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

REPORT TO

MONSANTO COMPANY

THREE-GENERATION REPRODUCTION STUDY WITH AROCLOR 1260 IN ALBINO RATS

NOVEMBER 4, 1971

IBT NO. B7297

0636649

TOXSTUDIES1477

REPORT TO

MONSANTO COMPANY

THREE-GENERATION REPRODUCTION STUDY WITH AROCLOR 1260 IN ALBINO RATS

NOVEMBER 4, 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 1260, Lot No. AK-3, 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.

TOXSTUDIES1478

II. Summary

A three-generation reproduction study employing albino rats fed diets containing 1, 10 or 100 ppm Aroclor 1260 was conducted. The following results were obtained during the investigation.

A. Parental Animals

1. Body Weights

Body weight gains revealed no differences between test and control animals which could be attributed to the ingestion of Aroclor 1260.

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 1260.

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 Fo and F1 males fed 100 ppm Aroclor 1260. This elevation was not found in the F2 males. 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 1260.

TOXSTUDIES1479

All lesions noted during histopathologic studies were similar for test and control animals.

4. Reproductive Performance

Reproductive indices of rats fed 1, 10 or 100 ppm Aroclor 1260 did not differ from those of the controls during any of the three generations.

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 1260 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.

TOXSTUDIES1480

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 1260.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Sandra Haley
Assistant Toxicologist
Rat Toxicity

Report approved by:

James B. Plank
Senior Group Leader
Rat Toxicity

Paul L. Wright, Ph.D.
Section Head, Toxicology

M. L. Keplinger, Ph.D.
Manager, Toxicology

November 4, 1971

sjn/jg/psh

0636653

TOXSTUDIES1481

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.

TOXSTUDIES1482

TABLE I

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Outline of Experiment

Fo Generation

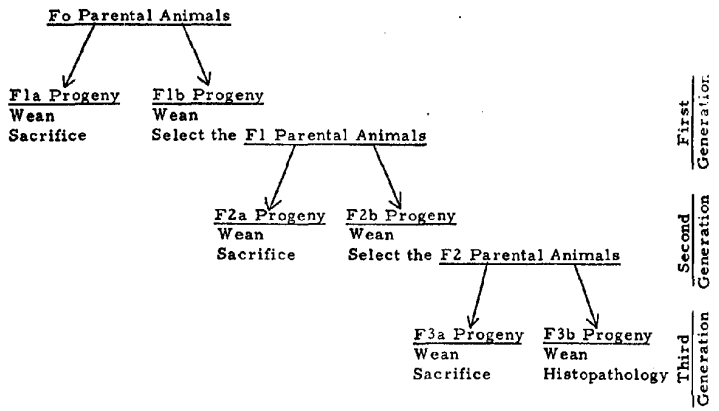
Group	Dietary Level (ppm)	Number of Animals Male	Female
Control	None	8	16
T-I	1	8	16
T-II	10	8	16
T-III	100	8	16

TOXSTUDIES1483

FIGURE 1

TEST MATERIAL: Aroclor 1260

Design of Experiment



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

TOXSTUDIES1484

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 1260 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; fresh diets were 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.

TOXSTUDIES1485

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.

TOXSTUDIES1486

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 from the control and T-III groups.

The following tissues and organs were examined:

TOXSTUDIES1487

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	

0636660

TOXSTUDIES1488

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 in body weight gains between test and control animals which could be related to the ingestion of Aroclor 1260.

TOXSTUDIES1489

TABLE II

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Mean Body Weight and Weight Gain Data

Parental Male Rats

Group	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
C	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
T-I	Fo	-	95	139	192	241	286	325	355	393	415	438	457	362	648
(1 ppm)	F1	48	73	101	141	185	232	272	312	345	376	397	422	374	626
	F2	55	89	132	175	216	269	302	328	358	378	398	407	352	624
T-II	Fo	-	95	135	187	233	290	343	382	431	457	485	510	415	709
(10 ppm)	F1	52	82	119	163	206	257	296	337	372	401	421	445	393	692
	F2	50	80	118	167	212	256	294	330	362	384	409	432	382	631
T-III	Fo	-	95	142	204	256	305	355	388	433	456	481	501	406	760
(100 ppm)	F1	49	80	126	173	223	271	321	344	373	406	441	364	315	696
	F2	49	72	101	142	176	234	265	293	326	359	384	401	352	633

