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

September 8, 1971

8TL-71-71

Mr. Elmer Wheeler
Monsanto Company
Medical Department
800 North Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Mr. Wheeler:

Re: IBT No. 9350 - Teratogenic Study with
Aroclor 1242 in Albino Rats

We are submitting herewith our laboratory report dated September 8, 1971, prepared in connection with the above study.

Very truly yours,

J. C. Calandra
President

JCC/kjl

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

REPORT TO

MONSANTO COMPANY

TERATOGENIC STUDY WITH
AROCLOR 1242
IN ALBINO RATS

SEPTEMBER 8, 1971

IBT NO. B9350

MONS 068703

Industrial BIO-TEST Laboratories Inc.

REPORT TO

MONSANTO COMPANY

TERATOGENIC STUDY WITH
AROCLOR 1242
IN ALBINO RATS

SEPTEMBER 8, 1971

BT NO. B9350

I. Introduction

At the request of Monsanto Company, a study was initiated to determine the potential teratogenicity of Aroclor 1242 using gravid albino rats. This report presents the results of the investigation.

II. Summary

A study was conducted to determine the potential teratogenic effects of Aroclor 1242 in albino rats. All pregnant rats were treated orally on Gestation Days 6 through 15 and sacrificed on Gestation Day 20. The day of insemination is defined as Gestation Day Zero. Dose levels of Aroclor 1242 were 10 and 30 mg/kg maternal body weight.

Investigation of the following parameters revealed no differences between test and control animals which could be attributed to the ingestion of Aroclor 1242.

A. Maternal Body Weight
B. Maternal Mortality
C. Implantation Sites
D. Resorption Sites
E. Viable Fetuses
F. Fetal Body Weight
G. Gross Abnormalities
H. Skeletal Development
I. Internal Development

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by: James B. Plank
James B. Plank
Senior Group Leader
Rat Toxicity

Report approved by: M. L. Koplinger
M. L. Koplinger, Ph.D.
Manager, Toxicology

III. Procedure

A. Experimental Animals

The animals employed were female Charles River [illegible] rats. The rats were bred at the Charles River Breeding [illegible] and confirmed pregnant by sperm-positive results of vaginal examinations. Day Zero is defined as the day of insemination. The animals were then shipped directly to the laboratory on Day One of gestation.

B. Organization Groups

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

TABLE I

TEST MATERIAL: Aroclor 1242

Teratogenic Study - Albino Rats

Outline of Experiment

Group	Dose Level (mg/kg/day)	Number of Females/Group
Control	-	26
T-I	10	22
T-II	30	20

C. Dosage and Feeding

Dilutions were prepared fresh daily by adding the appropriate weight of test material to corn oil. Doses were administered at 5 ml/kg via gavage to each test animal by means of a hypodermic syringe equipped with a ball-tipped intubation needle.

All test animals were given the material daily from the sixth day of the gestation period through the fifteenth day inclusive for a total of ten doses. Controls were treated in a similar manner with corn oil.

All animals were allowed food and water ad libitum.

D. Body Weight Data

Females were weighed daily during the dosing period and again at sacrifice. Data reported include the mean group body weights on Day 6 of gestation (initial dosing), Day 9, Day 12, Day 15 (final dosing) and sacrifice, Day 20.

E. Mortality and Reactions

Daily records of mortality and reactions were maintained throughout the investigation.

F. Reproductive and External Teratogenic Effects

All females were sacrificed by carbon dioxide asphyxiation on the 20th day of gestation. An incision was made in the abdominal wall and the full content of both uterine horns was removed [illegible]

paid to resorption sites or any other uterine abnormalities. The number of corpora lutea was determined and recorded at this time.

The number of viable fetuses present in the uterus was determined, spontaneous movement and a more ruddy color distinguishing live from dead animals. Each fetus was removed by placing a small hemostat on the umbilical cord, flush with the abdominal wall, and cutting the cord distal to the clamp. Blotting paper was used to remove excess amniotic fluid and blood prior to the weighing of the animals.

An external examination of the fetuses was conducted with special attention paid to detection of the following abnormalities: hydrocephaly, exencephaly, meningoencephalocele, simple meningocele, anophthalmia, microphthalmia, cleft lip, mandible or palate, oblique facial cleft, micrognathia, external ear abnormalities in size, shape or position, unusual size or position of the limbs, number and disposition of the digits, umbilical hernia, gastroschisis, myelomeningocele, spina bifida and scoliosis.

C. Skeletal Development

Two-thirds of the fetuses (from each litter) were used for evaluation of skeletal development. The method of alizarin staining of bone was that of Hurley[1].

[1] Hurley, Lucille S., "Demonstration A-Alizarin Staining of Bone," (revised) Supplement to Teratology Workshop 24 June 1, Berkeley, California, January 29-30, 1965, pp. 121-122.

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H. Internal Development

Internal development of remaining fetuses was evaluated by comparing those from treated females to those from untreated controls using the freehand razor blade section technique of Wilson et al.*

* Wilson, James G. and Warkany, Josef, Teratology Principles and Techniques, University of Chicago Press, Chicago, Illinois, 1965, pp. 271-277.

