REPORT TO

MONSANTO COMPANY

90-DAY SUBACUTE ORAL TOXICITY STUDY WITH AROCLOR 1221 IN ALBINO RATS

APRIL 28, 1972

IBT NO. B9888

I. Introduction

A sample identified as Aroclor 1221 was received from the Monsanto Company for the purpose of conducting a 90-day subacute oral toxicity study using albino rats as test animals. The following report presents the results of this investigation.

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II. Summary

Ninety days of feeding Aroclor 1221 to groups of albino rats at dietary levels of 10, 100 and 300 ppm revealed no abnormalities in any of the following parameters:

Body Weight Gain
Food Consumption
Survival
Hematologic, Clinical Blood Chemistry and Urologic Studies
Gross and Microscopic Pathologic Studies
Organ Weights and Ratios

Respectfully submitted,

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III. Procedure

A. Experimental Animals

The animals employed in the study were Charles River strain* albino rats. One hundred and twenty rats (60 males and 60 females) were selected for the experiment and housed individually in standard, wire-bottomed steel rat cages. Each cage bore a color-coded card identifying the animal with respect to project number, dietary level assignment, individual animal number and sex.

B. Organization of Groups

A structural outline of the experiment is shown in Table I.

TABLE I

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Outline of Experiment

Group	Number of Animals Males	Females	Dietary Level (ppm)
Control	15	15	None Administered
T-I	15	15	10
T-II	15	15	100
T-III	15	15	300

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

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C. Body Weights

Each animal used in the study was weighed on the first day of the test and at weekly intervals thereafter. The weights were recorded and served as an index to growth. Weight gains were computed at the conclusion of the 90-day test period and the data subjected to statistical analyses.

D. Food Consumption and Diet Preparation

Food consumption data were collected individually for five rats of each sex in every group weekly during the study and the data recorded.

The diet for any given group was prepared by blending the appropriate amount of Aroclor 1221 with standard rat ration in a Hobart Mixer.

Fresh diets were prepared each week. Each rat was offered an amount of diet sufficient for one week's ad libitum feeding. However, checks were made periodically to ensure that the food jars were not empty.

E. Mortality and Reactions

Abnormal reactions and deaths were recorded daily during the investigation.

F. Hematologic, Clinical Blood Chemistry Studies and Urine Analyses

Blood and urine samples collected individually from ten rats of each sex from both the control and T-III groups after 45 and 84 days of feeding were analyzed for the following:

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1. Hematologic Studies

   a. Hematocrit Value
   b. Erythrocyte Count
   c. Hemoglobin Concentration
   d. Total Leukocyte Count
   e. Differential Leukocyte Count

2. Clinical Blood Chemistry Studies

   a. Blood Urea Nitrogen (BUN) Concentration
   b. Serum Alkaline Phosphatase (SAP) Activity
   c. Serum Glutamic-Pyruvic Transaminase (SGPT) Activity
   d. Fasted Blood Glucose Concentration

3. Urine Analyses

   a. Glucose Concentr tion
   b. Albumin Concentration
   c. Microscopic Elements Examination
   d. pH
   e. Specific Gravity

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G. Pathologic Studies

Following 90 days of feeding, all surviving rats were sacrificed by carbon dioxide asphyxiation and autopsied. Animals which died during the study were examined grossly unless examination was precluded by postmortem autolysis. At the time of gross examination a complete set of organs and other tissues was removed from each rat and preserved in formalin solution. Also at autopsy the weights of the liver, kidneys, spleen, gonads, heart and brain of each rat were determined and recorded.

Microscopic examination of tissues taken from ten rats of each sex from both the control and T-III groups was conducted. The following tissues, stained with Hematoxylin-Eosin, were included: esophagus, stomach (cardia, fundus and pylorus), small intestine (duodenum, jejunum and ileum), cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary gland, adrenal gland, testes, seminal vesicle, ovary, bone marrow, thyroid gland, parathyroid gland, salivary gland, prostate gland, heart, aorta, lung, lymph node (cervical and mesenteric), skeletal muscle, peripheral nerve, bone (femur), spinal cord, uterus, trachea, eye, optic nerve and brain (cerebrum, cerebellum and pons).