0636662

TOXSTUDIES1490

TABLE III

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Mean Body Weight and Weight Gain Data

Parental Female Rats

Group	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
C	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
T-I	Fo	-	93	124	157	178	200	215	224	239	247	255	265	172	369
(1 ppm)	F1	45	69	95	120	147	170	188	205	219	231	238	249	204	329
	F2	53	79	111	136	154	174	181	188	201	208	215	221	168	321
T-II	Fo	-	93	125	158	180	202	221	231	244	250	257	266	173	410
(10 ppm)	F1	50	77	106	138	152	189	199	213	234	252	245	267	217	388
	F2	46	68	100	126	146	168	183	197	209	216	225	221	175	372*
T-III	Fo	-	93	124	155	177	198	215	226	237	247	253	264	171	360
(100 ppm)	F1	46	68	100	130	154	175	194	208	225	238	249	255	209	370
	F2	42	68	94	119	141	157	174	190	202	214	223	230	188	363*

* Statistically significant difference at the 95 percent confidence level.

TOXSTUDIES1491

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 1260 and the death of the animal.

TOXSTUDIES1492

TABLE IV

TEST MATERIAL: Aroclor 1260

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	0	0
	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	0	0
T-III	Fo	0	0	0	0	0	0
(100 ppm)	F1	0	0	0	0	0	0
	F2	1	0	0	0	1	2

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

0636665

TOXSTUDIES1493

TABLE V

TEST MATERIAL: Aroclor 1260

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	0	0	0
(1 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-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	1	0	0	1
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
	F2	1	0	0	0	0	0	0	0	1	0	0	2

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

0636666

TOXSTUDIES1494

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 Fo and F1 males fed 100 ppm Aroclor 1260. This increase was not found in the F2 males of this group. Both elevations and depressions in liver weights were found in several of the other treatment groups. These variations in liver weight did not follow a dose related pattern.

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 1260.

TOXSTUDIES1495

TABLE VI

TEST MATERIAL: Aroclor 1260

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	Fo	20.1**	14.5	3.12**	3.96	9.8**	7.30
(1 ppm)	F1	26.1	14.0	4.21	4.28	13.0	6.74**
	F2	22.2	14.2*	3.55*	4.43	10.6	7.14
T-II	Fo	23.3**	18.2	3.32**	4.44	11.2**	9.57
(10 ppm)	F1	29.8*	14.0	4.31*	3.63**	14.7*	7.56
	F2	22.2	15.6*	3.58*	4.20	10.6	7.87
T-III	Fo	35.3**	18.3	4.72**	5.12**	16.5**	9.72
(100 ppm)	F1	33.7**	16.6	4.84*	4.45	15.9*	8.55
	F2	25.0	14.9*	3.94	4.13	12.2	7.83

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

0636668

TOXSTUDIES1496

TABLE VII

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Mean Organ Weights and Ratios

Parental Animals

Organ: Kidneys

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	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	Fo	3.85**	2.76	0.598**	0.751	1.88**	1.39
(1 ppm)	F1	4.19	2.70	0.680	0.823	2.08	1.29
	F2	3.80	2.67	0.611	0.830	1.82	1.33
T-II	Fo	4.40*	2.97	0.623**	0.731	2.13	1.57
(10 ppm)	F1	4.61	2.85	0.668	0.774	2.26	1.54
	F2	3.73	2.83	0.619	0.763	1.78	1.43
T-III	Fo	4.95	2.79	0.660	0.783	2.31	1.49
(100 ppm)	F1	4.55	2.76	0.656	0.747	2.15	1.42
	F2	3.74	2.55	0.589	0.705*	1.82	1.33