IV. Results

A. Body Weight Data

Mean body weight data are presented in Table [illegible]. Animals which were not pregnant are not included in these data.

Body weight gain during gestation was not influenced by the administration of Aroclor 1242.

TABLE [illegible]

TEST MATERIAL: Amoco 1242

Teratogenic Study - Albino Rats

Body Weight Data

Summary of Mean Values

Group	Body Weight (grams) Day of Gestation 6	9	12	15	20	Weight Gain (grams)
Control	208	228	255	273	312	104
T-I	210	226	245	273	344	134
T-II	190	203	211	244	309	119

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B. Mortality

There were no deaths among the [illegible]

C. Reactions

No unusual reactions were noted among the [illegible]

D. Reproductive Effects

The results of the sacrifice at Day 20 of gestation are presented in Table III. Females which were not pregnant are not included in these data.

Females in all groups were free of gross uterine abnormalities. There were no significant differences in number of resorption sites or number of viable fetuses per female between the control group and those treated with Aroclor 1242. The incidence of females with resorption sites was higher among females receiving 10 mg Aroclor 1242 per kilogram than among females receiving 30 mg/kg or among control females.

TABLE III

TEST MATERIAL: Aroclor 1242

Teratogenic Study - Albino Rats

Reproductive Effects

Summary of Results

Females Examined	Corpora Lutea		Implantation Sites		Resorption Sites		Viable Fetuses		Females with One or More Resorption Sites	
	Total	Mean/Female	Total	Mean/Female	Total	Mean/Female	Total	Mean/Female	Total	Percent
26	305	11.7	267	10.3	13	0.5	254	9.8	6	23.1
22	268	12.2	244	11.1	15	0.7	229	10.4	12	54.5
20	240	12.0	220	11.0	4	0.2	216	10.8	3	15.0

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E. Fetal Development

1. Body Weight and Sex Ratio

Body weights of fetuses are summarized in Table IV.

There were no significant differences in fetal body weight between control and treated groups.

Chi square analysis showed that the sex ratio of control and treatment groups did not differ significantly from the expected ratio and was not altered by Aroclor 1242.

TABLE IV

TEST MATERIAL: Aroclor 1242

Teratogenic Study - Albino Rats

Fetal Body Weight and Sex Ratio

Summary of Results

Group	Number of Males	Mean Body Weight (grams)	Number of Females	Mean Body Weight (grams)	Number of Males per 100 Fetuses
Control	141	4.0	113	3.8	55.5
T-I	118	4.3	111	4.2	51.5
T-II	103	4.3	113	4.0	47.7

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2. Fetal External Development

All fetuses appeared normal and were free of gross abnormalities.

3. Skeletal Development:

The results of the examination for skeletal abnormalities are presented in Table V. Maternal treatment with Aroclor 1242 did not influence fetal skeletal development.

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TABLE V

TEST MATERIAL: Aroclor 1242

Teratogenic Study - Albino Rats

Fetal Skeletal Development

Summary of Results

Group	Fetuses Examined	Finding	Incidence	Percent of Total Examined
Control	169	Supernumerary ribs	8	4.7
		Incomplete ossification of sternum section(s)	30	17.8
		Non-ossified sternum section(s)	23	13.6
		Underdeveloped frontal and parietal skull bones	1	0.6
		Total abnormal fetuses	58	34.3
		Total normal fetuses	111	65.7
T-I	131	Supernumerary ribs	1	0.8
		Incomplete ossification of sternum section(s)	5	3.8
		Non-ossified sternum section(s)	5	3.8
		Total abnormal fetuses	11	8.4
		Total normal fetuses	120	91.6
T-II	143	Supernumerary ribs	1	0.7
		Incomplete ossification of sternum section(s)	15	10.5
		Non-ossified sternum section(s)	22	15.4
		Total abnormal fetuses	[illegible]	[illegible]
		Total normal fetuses	106	74.1

4. Internal Development

The results of the evaluation of fetal external development are summarized in Table VI.

Several of the fetuses examined from each of the groups had either large or small atria. The total incidence of these abnormalities was not significantly different among test or control groups.

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TABLE VI

TEST MATERIAL: Aroclor 1242

Teratogenic Study - Albino Rats

Fetal Internal Development

Summary of Findings

Group	Fetuses Examined	Finding	Incidence	Percent of Total Examined
Control	85	Small atria	6	7.1
		Large atria	7	8.2
		Undescended testes	2	2.4
		Total abnormal fetuses	15	17.6
		Total normal fetuses	70	82.4
[illegible]	98	Small atria	4	4.1
		Large atria	12	12.2
		One small testicle	2	2.0
		Total abnormal fetuses	19	19.2
		Total normal fetuses	79	80.8
[illegible]	73	Small atria	2	2.7
		Large atria	11	15.1
		One small testicle	3	4.1
		Total abnormal fetuses	15	20.5

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