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H. Organ Weights, Organ to Body Weight and Organ to Brain Weight Ratios

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

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IV. Results

A. Body Weights

Body weight data collected during the 90-day test period are summarized in Table II. Also included in the table are 90-day average total weight gains.

Statistical comparisons of final body weights and total weight gains revealed no significant differences between test and control rats.

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TABLE II

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Body Weight and Total Weight Gain Data

Summary of Mean Values

etary Level (ppm)	Sex	Body Weight (grams) Week: 0	1	2	3	4	5	6	7	8	9	10	11	12	13	Total Weight Gain (grams/rat)
Control	M	77	167	207	255	294	317	338	360	387	397	403	419	431	452	375
	F	85	141	164	190	204	211	218	236	243	251	253	256	263	269	184
10	M	82	160	206	254	293	309	323	334	352	367	385	389	391	427	345
	F	83	145	165	195	212	219	229	234	242	246	254	261	267	279	196
100	M	88	166	210	274	313	331	356	365	388	406	425	435	456	468	380
	F	90	157	177	201	216	222	233	236	247	249	257	273	274	292	202
300	M	85	168	214	264	299	321	344	366	383	394	402	417	416	452	367
	F	88	147	169	195	207	215	221	227	242	244	252	261	266	272	184

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B. Food Consumption

Food consumption data collected during the 90-day test period are summarized in Table III.

Test rats ate amounts of food equal to that consumed by control rats.

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TABLE III

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Food Consumption Data

Summary of Mean Values

Dietary Level (ppm)	Sex	Food Consumption (grams/rat/seven days) Week: 1	2	3	4	5	6	7	8	9	10	11	12	13	Total Food Consumption (grams/rat)
Control	M	88	92	131	144	161	170	144	158	163	159	179	185	165	1939
	F	86	98	118	122	113	134	93	133	132	130	172	146	145	1622
10	M	89	140	145	162	167	189	189	202	163	173	185	195	187	2186
	F	104	126	113	121	112	111	117	143	143	140	146	155	147	1678
100	M	110	146	164	188	183	197	182	197	171	182	177	199	204	2300
	F	113	127	103	122	177	117	125	144	153	164	166	138	181	1830
300	M	100	131	153	166	175	192	168	208	181	187	181	205	191	2238
	F	83	108	117	164	134	144	160	151	178	128	158	135	154	1814

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C. Mortality and Reactions

Seven deaths occurred during the study. One of these deaths was ascribed to an acute respiratory infection, while the other six resulted from trauma incurred during the collection of blood samples.

No untoward behavioral reactions were noted among any of the animals employed in the study.

D. Hematologic Studies

The results of the hematologic studies conducted on blood samples taken from ten rats of each sex in the control and T-III groups after 45 and 84 days of feeding are summarized in Tables IV and V.

No outstanding differences between test and control rats were noted with respect to any of the parameters investigated.

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TABLE IV

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data

Summary of Mean Values

Dietary Level (ppm)	Sex	Total Leukocyte Count (thousands/mm^3) Day: 45	84	Erythrocyte Count (millions/mm^3) Day: 45	84	Hemoglobin Concentration (g/100 ml) Day: 45	84	Hematocrit Value (percent) Day: 45	84
Control	M	20.8	20.8	7.85	8.46	15.4	15.1	40.6	41.4
	F	17.4	14.5	7.59	7.79	14.9	14.7	38.7	40.0
300	M	18.6	19.3	7.56	8.47	14.6	15.4	37.9	41.7
	F	13.6	12.1	7.81	7.84	15.0	15.0	39.7	41.1

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TABLE V

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data

Summary of Mean Values

Dietary Level (ppm)	Sex	Differential Leukocyte Count (Number of Cells per Hundred)									
		Lymphocytes Day:		Neutrophils Day:		Monocytes Day:		Eosinophils Day:		Basophils Day:	
		45	84	45	84	45	84	45	84	45	84
Control	M	92.8	85.5	5.0	10.6	1.6	3.2	0.6	0.7	0.0	0.0
	F	90.6	85.7	7.6	11.7	1.8	2.1	0.0	0.5	0.0	0.0
300	M	83.6	82.9	14.8	13.5	1.0	3.2	0.6	0.4	0.0	0.0
	F	80.8	81.7	17.2	14.2	1.8	3.1	0.2	1.0	0.0	0.0

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E. Clinical Blood Chemistry Studies

The results of the clinical chemistry studies conducted on blood samples obtained from ten rats of each sex in the control and T-III groups after 45 and 84 days of feeding are summarized in Tables VI and VII.