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

TOXSTUDIES1497

TABLE VIII

TEST MATERIAL: Aroclor 1260

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	0.95	0.63	0.16	0.20	0.47	0.35
T-I (1 ppm)	Fo	0.83	0.54	0.13	0.15	0.41	0.27
	F1	0.72	0.58	0.12	0.18	0.36	0.27
	F2	0.79	0.64	0.12**	0.20	0.37*	0.32
T-II (10 ppm)	Fo	0.84	0.59	0.12	0.15	0.41	0.31
	F1	0.79	0.49	0.11	0.13*	0.39	0.27
	F2	0.79	0.66	0.13*	0.17*	0.38*	0.33
T-III (100 ppm)	Fo	0.95	0.55	0.13	0.16	0.45	0.30
	F1	0.67	0.52	0.09	0.14*	0.32	0.27
	F2	0.71	0.57	0.11**	0.15*	0.35*	0.30

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

0636670

TOXSTUDIES1498

TABLE IX

TEST MATERIAL: Aroclor 1260

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	Fo	3.44	0.121	0.534	0.0332	1.68	0.0604
(1 ppm)	F1	3.33	0.103	0.545	0.0320	1.65*	0.0503
	F2	3.67	0.104	0.594	0.0330	1.76	0.0528*
T-II	Fo	3.68	0.136	0.524	0.0335	1.78	0.0710
(10 ppm)	F1	3.81	0.106	0.562	0.0284	1.88	0.0537
	F2	3.09	0.130	0.522	0.0353	1.47	0.0654
T-III	Fo	3.51	0.119	0.473	0.0332	1.64	0.0625
(100 ppm)	F1	4.11**	0.126	0.598	0.0339	1.94*	0.0648
	F2	3.59	0.121	0.568	0.0333	1.75	0.0630

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

D636671

TOXSTUDIES1499

TABLE X

TEST MATERIAL: Aroclor 1260

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	0.322	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	1.77	1.29	0.274	0.352	0.864	0.650
	F1	1.71	1.27	0.278	0.389	0.852	0.610
	F2	1.68	1.21	0.269	0.376	0.806	0.603
T-II (10 ppm)	Fo	1.96	1.40	0.277	0.346	0.947	0.740
	F1	1.75	1.18	0.255	0.310**	0.867	0.644
	F2	1.62	1.25	0.269	0.340	0.780	0.635
T-III (100 ppm)	Fo	2.05	1.32	0.277	0.370	0.961	0.704
	F1	1.89	1.16	0.272	0.315**	0.897	0.601
	F2	1.67	1.24	0.264	0.342	0.819	0.648

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

0636672

TOXSTUDIES1500

TABLE XI

TEST MATERIAL: Aroclor 1260

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	2.05	1.99	0.317	0.545
(1 ppm)	F1	2.01	2.09*	0.329	0.640
	F2	2.08	1.99**	0.336	0.625*
T-II	Fo	2.08	1.91	0.296	0.470
(10 ppm)	F1	2.03	1.85	0.297	0.487*
	F2	2.08	1.98**	0.359	0.536
T-III	Fo	2.15	1.89	0.290	0.533
(100 ppm)	F1	2.11	1.93	0.307	0.528
	F2	2.04	1.91**	0.323	0.534

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

0636673

TOXSTUDIES1501

TABLE XII

TEST MATERIAL: Aroclor 1260

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	0.025	0.035	0.045
T-I	Fo	0.062	0.090	0.009	0.024	0.030	0.046
(1 ppm)	F1	0.065	0.079	0.011	0.024	0.032	0.038*
	F2	0.061	0.100**	0.009	0.031	0.029	0.050
T-II	Fo	0.070	0.096	0.009	0.023	0.034	0.051
(10 ppm)	F1	0.063	0.083	0.009	0.022	0.031	0.045
	F2	0.065	0.083	0.011	0.022	0.031	0.042
T-III	Fo	0.076	0.090	0.010	0.025	0.036	0.049
(100 ppm)	F1	0.066	0.072	0.009	0.020*	0.031	0.037*
	F2	0.041	0.076	0.011	0.021	0.015	0.040*

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

0636674

TOXSTUDIES1502

TABLE XIII

TEST MATERIAL: Aroclor 1260

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	0.033	0.028	0.0056	0.0089	0.016	0.016
T-I	Fo	0.031	0.026	0.0048	0.0072	0.014	0.013
(1 ppm)	F1	0.029	0.021*	0.0047	0.0064	0.014	0.010
	F2	0.034	0.032	0.0055	0.0100*	0.016	0.016
T-II	Fo	0.031	0.028	0.0049	0.0070	0.015	0.015
(10 ppm)	F1	0.032**	0.024	0.0047*	0.0061	0.016**	0.013
	F2	0.034	0.028	0.0056	0.0076*	0.016	0.014
T-III	Fo	0.042	0.026	0.0057	0.0074	0.020	0.014
(100 ppm)	F1	0.046**	0.028	0.0065**	0.0078	0.022**	0.015
	F2	0.035	0.027	0.0056	0.0078	0.017	0.014

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

0636675

TOXSTUDIES1503

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.

