PROJECT NO: BT-71-68
REPORT FILE

Industrial **BIO-TEST** *Laboratories, Inc.*
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

BTL 71-68 #1

REPORT TO

MONSANTO COMPANY

THREE-GENERATION REPRODUCTION STUDY WITH AROCLOR 1242 IN ALBINO RATS

NOVEMBER 1, 1971

IBT NO. B7297

B7L-71-6

Industrial BIO-TEST Laboratories, Inc.
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

November 1, 1971

Mr. Elmer Wheeler
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Mr. Wheeler:

Re: IBT No. B7297 - Three-Generation Reproduction Study With Aroclor 1242 In Albino Rats

We are submitting herewith our laboratory report dated November 1, 1971, prepared in connection with the above study.

Very truly yours,

J. C. Calandra
President

JCC:sjn

REPORT TO

MONSANTO COMPANY

THREE-GENERATION REPRODUCTION STUDY WITH AROCLOR 1242 IN ALBINO RATS

NOVEMBER 1, 1971

IBT NO. B7297

I. Introduction

At the request of Monsanto Company, a reproduction study was initiated in order to ascertain potential toxicological effects of subacute oral administration of Aroclor 1242, Lot No. AK-255, upon the fertility and offspring of three consecutive generations of albino rats.

This report presents the data collected from the initiation of the investigation to the weaning of the second (F3b) litters obtained from the third (F2) parental generation.

II. Summary

A three-generation reproduction study employing albino rats fed diets containing 1, 10 or 100 ppm Aroclor 1242 was conducted. The following results were obtained during the investigation.

A. Parental Animals

1. Body Weights

Body weights and body weight gains revealed no differences between test and control animals which could be attributed to the ingestion of Aroclor 1242.

2. Mortality and Reactions

Several animals succumbed during each of the three generations. None of these deaths could be attributed to the ingestion of Aroclor 1242.

3. Pathologic Studies

Gross pathologic examination revealed no differences between test and control rats.

The absolute liver weights and liver to body weight or brain weight ratios were significantly elevated in both F1 males and females fed 100 ppm Aroclor 1242. Statistical evaluations of other organ weights, organ to body weight and organ to brain weight ratios disclosed several randomly occurring intergroup differences. The lack of any consistent dose or generation related response and the absence of any deleterious histopathologic change confirm that these differences were not related to the ingestion of Aroclor 1242.

All lesions noted during histopathologic studies were those of spontaneous disease.

4. Reproductive Performance

Reproductive indices of rats fed 1 or 10 ppm did not differ from those of the controls during any of the three generations. During the second generation (F2a and F2b litters), rats fed 100 ppm had lowered mating indices and a reduced incidence of pregnancy. Because only two T-III females produced F2b litters, it was not possible to continue this level through the third generation.

B. Progeny

1. Population Data

The number of live pups born per litter and the average number of pups weaned were not affected at any level of Aroclor 1242 tested. No external abnormalities were present that could be attributed to treatment. No untoward behavioral reactions were observed among test or control progeny.

2. Survival

Twenty-four hour and five day survival indices and the lactation index were normal for all groups.

3. Body Weights

Body weights for all progeny were normal at weaning.

4. Pathologic Studies

At autopsy of the F3b weanlings no gross or microscopic tissue changes were present which could be associated with the ingestion of Aroclor 1242.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

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Rat Toxicity

Report approved by:

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Manager, Toxicology

November 1, 1971

jg:sjn:psh

III. Procedure

A. Experimental Animals

The animals employed were weanling Charles River albino rats*. A total of 96 weanling rats (32 males and 64 females) was selected to form three test groups and a control group of Fo generation animals. Parental animals were allowed to reach maturity, mate and produce two litters. Eight males and 16 females from the second litters of each dietary group (F1b and F2b) were selected at weaning as parental animals for the succeeding generations. The study terminated following the weaning of the F3b litters.

B. Organization of Groups

A structural outline of the experiment is given in Table I. A flow chart depicting the three generations is shown in Figure 1.

* Charles River Breeding Laboratories, Inc., North Wilmington, Mass.

TABLE I

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

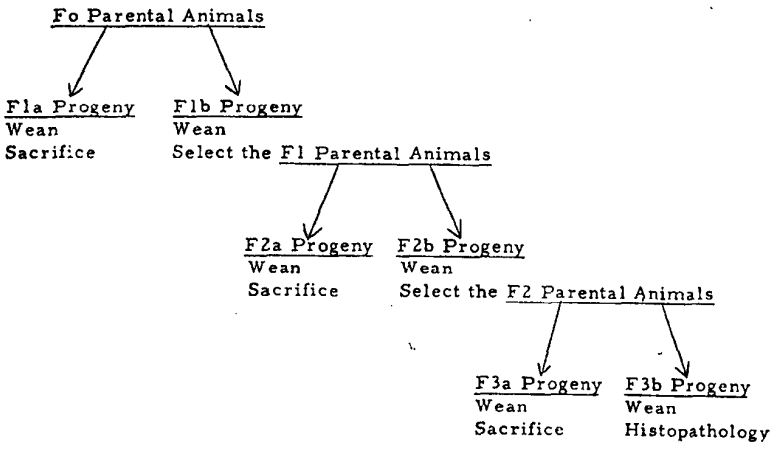
Outline of Experiment

Group	Dietary Level (ppm)	Number of Animals Male	Female
Control	None	8	16
T-I	1	8	16
T-II	10	8	16
T-III	100	8	16

FIGURE 1

TEST MATERIAL: Aroclor 1242

Design of Experiment



Gross and histopathologic examinations were conducted upon parental animals of all three generations following the weaning of the second (b) litters.

