	99.5%	100.0%	98.5%
F_2B	99.0%	99.2%	97.4%	98.1%
F_3A	99.7%	100.0%	98.5%	98.8%
F_3B	99.2%	97.9%	97.0%*	93.6%**

[a]Based on 232-329 pups per group.

*Statistically different from control value ($p \leq 0.05$).

**Statistically different from control value ($p \leq 0.01$).

TABLE 7. Effects of Cyhalothrin on Mean Percentage of Pups Alive on Postnatal Day 22 in Rats

Litter	Dose Level (ppm)			
	0	10	30	100
F_1A	85.7%	94.0%	91.5%	91.0%
F_1B	90.3%	96.8%	95.6%	88.2%
F_2A	89.1%	92.8%	99.7%	86.8%
F_2B	94.9%	96.5%	95.5%	95.7%
F_3A	97.0%	98.3%	98.7%	96.6%
F_3B	96.8%	96.7%	95.2%	93.9%

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TABLE 8. Effects of Cyhalothrin on Mean Initial Pup Body Weight (g) and Weight Gain (g) in Rats

Weight Gain	Dose Level (ppm) 0	10	30	100
		F_1A Females		
Initial weight	5.4	5.7	5.7	5.7
Postnatal day				
5	2.9	2.3*	2.5	2.5
11	11.3	10.6	10.7	10.5
22	32.4	30.8	30.9	31.1
29	61.6	59.9	61.1	59.8
		F_1A Males		
Initial weight	5.8	6.2	6.1	6.1
Postnatal day				
5	2.9	2.6	2.8	2.7
11	12.1	11.4	11.5	11.0
22	34.2	33.1	32.3	34.0
29	67.0	65.9	65.9	66.6
		F_1B Females		
Initial weight	5.9	6.0	5.9	5.9
Postnatal day				
5	2.5	3.0	2.7	2.5
11	11.8	12.5	11.4	10.8
22	36.6	37.1	32.9*	33.2*
29	67.3	68.8	61.8*	62.2*
		F_1B Males		
Initial weight	6.2	6.4	6.3	6.0
Postnatal day				
5	2.6	3.1	3.0	2.5
11	11.9	13.0	12.0	11.4
22	37.5	38.5	35.2	34.8
29	71.2	72.9	66.8	66.4*

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(Continued)

*Statistically different from control value ($p \leq 0.05$).

TABLE 8. Effects of Cyhalothrin on Mean Initial Pup Body Weight (g) and Weight Gain (g) in Rats (Continued)

Weight Gain	Dose Level (ppm) 0	10	30	100
		F_2A Females		
Initial weight	5.8	5.9	5.8	5.8
Postnatal day				
5	3.3	3.1	3.0	3.0
11	12.6	12.4	12.2	12.7
22	36.7	36.9	33.6	36.5
29	69.0	70.8	67.6	70.0
		F_2A Males		
Initial weight	6.1	6.2	6.2	6.2
Postnatal day				
5	3.2	3.1	2.9	3.3
11	13.1	12.6	12.4	13.6
22	37.1	36.7	35.3	38.9
29	71.8	73.2	72.5	75.8
		F_2B Females		
Initial weight	6.0	5.9	6.0	6.0
Postnatal day				
5	2.6	2.8	3.3	2.7
11	12.4	12.8	13.9	12.1
22	37.9	39.2	38.5	36.6
29	72.5	72.6	73.6	70.4
		F_2B Males		
Initial weight	6.5	6.6	6.4	6.3
Postnatal day				
5	2.9	2.9	3.4	2.7
11	13.5	13.4	14.2	12.2
22	41.0	41.8	41.0	37.4*
29	80.1	79.4	80.0	73.9*

*Statistically different from control value ($p \leq 0.05$).

(Continued)

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TABLE 8. Effects of Cyhalothrin on Mean Initial Pup Body Weight (g) and Weight Gain (g) in Rats (Continued)

Weight Gain	Dose Level (ppm) 0	10	30	100
		F_3A Females		
Initial weight	5.8	5.7	5.7	5.8
Postnatal day				
5	3.2	3.0	2.9	2.9
11	13.3	12.8	12.2	11.7*
22	38.5	36.5	34.7**	34.7*
29	73.7	71.2	67.8**	67.6**
		F_3A Males		
Initial weight	6.2	6.2	6.1	6.1
Postnatal day				
5	3.4	3.1	2.9*	2.9*
11	14.0	12.1**	12.4*	11.7**
22	39.8	37.1*	35.8**	34.8**
29	79.1	75.2	72.1**	69.9**
		F_3B Females		
Initial weight	6.0	6.2	6.1	5.9
Postnatal day				
5	3.4	3.3	3.3	3.5
11	13.7	12.8	13.4	13.3
22	39.3	36.9	37.0	37.7
29	74.7	70.8	70.4*	71.9
		F_3B Males		
Initial weight	6.4	6.5	6.4	6.4
Postnatal day				
5	3.6	3.4	3.3	3.4
11	14.3	13.6	13.0*	13.4
22	40.9	39.0	37.6*	38.4
29	80.0	76.4	74.1*	75.7

(Concluded)

*Statistically different from control value ($p \leq 0.05$).