TOXSTUDIES1504

TABLE XIV

TEST MATERIAL: Aroclor 1260

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

TOXSTUDIES1505

TABLE XIV continued

TEST MATERIAL: Aroclor 1260

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	Tracheitis	5	1.0
	5 Females	Tracheitis	3	2.0
Lung	5 Males	Focal inflammation	3	1.0
		Hyperemia	2	0.5
	5 Females	Focal inflammation	3	0.5
		Hyperemia	5	3.0
Liver	5 Males	Focal inflammation	1	1.0
Kidney	5 Males	Nephritis	2	1.0
	5 Females	Focal inflammation	1	0.5
		Nephritis	1	0.5
		Calcification	1	0.5
Adrenals	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
3.0 = moderate
4.0 = severe
5.0 = extreme

0636678

TOXSTUDIES1506

TABLE XV

TEST MATERIAL: Aroclor 1260

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

Industrial BIO-TEST Laboratories, Inc.

0636679

TOXSTUDIES1507

TABLE XV continued

TEST MATERIAL: Aroclor 1260

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	2	2.0
		Focal inflammation	1	0.5
	5 Females	Focal inflammation	3	1.0
Lung	5 Males	Focal inflammation	4	1.0
		Hyperemia	1	1.0
	5 Females	Focal inflammation	3	1.0
		Focal inflammation with dilatation of bronchi	1	3.0
		Hyperemia	2	2.0
Liver	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
3.0 = moderate
4.0 = severe
5.0 = extreme

0636680

TOXSTUDIES1508

TABLE XVI

TEST MATERIAL: Aroclor 1260

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
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

TOXSTUDIES1509

TABLE XVI continued

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Histopathologic Changes

Test Group III - F2 Generation

Organ	Number of Animals Examined	Findings	Incidence	Average Grade
Trachea	5 Males	Focal inflammation	3	0.5
	5 Females	Focal inflammation	3	0.5
Lung	5 Males	Focal inflammation	1	1.0
	5 Females	Focal inflammation	5	2.0
Pancreas	5 Males	Focal inflammation	1	1.0
		Focal fibrosis	1	1.0
Liver	5 Females	Hyperemia	1	1.0
Kidney	5 Males	Hyperemia	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

0636682

TOXSTUDIES1510

TABLE XVII

TEST MATERIAL: Aroclor 1260

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	12	Focal epithelial hyperplasia associated with focal cystitis (11)	1	1.0
T-I (1 ppm)	M	8	Proteinaceous plug (170, 174, 175, and 176)	4	-
	F	15	None	-	-
T-II 10 ppm)	M	7	Proteinaceous plug (193, 195, and 196)	3	-
	F	13	None	-	-
T-III (100 ppm)	M	6	Proteinaceous plug (224)	1	-
	F	14	Focal epithelial hyperplasia associated with focal cystitis and mineralized calculi	1	3.0

* 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

0636683

TOXSTUDIES1511

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, 10 or 100 ppm Aroclor 1260 to the diet did not affect the reproductive performance of rats during the three-generation study.