C. Diets and Feeding

Diets were prepared in the central diet room of this laboratory. The diet for any given test group was prepared by incorporating a calculated weight of Aroclor 1242 into a standard pulverized stock ration*, so that the final concentrations of test material in the diets were 1, 10 and 100 parts per million respectively. The animals in the control group were fed the basic ration without test material. Animals in all groups were maintained on their respective diets without interruption until their sacrifice, which followed the weaning of the second litters. Feeding was conducted on an ad libitum basis with fresh diets prepared weekly.

D. Body Weights and Weight Gains

Initially, the body weight of each rat was determined and recorded at 21 days of age. All animals were then weighed weekly until mating trials commenced. No further body weight data were obtained until the sacrifice of each parental generation, at which time final body weights were recorded.

E. Mortality, Reactions and General Observations

Observations among animals of each generation for mortality and abnormal behavioral reactions were made daily. In addition, these animals were observed for fertility, length of gestation and lactation performance.

* Special Mix Mouse Chow, Ralston Purina Company, St. Louis, Missouri.

All pups were examined for physical abnormalities at birth and the numbers of viable and stillborn members of each litter were recorded. Records of survival at designated intervals during the lactation period were maintained and a final examination for physical abnormalities was made at the weaning of each litter. Litters of more than ten pups were reduced to that number by random sacrifice on the fifth day of the lactation period.

F. Mating Procedure

Mating trials were initiated when the parental animals were 100 days old. Females were caged in pairs and mated with a male from within the same treatment group. Daily examinations were conducted to determine if copulation had occurred. Males were rotated within their dietary group at ten day intervals until conception was confirmed or until each female had been paired with a maximum of three males.

The first litters (F1a, F2a and F3a) obtained were weaned at 21 days post-partum. The parental females were then given a ten-day rest period and again mated, the above procedure being repeated in order to obtain second litters (F1b, F2b and F3b). Females failing to become pregnant during the first mating trials were not rebred.

Eight males and 16 females from the second litters of each group were selected at weaning on the basis of health and body weight as parental animals for each succeeding generation.

G. Gross and Microscopic Pathologic Studies

Whenever a parental animal succumbed during the test period, a gross autopsy was performed. In those instances when postmortem changes were not advanced, representative tissues were taken for microscopic study.

After the second litters were weaned, all surviving males and eight females from each group were sacrificed and subjected to gross pathologic examination. The weights of the liver, kidneys, spleen, gonads, heart and brain were recorded, along with the final body weight of each rat.

Statistical analyses were conducted upon the absolute organ weights of the sacrificed animals and upon the corresponding organ to body weight and organ to brain weight ratios. An Analysis of Variance was conducted first and significant effects disclosed by that treatment were further studied by "t"-tests.

Microscopic pathologic studies were conducted upon five males and five females (Fo and F1) from the control and T-III groups; the T-II and control groups were examined following sacrifice of the F2 generation.

The following tissues and organs were examined:

Tissues and Organs Examined Grossly	Tissues and Organs Examined Microscopically
Skin	Heart (right and left ventricles)
Heart	Trachea
Trachea	Lung
Lungs	Liver
Liver	Pancreas
Pancreas	Stomach (cardiac, fundic and pyloric regions)
Esophagus	Small Intestine (duodenum, jejunum and ileum)
Stomach	Caecum
Intestinal Tract	Colon
Spleen	Spleen
Lymph Nodes	Lymph Node (cervical and mesenteric)
Kidneys	Kidney
Urinary Bladder	Urinary Bladder
Testes	Testis
Ovaries	Ovary
Prostate	Prostate
Seminal Vesicles	Uterus
Uterus	Pituitary Gland
Vagina	Adrenal Gland
Pituitary Gland	Salivary Gland (submaxillary)
Adrenal Glands	Thyroid Gland
Salivary Glands	Parathyroid Gland
Thyroid Gland	Skeletal Muscle
Skeletal Muscle	Bone Marrow (sternum and femur)
Bone	Peripheral Nerve (sciatic)
Peripheral Nerve	Brain (cerebrum, cerebellum and pons)
Eyes	Seminal Vesicles
Brain	Esophagus
Thymus	Spinal Cord
Optic Nerve	
Aorta	

IV. Results

A. Parental Animals

1. Body Weights

Body weight data are presented in Tables II and III. Included in the data on these tables are total weight gains over the first 77 days of the feeding period.

There were no differences between test and control animals which could be related to the ingestion of Aroclor 1242.

TABLE II

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Parental Male Rats

oup	Generation	Mean Body Weight (grams) Day Number: 0	7	14	21	28	35	42	49	56	63	70	77	Total Weight Gain (grams)	Final Body Weight at Sacrifice
	Fo	-	95	142	202	253	309	354	393	426	456	480	492	397	709
	F1	47	77	112	152	192	234	271	316	349	382	416	438	391	636
	F2	49	77	108	140	164	200	234	265	295	319	345	354	305	592
-I	Fo	-	95	137	192	242	292	336	374	409	435	458	475	380	707
ppm)	F1	48	76	115	164	212	259	297	335	371	393	421	444	396	639
	F2	58	98	149	195	234	280	327	357	390	408	436	455	397	680
-II	Fo	-	95	141	200	249	297	341	366	394	422	447	466	371	661
0 ppm)	F1	50	85	123	169	221	271	306	346	394	422	438	455	405	636
	F2	52	92	136	176	221	262	285	313	341	362	380	394	342	574
-III	Fo	-	95	139	196	224	292	340	375	400	433	461	474	379	720
00 ppm)	F1	45	73	112	153	194	245	291	339	366	409	432	450	405	652

ote: All animals were 28 days old at day number seven.