The values obtained for all the parameters investigated were within normal limits for the albino rat.

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TABLE VI

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Clinical Blood Chemistry Data

Summary of Mean Values

Dietary Level (ppm)	Sex	Serum Alkaline Phosphatase Activity (King-Armstrong Units) Day: 45	84	Serum Glutamic-Pyruvic Transaminase Activity (Dade Units) Day: 45	84
Control	M	27	25	41	31
	F	18	18	46	31
300	M	24	28	23	34
	F	15	20	31	34

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TABLE VII

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Clinical Blood Chemistry Data

Summary of Mean Values

Dietary Level (ppm)	Sex	Blood Urea Nitrogen Concentration (mgs %) Day: 45	84	Fasted Blood Glucose Concentration (mgs %) Day: 45	84
Control	M	13	17	113	134
	F	16	19	118	116
300	M	15	18	109	135
	F	14	15	113	133

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F. Urine Analyses

The results of the periodic examinations of urine specimens collected from ten rats of each sex in the control and T-III groups after 45 and 84 days of feeding are summarized in Table VIII.

No significant differences between the urine of test rats and control rats were observed.

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TABLE VIII

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Urine Analysis Data

Summary of Mean Values

Dietary Level (ppm)	Sex	Glucose Day: 45	Glucose Day: 84	Albumin Day: 45	Albumin Day: 84	Microscopic Elements Day: 45	Microscopic Elements Day: 84	pH Day: 45	pH Day: 84	Specific Gravity Day: 45	Specific Gravity Day: 84
Control	M	neg	neg	t	t	N	+2	6.8	8.0	1.015	1.031
	F	neg	neg	t	t	N	+3	7.0	8.1	1.016	1.024
300	M	neg	neg	neg	t	N	N	6.8	6.8	1.020	1.036
	F	neg	neg	neg	neg	N	+2	6.8	7.2	1.015	1.024

Glucose and Albumin

neg = negative
t = trace; less than 30 mg/100 ml urine
+1 = 30 to 100 mg/100 ml urine
+2 = 100 to 300 mg/100 ml urine
+3 = 300 to 500 mg/100 ml urine
+4 = more than 500 mg/100 ml urine

Microscopic Elements

N = normal
t = trace; less than 5 per low power field
+1 = 5-10 per low power field
+2 = 10-15 per low power field
+3 = more than 15 per low power field

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STLCOPCB4021015

G. Pathologic Studies

1. Gross Pathologic Findings

No outstanding differences were noted between test and control rats upon gross pathological examination.

2. Organ Weight and Organ to Body and Organ to Brain Weight Ratio Data

The results of the statistical analyses conducted on absolute organ weights, organ to body weight and organ to brain weight ratios are summarized in Tables IX through XIV.

There were no significant differences noted between the test groups and the control group.

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TABLE IX

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Organ Weight and Ratio Data

Summary of Mean Values

Organ: Liver

ietary Level (ppm)	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
	Males	Females	Males	Females	Males	Females
Control	15.2	8.7	3.36	3.21	7.73	4.73
10	14.3	9.5	3.34	3.40	7.22	5.19
100	14.3	9.6	3.07	3.25	7.18	5.25
300	14.6	9.3	3.26	3.40	7.59	5.16

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STLCOPCB4021017

TABLE X

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Organ Weight and Ratio Data

Summary of Mean Values

Organ: Kidneys

tary Level (ppm)	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
	Males	Females	Males	Females	Males	Females
Control	3.02	1.91	0.668	0.708	1.53	1.03
10	2.87	1.95	0.674	0.703	1.45	1.06
100	3.06	1.93	0.655	0.664	1.53	1.05
300	2.89	1.97	0.643	0.725	1.49	1.09