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

TOXSTUDIES1512

TABLE XVIII

TEST MATERIAL: Aroclor 1260

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-I (1 ppm)	F1a	16/25	64.0	16/16	100.0	16/16	100.0	16/16	100.0	22	20-23
	F1b	16/21	76.2	16/16	100.0	16/16	100.0	15/16	93.8	22	21-22
	F2a	13/53	24.5	13/16	81.2	13/13	100.0	13/13	100.0	22	21-23
	F2b	13/25	52.0	12/13	92.3	12/13	92.3	12/12	100.0	22	21-22
	F3a	17/69	24.6	11/16	68.8	11/17	64.7	10/11	90.9	22	21-22
	F3b	12/29	41.4	10/11	90.9	10/12	83.3	10/10	100.0	22	22-23

0636685

TOXSTUDIES1513

TABLE XVIII continued

TEST MATERIAL: Aroclor 1260

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
I-II	F1a	17/42	40.5	16/16	100.0	16/17	94.1	16/16	100.0	22	21-22
10 ppm)	F1b	16/23	69.6	16/16	100.0	16/16	100.0	16/16	100.0	22	21-22
	F2a	12/54	22.2	12/16	75.0	12/12	100.0	12/12	100.0	21	21-22
	F2b	10/28	35.7	10/12	83.3	10/10	100.0	10/10	100.0	22	21-22
	F3a	13/63	20.6	12/16	75.0	12/13	92.3	12/12	100.0	22	21-22
	F3b	12/34	35.3	11/12	91.7	11/12	91.7	11/11	100.0	22	21-22
-III	F1a	14/53	26.4	14/16	87.5	14/14	100.0	13/14	92.9	22	21-23
100 ppm)	F1b	14/31	45.2	14/14	100.0	14/14	100.0	14/14	100.0	21	20-22
	F2a	16/54	29.6	13/16	81.2	13/16	81.2	13/13	100.0	22	20-23
	F2b	12/32	37.5	12/13	92.3	12/12	100.0	11/12	91.7	22	20-22
	F3a	16/52	30.8	13/15	86.7	13/16	81.2	12/13	92.3	23	22-23
	F3b	12/40	30.0	10/10	100.0	10/12	83.3	10/10	100.0	23	22-23

0636686

TOXSTUDIES1514

B. Progeny

1. Population Data

Popululation 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 1260. 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.

TOXSTUDIES1515

TABLE XIX

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups Delivered Total	Number of Pups Delivered Mean/Litter	Number of Pups Stillborn Total	Number of Pups Stillborn Mean/Litter	Number of Pups Cannibalized Total	Number of Pups Cannibalized Mean/Litter	Number of Viable Pups Born Total	Number of Viable Pups Born Mean/Litter
C	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
T-1 (1 ppm)	F1a	204	12.8	6	0.4	0	-	198	12.4
	F1b	197	13.1	15	1.0	1	0.1	181	12.1
	F2a	129	9.9	1	0.1	0	-	128	9.8
	F2b	127	10.6	0	-	0	-	127	10.6
	F3a	87	8.7	8	0.8	0	-	79	7.9
	F3b	90	9.0	1	0.1	0	-	89	8.9

0636688

TOXSTUDIES1516

TABLE XIX continued

TEST MATERIAL: Aroclor 1260

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	187	11.7	1	0.1	0	-	186	11.6
(10 ppm)	F1b	209	13.1	4	0.3	0	-	205	12.8
	F2a	122	10.2	1	0.1	0	-	121	10.1
	F2b	116	11.6	1	0.1	0	-	115	11.5
	F3a	101	8.4	7	0.6	0	-	94	7.8
	F3b	92	8.4	6	0.5	0	-	86	7.8
T-III	F1a	173	13.3	2	0.2	0	-	171	13.2
(100 ppm)	F1b	160	11.4	23	1.6	0	-	137	9.8
	F2a	135	10.4	1	0.1	2	0.2	132	10.2
	F2b	127	11.5	1	0.1	0	-	126	11.4
	F3a	110	9.2	12	1.0	3	0.2	95	7.9
	F3b	98	9.8	7	0.7	1	0.1	88	8.8

0636689

TOXSTUDIES1517

TABLE XX

TEST MATERIAL: Aroclor 1260

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
C	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
T-I	F1a	193	12.1	152	9.5	129	8.1	63	57	120	7.5
(1 ppm)	F1b	181	12.1	150	10.0	123	8.2	32	42	74	4.9
	F2a	126	9.7	107	8.2	103	7.9	48	48	96	7.4
	F2b	127	10.6	99	8.2	91	7.6	40	36	76	6.3
	F3a	76	7.6	59	5.9	54	5.4	16	24	40	4.0
	F3b	88	8.8	63	6.3	57	5.7	25	28	53	5.3

Industrial BIO-TEST Laboratories, Inc.