TABLE III

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Parental Female Rats

up	Generation	Mean Body Weight (grams) Day Number: 0	7	14	21	28	35	42	49	56	63	70	77	Total Weight Gain (grams)	Final Body Weight at Sacrifice
	Fo	-	93	127	158	182	203	220	233	240	250	257	266	173	388
	F1	45	73	104	134	156	180	197	220	229	237	246	248	203	349
	F2	44	66	89	113	134	152	163	178	183	193	199	212	168	316
	Fo	-	93	126	155	179	203	221	232	243	252	262	270	177	388
)pm)	F1	46	75	107	140	156	176	196	216	225	229	248	252	206	304
	F2	48	76	104	134	144	169	177	186	191	205	213	214	166	318
I	Fo	-	93	127	158	181	200	219	230	241	248	256	263	170	387
ppm)	F1	49	78	107	138	167	176	204	222	237	249	256	263	214	338
	F2	49	79	116	137	160	177	189	200	212	223	231	237	188	360
II	Fo	-	93	127	160	184	207	224	236	247	254	264	272	179	372
0 ppm)	F1	42	69	103	136	160	182	206	223	237	252	261	270	228	392

e: All animals were 28 days old at day number seven.

MONS 089333

2. Mortality

Mortality data are presented in Tables IV and V.

Gross autopsy performed on animals which succumbed during the test period failed to reveal any relationship between the ingestion of Aroclor 1242 and the death of the animal.

TABLE IV

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mortality Data

Parental Generation Males

Group	Generation	First Mating			Second Mating		
		Pre-M	M	Post-M	M	Post-M	Total
C	Fo	0	0	0	0	0	0
	F1	0	0	0	0	0	0
	F2	0	0	0	0	1	1
T-I	Fo	0	0	0	0	0	0
(1 ppm)	F1	0	0	0	0	1	1
	F2	0	0	0	0	0	0
T-II	Fo	0	0	0	0	0	0
(10 ppm)	F1	0	0	0	0	0	0
	F2	0	0	0	0	1	1
T-III	Fo	1	0	0	0	0	1
(100 ppm)	F1	0	0	0	0	1	1

Pre-M = Pre-Mating Period
M = Mating Period
Post-M = Post-Mating Period

MONS 080335

TABLE V

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mortality Data

Parental Generation Females

Group	Generation	First Mating						Second Mating					
		Pre-M	M	G	P	L	R	M	G	P	L	Post-W	Total
C	Fo	0	0	0	1	0	0	0	0	0	0	0	1
	F1	0	0	0	0	0	0	0	0	0	0	0	0
	F2	0	0	0	0	0	1	0	0	0	0	0	1
T-I	Fo	0	0	0	0	0	0	0	0	0	1	0	1
(1 ppm)	F1	0	0	0	0	0	0	0	0	0	0	1	1
	F2	0	0	0	0	0	0	0	0	0	0	0	0
T-II	Fo	0	0	0	0	0	0	0	0	0	0	0	0
(10 ppm)	F1	0	0	0	0	0	0	0	0	0	0	0	0
	F2	0	0	0	0	0	0	0	0	0	0	0	0
T-III	Fo	0	0	0	0	0	0	0	0	0	0	0	0
(100 ppm)	F1	0	0	0	0	0	0	0	0	0	0	0	0

Pre-M = Pre-Mating Period
M = Mating Period
G = Gestation Period
P = Parturition
L = Lactation Period
R = Resting Period
Post-W = Post-Weaning Period

MONS 0093336

Industrial BIO-TEST Laboratories, Inc.

3. Reactions

No untoward reactions were noted among the parental animals during the investigation.

4. Pathologic Findings

a. Gross Pathologic Findings

There were no gross pathologic findings which could be correlated with ingestion of the test material. Findings among test animals were comparable to those noted among control animals.

b. Organ Weights and Ratios

Mean organ weights, organ to body weight ratios and organ to brain weight ratios are assembled in Tables VI through XIII.

The absolute liver weights and liver to body weight or brain weight ratios were significantly elevated in both F1 males and females fed 100 ppm Aroclor 1242.

Statistical evaluations of the other organ weights and ratios revealed several intergroup differences. There was no consistent dose or generation related response and these differences were not attributed to the ingestion of Aroclor 1242.

TABLE VI

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Liver

Group	Generation	Organ Weight (g) Males	Organ Weight (g) Females	Organ/Body Weight Ratio (g/100 g) Males	Organ/Body Weight Ratio (g/100 g) Females	Organ/Brain Weight Ratio (g/g) Males	Organ/Brain Weight Ratio (g/g) Females
C	Fo	28.0	16.3	3.96	4.26	12.9	8.68
	F1	24.7	15.2	3.90	4.41	11.9	7.92
	F2	23.6	12.2	3.97	3.87	11.6	6.97
T-I (1 ppm)	Fo	26.8	16.8	3.80	4.33	12.6	8.61
	F1	24.4	13.4**	3.87	4.45	11.8	7.06*
	F2	22.7	12.0	3.38**	3.80	10.5	6.02
T-II (10 ppm)	Fo	26.5	16.0	4.02	4.18	12.0	7.77
	F1	26.7	16.1	4.20*	4.78	12.4	8.36
	F2	22.5	15.1	3.94	4.25	10.6	7.80
T-III (100 ppm)	Fo	29.9	17.6	4.18	4.75	14.4*	7.90
	F1	30.8*	18.3**	4.75*	4.73	15.8**	10.30**

MONS 089338

* Statistically significant difference at the 95 percent confidence level.
** Statistically significant difference at the 99 percent confidence level.