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STLCOPCB4021018

TABLE XI

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Organ Weight and Ratio Data

Summary of Mean Values

Organ: Spleen

tary Level (ppm)	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
	Males	Females	Males	Females	Males	Females
Control	0.85	0.55	0.187	0.204	0.429	0.300
10	0.73	0.57	0.171	0.205	0.368	0.311
100	0.78	0.70	0.168	0.239	0.390	0.384
300	0.81	0.62	0.179	0.231	0.415	0.344

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STLCOPCB4021019

TABLE XII

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Organ Weight and Ratio Data

Summary of Mean Values

Organ: Gonads

stary Level (ppm)	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
	Males	Females	Males	Females	Males	Females
Control	3.19	0.135	0.708	0.0501	1.61	0.0733
10	3.28	0.134	0.767	0.0480	1.65	0.0733
100	3.25	0.123	0.698	0.0425	1.62	0.0675
300	3.33	0.111	0.746	0.0408	1.71	0.0622

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TABLE XIII

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Organ Weight and Ratio Data

Summary of Mean Values

Organ: Heart

etary Level (ppm)	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)		Organ/Brain Weight Ratio (g/g)	
	Males	Females	Males	Females	Males	Females
Control	1.43	0.98	0.318	0.361	0.727	0.531
10	1.42	1.02	0.332	0.367	0.716	0.558
100	1.48	1.01	0.317	0.350	0.738	0.559
300	1.39	0.96	0.310	0.355	0.720	0.534

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TABLE XIV

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Organ Weight and Ratio Data

Summary of Mean Values

Organ: Brain

Dietary Level (ppm)	Organ Weight (g)		Organ/Body Weight Ratio (g/100 g)	
	Males	Females	Males	Females
Control	1.97	1.84	0.441	0.687
10	1.98	1.83	0.468	0.665
100	2.01	1.82	0.433	0.634
300	1.96	1.79	0.436	0.675

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3. Histopathologic Findings

Histopathologic examination of tissues and organs taken from ten rats of each sex in both the control and T-III groups was conducted.

Tables XV and XVI list all histopathologic changes noted.

All of the lesions noted in the microscopic examination of tissues were those of spontaneous disease and are not unusual for the albino rat. The most frequent findings were lesions in the trachea and lungs, indicating chronic murine pneumonia. These occurred in the control as well as the rats fed Aroclor 1221.

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IBT No. B9888
Monsanto

I have completed a histopathologic evaluation of a series of rat tissues from IBT B9888. There are no changes which can be attributed to the test material. The lesions described are those of spontaneous disease and they are not unusual for the rat.

Ward R. Richter

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STLCOPCB4021024

TABLE XV

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Histopathologic Changes

Group: Control

Number of Animals	Organ Examined	Findings	Incidence	Average Grade
10 Males	Trachea	Tracheitis	4	1.0
	Lung	Chronic respiratory disease	5	1.0
	Kidney	Focal interstitial nephritis	1	1.0
	Urinary bladder	Calculus	5	1.0
	Prostate	Inflammation	1	1.0
10 Females	Trachea	Tracheitis	2	1.0
	Lung	Chronic respiratory disease	2	1.0
	Liver	Focal hepatitis	3	1.0

All other tissues and organs, as listed on page 6, were normal histologically.

Grading System
0.5 = minimal
1.0 = slight
2.0 = mild
3.0 = moderate
4.0 = severe
5.0 = extreme

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TABLE XVI

TEST MATERIAL: Aroclor 1221

90-Day Subacute Oral Toxicity Study - Albino Rats

Histopathologic Changes

Group: 300 ppm

Number of Animals	Organ Examined	Findings	Incidence	Average Grade
10 Males	Trachea	Tracheitis	4	1.0
	Lung	Chronic respiratory disease	3	1.0
	Urinary bladder	Calculus	5	1.0
10 Females	Trachea	Tracheitis	5	1.0
	Lung	Chronic respiratory disease	3	1.0
		Congestion	1	1.0
	Liver	Focal lymphoid infiltration	1	1.0
		Ductile hyperplasia	1	1.0
	Stomach	Gastritis with severe edema and focal hemorrhage in non-glandular stomach	1	-
	Kidney	Focal lymphoid hyperplasia	1	1.0

All other tissues and organs, as listed on page 6, were normal histologically.

Grading System

0.5 = minimal 2.0 = mild 4.0 = severe
1.0 = slight 3.0 = moderate 5.0 = extreme

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