0636690

TOXSTUDIES1518

TABLE XX continued

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Population Data

Progeny

Group	Litter	Number of Pups at Lactation Day 1 Total	Mean/Litter	Number of Pups at Lactation Day 5 Total	Mean/Litter	Number of Pups Retained at Lactation Day 5 Total	Mean/Litter	Male	Number of Weanlings Female	Total	Mean/Litter
T-II	F1a	183	11.4	179	11.2	148	9.3	78	64	142	8.9
(10 ppm)	F1b	204	12.8	199	12.4	154	9.6	58	77	135	8.4
	F2a	111	9.2	104	8.7	93	7.8	36	39	75	6.2
	F2b	111	11.1	77	7.7	70	7.0	36	24	60	6.0
	F3a	77	6.4	67	5.6	67	5.6	29	30	59	4.9
	F3b	82	7.4	44	4.0	42	3.8	18	15	33	3.0
T-III	F1a	156	12.0	116	8.9	92	7.1	39	44	83	6.4
(100 ppm)	F1b	129	9.2	95	6.8	78	5.6	28	31	59	4.2
	F2a	119	9.2	107	8.2	99	7.6	29	47	76	5.8
	F2b	112	10.2	111	10.1	99	9.0	40	43	83	7.5
	F3a	94	7.8	86	7.2	83	6.9	25	45	70	5.8
	F3b	86	8.6	66	6.6	63	6.3	14	18	32	3.2

Industrial BIO-TEST Laboratories, Inc.

0636691

TOXSTUDIES1519

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.

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

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

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

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

TOXSTUDIES1520

TABLE XXI

TEST MATERIAL: Aroclor 1260

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	93.2	98.9	65.7	64.1
	F2a	95.2	94.3	64.3	82.0
	F2b	100.0	99.4	82.3	73.9
	F3a	90.2	97.8	75.0	78.5
	F3b	85.3	97.8	84.9	56.0
T-I	F1a	97.1	97.5	76.8	93.0
(1 ppm)	F1b	91.9	100.0	82.9	60.2
	F2a	99.2	98.4	83.6	93.2
	F2b	100.0	100.0	77.9	83.5
	F3a	90.8	96.2	74.7	74.1
	F3b	98.9	98.9	70.8	93.0
T-II	F1a	99.5	98.4	96.2	95.9
(10 ppm)	F1b	98.1	99.5	97.1	87.7
	F2a	99.2	91.7	86.0	80.6
	F2b	99.1	96.5	67.0	85.7
	F3a	93.1	81.9	71.3	88.0
	F3b	93.5	95.3	51.2	78.6
T-III	F1a	98.8	91.2	67.8	90.2
(100 ppm)	F1b	85.6	94.2	69.3	75.6
	F2a	97.8	90.1	81.1	76.8
	F2b	99.2	88.9	88.1	83.8
	F3a	86.4	98.9	90.5	84.3
	F3b	89.8	97.7	75.0	50.8

TOXSTUDIES1521

3. Body Weight Data

Body weight data for weanlings are presented in Table XXII. There were no significant differences between test and control weanling body weights.

TOXSTUDIES1522

TABLE XXII

TEST MATERIAL: Aroclor 1260

Three-Generation Reproduction Study - Albino Rats

Progeny

Weanling Body Weight Data

Group	Litter	Mean Body Weight (grams) Male	Female
C	F1a	48	44
	F1b	47	43
	F2a	46	43
	F2b	41	39
	F3a	45	44
	F3b	42	42
T-I (1 ppm)	F1a	44	42
	F1b	47	44
	F2a	46	46
	F2b	48	46
	F3a	48	46
	F3b	46	41
T-II (10 ppm)	F1a	50	46
	F1b	49	47
	F2a	52	49
	F2b	44	43
	F3a	44	40
	F3b	34	51
T-III (100 ppm)	F1a	47	45
	F1b	51	47
	F2a	49	43
	F2b	47	43
	F3a	40	41
	F3b	42	40

TOXSTUDIES1523

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 1260.

TOXSTUDIES1524