TABLE VII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Kidneys

Group	Generation	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
		Males	Females	Males	Females	Males	Females
C	Fo	4.82	2.77	0.680	0.724	2.22	1.48
	F1	4.44	2.68	0.709	0.771	2.14	1.40
	F2	4.01	2.43	0.681	0.774	1.99	1.39
T-I (1 ppm)	Fo	4.30	2.72	0.610*	0.704	2.02	1.39
	F1	4.47	2.65	0.709	0.882**	2.17	1.39
	F2	4.03	2.37	0.601**	0.755	1.87	1.19
T-II (10 ppm)	Fo	4.59	2.95	0.693	0.771	2.08	1.44
	F1	4.56	2.74	0.723*	0.813	2.13	1.42
	F2	3.71	2.68	0.647	0.755	1.74	1.38
T-III (100 ppm)	Fo	4.26	3.02	0.593**	0.816**	2.05	1.33
	F1	4.09	2.74	0.626*	0.711	2.09	1.55

* Statistically significant difference at the 95 percent confidence level.
** Statistically significant difference at the 99 percent confidence level.

MONS 089339

TABLE VIII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Spleen

Group	Generation	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
		Males	Females	Males	Females	Males	Females
C	Fo	0.83	0.63	0.12	0.16	0.38	0.33
	F1	0.74	0.61	0.12	0.18	0.36	0.32
	F2	0.96	0.63	0.16	0.20	0.48	0.36
T-I (1 ppm)	Fo	0.85	0.59	0.12	0.15	0.40	0.30
	F1	0.73	0.53	0.12	0.18	0.35	0.28
	F2	0.83*	0.57	0.12**	0.18	0.38**	0.28
T-II (10 ppm)	Fo	0.89	0.59	0.14	0.15	0.41	0.29
	F1	0.78	0.64	0.12	0.19	0.36	0.33
	F2	0.76*	0.62	0.13*	0.18	0.35**	0.32
T-III (100 ppm)	Fo	0.82	0.58	0.11	0.16	0.40	0.25
	F1	0.82	0.60	0.13	0.15	0.42	0.34

* Statistically significant difference at the 95 percent confidence level.
** Statistically significant difference at the 99 percent confidence level.

MONS 0893940

TABLE IX

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Gonads

Group	Generation	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
		Males	Females	Males	Females	Males	Females
C	Fo	3.62	0.117	0.510	0.0302	1.67	0.0627
	F1	3.57	0.099	0.576	0.0283	1.72	0.0524
	F2	3.18	0.132	0.530	0.0424	1.57	0.0757
T-I (1 ppm)	Fo	3.59	0.116	0.512	0.0303	1.69	0.0590
	F1	3.66	0.080	0.581	0.0263	1.77	0.0415
	F2	3.56	0.111	0.536	0.0353	1.65	0.0561
T-II (10 ppm)	Fo	3.61	0.131	0.549	0.0338	1.64	0.0637
	F1	3.78	0.119	0.630	0.0361	1.76	0.0620
	F2	3.74	0.130	0.652*	0.0375	1.75	0.0668
T-III (100 ppm)	Fo	3.55	0.114	0.501	0.0310	1.70	0.0505
	F1	3.69	0.102	0.571	0.0274	1.89	0.0579

* Statistically significant difference at the 95 percent confidence level.

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TABLE X

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Heart

Group	Generation	Organ Weight (g) Males	Organ Weight (g) Females	Organ/Body Weight Ratio (g/100 g) Males	Organ/Body Weight Ratio (g/100 g) Females	Organ/Brain Weight Ratio (g/g) Males	Organ/Brain Weight Ratio (g/g) Females
C	Fo	1.86	1.28	0.261	0.332	0.858	0.684
	F1	1.74	1.24	0.276	0.360	0.844	0.647
	F2	1.84	1.19	0.314	0.379	0.914	0.682
T-I (1 ppm)	Fo	1.79	1.28	0.254	0.333	0.843	0.655
	F1	1.87	1.32	0.297	0.440**	0.918	0.695
	F2	1.93	1.12	0.288	0.355	0.891	0.563
T-II (10 ppm)	Fo	1.71	1.25	0.259	0.331	0.775	0.611
	F1	1.82	1.10**	0.289	0.328*	0.851	0.574*
	F2	1.57	1.18	0.274	0.337	0.739	0.608
T-III (100 ppm)	Fo	1.92	1.25	0.267	0.337	0.927	0.561
	F1	1.83	1.28	0.284	0.332	0.944	0.727*

* Statistically significant difference at the 95 percent confidence level.
** Statistically significant difference at the 99 percent confidence level.