**Statistically different from control value ($p \leq 0.01$).

significance. No compound-related effects on parental fertility or maternal neglect were noted. However, we assess that the statistically significant reductions in the number of viable pups in the 100-ppm groups from the F_2A and F_3B generations were compound related.

B. Our conclusions differed from those of the study authors in that we assess that the NOEL for parental toxicity is 10 ppm, based on the statistically significant reductions in body weights at 30 and 100 ppm; we assess that the LOEL for parental toxicity is 30 ppm. The NOEL for offspring toxicity could not be determined because there were statistically significant reductions in pup body weight, even in some groups dosed with 10 ppm; therefore, this dose (the lowest used) is the LOEL for offspring toxicity in this study.

Although the study authors stated that no other parameters were affected, we conclude that the reductions in viable fetuses noted in two generations dosed with 100 ppm suggest a lethal effect of the test material on the offspring at this dose level.

C. The summary tables had several arithmetic errors when compared to the individual animal data. Specific examples of the errors include:

1. Tables 23-24 (fertility tables): The source of the denominators is not clear. In Table 23 (p. 50), male fertility during production of litter F_1A at 30 ppm was reported as 11/12, but information from Appendix F (pp. 108-109) indicates it should have been 11/14 (male No. 132 was infertile, no litters or positive vaginal smear).

   Litter F_2A (control), the value of 13/14 should have been reported as 13/15 (Appendix N, pp. 297-298).

   Litter F_2A (100 ppm), the value of 14/15 should have been reported as 14/14 (Appendix N, pp. 299-300).

   Litter F_1A (100 ppm), the value reported as 26/27 should have been reported as 26/28 (Appendix F, pp. 110-111).

   Litter F_2A (10 ppm), the value reported as 24/30 should have been reported as 24/29 (Appendix N, pp. 299-300).

2. The following discrepancies were noted in Table 28 (p. 55):

Litter Size, F_1 Generation

Group	Reported as	Should be	Individual Animal Reference
A, control, day 1	12.0 (22)	11.5 (23)	App. F, pp. 104-105
A, 10 ppm, day 1	11.8 (25)	11.3 (26)	App. P, pp. 106-107
A, 30 ppm, day 1	12.1 (21)	12.3 (22)	App. F, pp. 108-109
A, 100 ppm, day 1	10.9 (25)	11.0 (26)	App. F, pp. 110-111
B, control, day 1	9.8 (21)	9.9 (22)	App. F, pp. 112-113
B, control, day 29	8.6 (21)	9.1 (21)	App. F, pp. 112-113
B, 10 ppm, day 1	10.1 (23)	10.1 (25)	App. F, pp. 114-115
B, 10 ppm, day 29	9.5 (23)	9.8 (22)	App. F, pp. 114-115
B, 30 ppm, day 29	11.5 (23)	11.1 (21)	App. F, pp. 116-117
B, 100 ppm, day 1	11.5 (22)	11.5 (24)	App. F, pp. 118-119
B, 100 ppm, day 29	9.9 (22)	9.7 (21)	App. F, pp. 118-119

3. The following discrepancies were noted in Table 29 (p. 26):

Litter Size, F_2 Generation

Litter/Group	Reported as	Should be	Individual Animal Reference
A, control day 1	11.6 (23)	11.0 (25)	App. N, pp. 297-298
A, 30 ppm, day 29	11.2 (21)	11.2 (20)	App. N, pp. 301-302
A, 100 ppm, day 1	10.0 (23)	9.9 (26)	App. N, pp. 303-304
A, 100 ppm, day 29	8.6 (23)	8.5 (21)	App. N, pp. 303-304
B, 10 ppm, day 1	10.3 (20)	10.5 (21)	App. N, pp. 307-308
B, 10 ppm, day 29	9.7 (20)	9.8 (17)	App. N, pp. 311-312
B, 100 ppm, day 29	9.4 (27)	9.6 (25)	

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4. The following discrepancies were noted in Table 30 (p. 57):

Litter Size, F_3 Generation

Litter/Group	Reported as	Should be	Individual Animal Reference
B, 100 ppm, day 1	10.0 (24)	9.6 (25)	App. V, pp. 515-516

5. The following discrepancies were noted in Table 31 (p. 58):

Pups Born Live

Litter/Group	Reported as	Should be	Individual Animal Reference
F_1A, control	264/274	264/276	App. F, pp. 104-105
F_2B, 100 ppm	269/275	269/279	App. N, pp. 311-312

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Item 15--see footnote 1.

16. CBI APPENDIX: Appendix A, Materials and Methods, CBI pp. 3-14.