MUNS 089342

TABLE XI

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Brain

Group	Generation	Organ Weight (g) Males	Organ Weight (g) Females	Organ/Body Weight Ratio (g/100 g) Males	Organ/Body Weight Ratio (g/100 g) Females
C	Fo	2.17	1.90	0.307	0.509
	F1	2.07	1.93	0.334	0.566
	F2	2.01	1.74	0.345	0.557
T-I	Fo	2.12	1.96	0.303	0.510
(1 ppm)	F1	2.07	1.91	0.329	0.637
	F2	2.17	1.99	0.328	0.633
T-II	Fo	2.21	2.05	0.338	0.542
(10 ppm)	F1	2.15	1.93	0.346	0.577
	F2	2.12	1.94	0.371	0.559
T-III	Fo	2.08	2.01	0.294	0.540
(100 ppm)	F1	1.95	1.77*	0.302	0.464*

MGNS 089343

* Statistically significant difference at the 95 percent confidence level.

TABLE XII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Adrenal Glands

Group	Generation	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
		Males	Females	Males	Females	Males	Females
C	Fo	0.072	0.095	0.010	0.025	0.033	0.050
	F1	0.066	0.091	0.010	0.026	0.032	0.047
	F2	0.071	0.080	0.012	0.026	0.035	0.046
T-I (1 ppm)	Fo	0.065	0.102	0.009	0.026	0.030	0.052
	F1	0.063	0.077	0.010	0.026	0.031	0.040
	F2	0.061	0.075	0.009	0.024	0.028	0.038
T-II (10 ppm)	Fo	0.076	0.093	0.011	0.024	0.034	0.045
	F1	0.084*	0.088	0.013*	0.026	0.039**	0.045
	F2	0.063	0.088	0.011	0.025	0.030	0.045
T-III (100 ppm)	Fo	0.063	0.090	0.008	0.024	0.030	0.039
	F1	0.069	0.078	0.011	0.020	0.035	0.044

*Statistically significant difference at the 95 percent confidence level.
**Statistically significant difference at the 99 percent confidence level.

MONS 089344

TABLE XIII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Thyroid Gland

Group	Generation	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
		Males	Females	Males	Females	Males	Females
C	Fo	0.035	0.028	0.0050	0.0075	0.016	0.015
	F1	0.025	0.025	0.0040	0.0074	0.012	0.013
	F2	0.034	0.028	0.0056	0.0089	0.016	0.016
T-I (1 ppm)	Fo	0.036	0.031	0.0051	0.0081	0.017	0.016
	F1	0.034**	0.026	0.0054**	0.0087	0.016**	0.014
	F2	0.038	0.030	0.0059	0.0095	0.017	0.015
T-II (10 ppm)	Fo	0.042	0.026	0.0063*	0.0067	0.019	0.013
	F1	0.043**	0.029*	0.0069**	0.0087	0.020**	0.015*
	F2	0.040	0.035	0.0070	0.0099	0.019	0.018
T-III (100 ppm)	Fo	0.041	0.028	0.0057	0.0077	0.020	0.014
	F1	0.037*	0.032*	0.0057*	0.0082	0.019**	0.018**

* Statistically significant difference at the 95 percent confidence level.
** Statistically significant difference at the 99 percent confidence level.

MONS 089345

c. Histopathologic Findings

Histopathologic findings among sacrificed animals are summarized in Tables XIV through XVI. Table XVII summarizes the histopathologic examination of the urinary bladder conducted on all animals sacrificed from the final generation.

No tissue changes were observed microscopically which could be correlated with ingestion of test material. Findings among treated animals were essentially the same as those of control animals.

TABLE XIV

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Control Group - Fo Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Focal inflammation	3	0.5
		Tracheitis	1	2.0
	5 Females	Focal inflammation	1	1.0
Lung	5 Males	Focal inflammation	2	1.0
		Hyperemia	5	2.0
	5 Females	Focal inflammation	2	0.5
		Hyperemia	5	1.0
Pancreas	5 Males	Prominent islands of Langerhans	1	1.0
Kidney	5 Males	Focal inflammation	1	0.5
		Hyperemia	1	0.5
	5 Females	Hyperemia	2	1.0
Adrenal gland	5 Females	Hyperemia	3	1.0

MONS 089347

TABLE XIV continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Test Group III - Fo Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Focal inflammation	2	1.0
		Tracheitis	2	2.0
	5 Females	Focal inflammation	3	0.5
Lung	5 Males	Focal inflammation	1	1.0
		Brown macrophages	1	1.0
		Hyperemia	1	1.0
	5 Females	Focal inflammation	1	1.0
		Hyperemia	4	2.0
Liver	5 Males	Focal vacuolization	1	0.5
	5 Females	Focal pericholangitis	1	0.5
		Hyperemia	2	1.0

MONS 089348

TABLE XIV continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Test Group III - Fo Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Kidney	5 Males	Focal inflammation	1	0.5
		Nephritis	1	0.5
		Hyperemia	2	0.5
	5 Females	Nephritis	1	0.5
		Hyperemia	2	1.0
Adrenal gland	5 Males	Hyperemia	1	0.5
	5 Females	Hyperemia	1	0.5

All other tissues and organs examined were normal.

Grading System
0.5 = Minimal
1.0 = Slight
2.0 = Mild
3.0 = Moderate
4.0 = Severe
5.0 = Extreme

MONS 089349

TABLE XV

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Control Group - F1 Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Tracheitis	3	2.0
		Focal inflammation	1	1.0
	5 Females	Tracheitis	3	2.0
Lung	5 Males	Focal inflammation	5	2.0
	5 Females	Focal inflammation	4	1.0
		Focal inflammation with abscess	1	5.0
		Hyperemia	1	2.0
Liver	5 Females	Hyperemia	1	0.5
Kidney	5 Males	Nephrosis	2	0.5
		Nephritis	1	0.5
	5 Females	Nephrosis	1	0.5
Prostate	5 Males	Focal inflammation	1	0.5

MONS 089350

TABLE XV continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Test Group III - F1 Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Tracheitis	3	2.0
	5 Females	Tracheitis	2	1.0
		Focal inflammation	2	0.5
Lung	5 Males	Focal inflammation	5	2.0
		Hyperemia	3	1.0
	5 Females	Focal inflammation	4	0.5
		Focal inflammation with abscess	1	3.0
		Hyperemia	4	2.0
Liver	5 Males	Hyperemia	1	1.0
	5 Females	Hyperemia	1	1.0
Kidney	5 Males	Nephrosis	1	0.5
		Nephritis	1	0.5
	5 Females	Nephritis	1	0.5
Adrenal gland	5 Females	Hyperemia	1	1.0

All other tissues and organs examined were normal.

Grading System

0.5 = Minimal
1.0 = Slight
2.0 = Mild
4.0 = Severe
5.0 = Extreme

MONS 089351

TABLE XVI

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Control Group - F2 Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Focal inflammation	1	0.5
		Inflammation	2	3.0
	5 Females	Focal inflammation	1	0.5
		Inflammation	1	1.0
Lung	5 Males	Focal inflammation	4	1.0
		Inflammation with abscess	1	3.0
		Hyperemia	2	1.0
	5 Females	Focal inflammation	1	2.0
		Inflammation with abscess	1	4.0
		Hyperemia	3	2.0

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TABLE XVI continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Control Group - F2 Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Colon	5 Males	Focal inflammation	2	0.5
Liver	5 Females	Hyperemia	1	0.5
Kidney	5 Males	Focal inflammation	1	0.5
	5 Females	Nephrocalcinosis	1	0.5

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TABLE XVI continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Test Group II - F2 Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Focal inflammation	4	1.0
	5 Females	Focal inflammation	2	0.5
		Inflammation	1	2.0
Lung	5 Males	Focal inflammation	2	1.0
		Focal hyperemia	1	1.0
		Hyperemia	2	1.0
	5 Females	Focal inflammation	3	1.0
		Hyperemia	3	2.0
Colon	5 Males	Focal inflammation	1	1.0

All other tissues and organs examined were normal.

Grading System
0.5 = Minimal
1.0 = Slight
2.0 = Mild
3.0 = Moderate
4.0 = Severe
5.0 = Extreme

MONS 089354

TABLE XVII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes of the Urinary Bladder

F2 Generation

Group	Sex	Number Examined	Findings*	Incidence	Average Grade
C	M	7	None	-	-
	F	10	Focal epithelia hyperplasia associated with focal cystitis (11)	1	1.0
T-I (1 ppm)	M	7	Proteinaceous plug (30)	1	-
	F	15	None	-	-
T-II (10 ppm)	M	5	Proteinaceous plug (55)	1	-
			Focal epithelial hyperplasia (69)	1	1.0
	F	13	None	-	-

* Individual animal numbers are shown in parenthesis.

Grading System
1.0 = Minimal or Trace
2.0 = Mild
3.0 = Moderate
4.0 = Severe
5.0 = Extreme

MONS 089355

5. Reproductive Data

Reproductive data for parental animals are presented in Table XVIII. The indices employed are defined below:

$$\text{Mating Index} = \frac{\text{Number of Copulations*}}{\text{Number of Estrus Cycles Required}} \times 100$$

$$\text{Fertility Index} = \frac{\text{Number of Pregnancies}}{\text{Number of Copulations}} \times 100$$

$$\text{Incidence of Pregnancy} = \frac{\text{Number of Pregnancies}}{\text{Number of Females Mated}} \times 100$$

$$\text{Incidence of Parturition} = \frac{\text{Number of Parturitions}}{\text{Number of Pregnancies}} \times 100$$

The addition of 1 or 10 ppm Aroclor 1242 to the diet did not affect the reproductive performance of rats during the three-generation study. During the second generation (F2a and F2b litters) rats fed 100 ppm (T-III) had lowered mating indices and a reduced incidence of pregnancy. Because only two T-III females produced F2b litters it was not possible to continue this level through the third generation.

* Only one copulation counted per estrus cycle. Five days equal one estrus cycle.

TABLE XVIII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Parental Animals

Reproductive Performance

Group	Litter	Mating Index Fraction	Mating Index Percent	Incidence of Pregnancy Fraction	Incidence of Pregnancy Percent	Fertility Index Fraction	Fertility Index Percent	Incidence of Parturition Fraction	Incidence of Parturition Percent	Gestation Time (Days) Mean	Gestation Time (Days) Range
C	F1a	17/25	68.0	16/16	100.0	16/17	94.1	15/16	93.8	22	19-22
	F1b	15/20	75.0	15/15	100.0	15/15	100.0	15/15	100.0	22	21-22
	F2a	16/37	43.2	14/16	87.5	14/16	87.5	14/14	100.0	21	20-22
	F2b	14/26	53.8	14/14	100.0	14/14	100.0	14/14	100.0	22	21-23
	F3a	15/66	22.7	13/16	81.2	13/15	86.7	11/13	84.6	22	21-22
	F3b	12/16	75.0	12/12	100.0	12/12	100.0	11/12	91.7	22	21-22
T-1 (1 ppm)	F1a	16/37	43.2	16/16	100.0	16/16	100.0	16/16	100.0	22	21-23
	F1b	15/21	71.4	15/15	100.0	15/16	93.8	15/15	100.0	22	21-24
	F2a	15/27	55.6	15/16	93.8	15/15	100.0	15/15	100.0	22	20-22
	F2b	15/18	83.3	14/15	93.3	14/15	93.3	14/14	100.0	22	21-23
	F3a	13/77	16.9	9/16	56.2	9/13	69.2	9/9	100.0	22	21-22
	F3b	9/23	39.1	8/9	88.8	8/9	88.9	8/8	100.0	21	20-22

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TABLE XVIII continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Parental Animals

Reproductive Performance

Group	Litter	Mating Index Fraction	Mating Index Percent	Incidence of Pregnancy Fraction	Incidence of Pregnancy Percent	Fertility Index Fraction	Fertility Index Percent	Incidence of Parturition Fraction	Incidence of Parturition Percent	Gestation Time (Days) Mean	Gestation Time (Days) Range
T-II	F1a	16/43	37.2	16/16	100.0	16/16	100.0	15/16	93.8	22	21-23
(10 ppm)	F1b	16/24	66.7	16/16	100.0	16/16	100.0	16/16	100.0	22	21-23
	F2a	13/53	24.5	12/16	75.0	12/13	92.3	12/12	100.0	22	21-22
	F2b	13/24	54.2	12/12	100.0	12/13	92.3	12/12	100.0	22	21-22
	F3a	16/43	37.2	16/16	100.0	16/16	100.0	15/16	93.8	22	21-22
	F3b	16/28	57.1	15/16	93.8	15/16	93.8	15/15	100.0	22	22-23
T-III	F1a	15/43	34.9	15/16	93.8	15/15	100.0	14/15	93.3	22	21-23
(100 ppm)	F1b	15/24	62.5	15/15	100.0	15/15	100.0	15/15	100.0	22	21-23
	F2a	11/78	14.1	7/16	43.8	7/11	63.6	7/7	100.0	21	-
	F2b	2/37	5.4	2/7	28.6	2/2	100.0	2/2	100.0	22	-

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B. Progeny

1. Population Data

Population data for all litters are presented in Tables XIX and XX. The number of live pups born per litter and the number of pups weaned per litter were not affected by feeding 1, 10 or 100 ppm Aroclor 1242. All pups delivered appeared outwardly normal and displayed normal growth through the lactation period. At weaning, an examination of each pup for external abnormalities was conducted and all pups were judged to be free of gross external abnormalities.

TABLE XIX

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups Delivered		Number of Pups Stillborn		Number of Pups Cannibalized		Number of Viable Pups Born	
		Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter
;	F1a	178	11.9	13	0.9	0	-	165	11.0
	F1b	191	12.7	12	0.8	1	0.1	178	11.9
	F2a	147	10.5	7	0.5	0	-	140	10.0
	F2b	164	11.7	0	-	0	-	164	11.7
	F3a	102	9.3	10	0.9	0	-	92	8.4
	F3b	109	9.9	15	1.4	1	0.1	93	8.5
'-I	F1a	184	11.5	9	0.6	1	0.1	174	10.9
l ppm)	F1b	208	13.9	11	0.7	4	0.3	193	12.9
	F2a	158	10.5	3	0.2	1	0.1	154	10.3
	F2b	142	10.1	2	0.1	0	-	140	10.0
	F3a	86	9.5	11	1.2	0	-	75	8.3
	F3b	80	10.0	7	0.9	4	0.5	71	8.9

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TABLE XIX continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups Delivered		Number of Pups Stillborn		Number of Pups Cannibalized		Number of Viable Pups Born	
		Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter	Total	Mean/Litter
T-II	F1a	176	11.7	3	0.2	0	-	173	11.5
(10 ppm)	F1b	207	12.9	4	0.2	0	-	203	12.7
	F2a	126	10.5	8	0.7	0	-	118	9.8
	F2b	138	11.5	5	0.4	0	-	133	11.1
	F3a	149	9.9	17	1.1	5	0.3	127	8.5
	F3b	171	11.4	8	0.5	3	0.2	160	10.7
T-III	F1a	168	12.0	8	0.6	4	0.3	156	11.1
(100 ppm)	F1b	203	13.5	3	0.2	0	-	200	13.3
	F2a	53	7.6	6	0.9	2	0.3	45	6.4
	F2b	20	10.0	2	1.0	2	1.0	16	8.0

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TABLE XX

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups at Lactation Day 1 Total	Number of Pups at Lactation Day 1 Mean/Litter	Number of Pups at Lactation Day 5 Total	Number of Pups at Lactation Day 5 Mean/Litter	Number of Pups Retained at Lactation Day 5 Total	Number of Pups Retained at Lactation Day 5 Mean/Litter	Number of Weanlings Male	Number of Weanlings Female	Number of Weanlings Total	Number of Weanlings Mean/Litter
;	F1a	146	9.7	70	4.7	66	4.4	34	28	62	4.1
	F1b	176	11.7	117	7.8	103	6.9	31	35	66	4.4
	F2a	132	9.4	90	6.4	78	5.6	30	34	64	4.6
	F2b	163	11.6	135	9.6	115	8.2	39	46	85	6.1
	F3a	90	8.2	69	6.3	65	5.9	26	25	51	4.6
	F3b	91	8.3	79	7.2	75	6.8	16	26	42	3.8
Γ-I	F1a	176	11.0	103	6.4	91	5.7	36	53	89	5.6
1 ppm)	F1b	175*	12.5	148	10.6	120	8.6	46	40	86	6.1
	F2a	152	10.1	107	7.1	99	6.6	37	39	76	5.1
	F2b	133	9.5	100	7.1	90	6.4	37	30	67	4.8
	F3a	69	7.7	46	5.1	39	4.3	12	13	25	2.8
	F3b	66	8.2	46	5.8	45	5.6	12	11	23	2.9

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* One female died on Day 1 of lactation. Pups from this litter were sacrificed and are not included in the totals and means.

TABLE XX continued

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups at Lactation Day 1 Total	Number of Pups at Lactation Day 1 Mean/Litter	Number of Pups at Lactation Day 5 Total	Number of Pups at Lactation Day 5 Mean/Litter	Number of Pups Retained at Lactation Day 5 Total	Number of Pups Retained at Lactation Day 5 Mean/Litter	Number of Weanlings Male	Number of Weanlings Female	Number of Weanlings Total	Number of Weanlings Mean/Litter
T-II	F1a	170	11.3	133	8.9	118	7.9	59	49	108	7.2
(10 ppm)	F1b	202	12.6	163	10.2	134	8.4	46	60	106	6.6
	F2a	109	9.1	96	8.0	90	7.5	38	39	77	6.4
	F2b	132	11.0	115	9.6	103	8.6	37	37	74	6.2
	F3a	126	8.4	114	7.6	105	7.0	44	60	104	6.9
	F3b	152	10.1	119	7.9	102	6.8	51	46	87	5.8
T-III	F1a	149	10.6	133	9.5	122	8.7	44	51	95	6.8
(100 ppm)	F1b	196	13.1	133	8.9	111	7.4	31	28	59	3.9
	F2a	37	5.3	36	5.1	36	5.1	14	21	35	5.0
	F2b	15	7.5	15	7.5	13	6.5	5	6	11	5.5

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2. Survival Data

Survival data for progeny are presented in Table XXI. Live birth, 24 hour, five day and lactation indices were normal for all groups.

The indices employed are defined below.

$$\text{Live Birth Index} = \frac{\text{Number of Viable Pups Born}}{\text{Total Number of Pups Born}} \times 100$$

$$\text{24-Hour Survival Index} = \frac{\text{Number of Pups Viable at Lactation Day 1}}{\text{Number of Viable Pups Born}} \times 100$$

$$\text{5-Day Survival Index} = \frac{\text{Number of Pups Viable at Lactation Day 5}}{\text{Number of Viable Pups Born}} \times 100$$

$$\text{Lactation Index} = \frac{\text{Number of Pups Viable at Lactation Day 21}}{\text{Number of Pups Viable at Lactation Day 5}} \times 100$$

TABLE XXI

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Survival Indices

Progeny

Group	Litter	Live Birth Index	24-Hour Survival Index	5-Day Survival Index	Lactation Index
C	F1a	92.7	88.5	42.4	93.9
	F1b	93.4	98.9	65.7	64.1
	F2a	95.2	94.3	64.3	81.2
	F2b	100.0	99.3	82.3	73.9
	F3a	90.2	97.8	75.0	78.5
	F3b	85.3	97.8	85.0	56.0
T-I (1 ppm)	F1a	94.6	98.3	59.2	97.8
	F1b	92.8	97.2	82.2	71.7
	F2a	97.5	98.7	69.5	76.8
	F2b	95.5	95.0	71.4	74.4
	F3a	87.2	92.0	61.3	64.1
	F3b	88.8	93.0	63.4	51.1
T-II (10 ppm)	F1a	98.3	98.3	76.9	91.5
	F1b	98.1	99.5	80.3	79.1
	F2a	93.7	92.4	81.4	85.6
	F2b	96.3	99.2	86.4	71.8
	F3a	85.2	99.2	82.7	99.0
	F3b	94.1	95.0	74.4	85.3
T-III (100 ppm)	F1a	92.9	95.5	85.3	77.9
	F1b	98.5	98.0	66.5	53.2
	F2a	84.9	82.2	80.0	97.2
	F2b	80.8	93.8	93.8	84.6

3. Body Weight Data

Body weight data for weanlings are presented in Table XXII.

There are no significant differences between test and control weanling body weights.

TABLE XXII

TEST MATERIAL: Aroclor 1242

Three-Generation Reproduction Study - Albino Rats

Progeny

Weanling Body Weight Data

Group	Litter	Mean Body Weight (grams) Male	Female
C	F1a	44	44
	F1b	47	43
	F2a	46	43
	F2b	41	39
	F3a	45	44
	F3b	42	42
T-I (1 ppm)	F1a	46	46
	F1b	46	45
	F2a	47	44
	F2b	45	40
	F3a	38	38
	F3b	35	39
T-II (10 ppm)	F1a	49	47
	F1b	52	47
	F2a	48	47
	F2b	41	45
	F3a	49	46
	F3b	39	43
T-III (100 ppm)	F1a	45	43
	F1b	42	42
	F2a	55	48
	F2b	38	37

4. Pathologic Studies

At autopsy of the F3b weanlings no gross or microscopic tissue changes were present which could be associated with the ingestion of Aroclor 1242.