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REPORT FILE

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

REPORT TO

MONSANTO COMPANY

TERATOGENIC STUDY WITH AROCLOR 1260 IN ALBINO RATS

SEPTEMBER 9, 1971

IBT NO. B9352

MONS 068720

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

September 9, 1971

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

Dear Mr. Wheeler:

Re: IBT No. B9352 - Teratogenic Study
with Aroclor 1260 in Albino Rats

We are submitting herewith our laboratory report dated September 9, 1971, prepared in connection with the above study.

Very truly yours,

J. C. Calandra
President

JCC/kjl

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REPORT TO

MONSANTO COMPANY

TERATOGENIC STUDY WITH
AROCLOR 1260
IN ALBINO RATS

SEPTEMBER 9, 1971

IBT NO. B9352

I. Introduction

At the request of Monsanto Company, a study was initiated to determine the potential teratogenicity of Aroclor 1260 using gravid albino rats. This report presents the results of the investigation.

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II. Summary

A study was conducted to determine the potential teratogenic effects of Arocior 1260 in albino rats. All pregnant rats were treated from Gestation Days 6 through 15 and sacrificed on Gestation Day 20. The day of insemination is defined as Gestation Day Zero. Dose levels of Arocior 1260 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 Arocior 1260.

Maternal Body Weight
Maternal Mortality
Implantation Sites
Resorption Sites
Viable Fetuses
Fetal Body Weight
Gross Abnormalities
Skeletal Development
Internal Development

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

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

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

Otis E. Fancher, Ph.D.
Scientific Director

September 9, 1971

ejm:peh

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III. Investigational Procedure

A. Experimental Animals

The animals employed were female Charles River albino rats. The rats were bred at the Charles River Breeding Laboratories* 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 this 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 1260

Teratogenic Study - Albino Rats

Outline of Experiment

Group	Dose Level (mg/kg/day)	Number of Females/Group
Control	-	26
T-I	10	17
T-II	30	19

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

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C. Dosage and Feeding

Dilutions were prepared fresh daily by adding the appropriate weight of test material to corn oil. Doses were administered orally 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 (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 at 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 extent of both uterine horns was exposed immediately. Fetal swellings and implantation sites were counted, special attention being paid to resorption sites or any other uterine abnormalities. The number of corpora lutea was determined and recorded at this time.

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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.

G. 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*.

* Hurley, Lucille S., "Demonstration A-Alizarin Staining of Bone," (revised) Supplement To Teratology Workshop Manual, Berkeley, California, January 25-30, 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 females using the free-hand razor blade section technique of Wilson and Warkany*.

* 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 II. Females which were not pregnant are not included in these data.

A slight reduction in weight gain of pregnant females treated with Aroclor 1260 was observed. This reduction in weight gain was not dose related.

TABLE II

TEST MATERIAL: Aroclor 1260

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	198	206	237	255	283	85
T-II	195	200	231	247	280	85

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B. Mortality

There were no deaths among test or control females.

C. Reactions

No unusual reactions were noted among test or control females.

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 viable fetuses per female between the control group and those treated with Aroclor 1260. The number of females with resorption sites was higher in the group receiving 30 mg Aroclor 1260 per kilogram than in either the group receiving 10 mg/kg or the control group. The average number of resorption sites did not differ greatly among any of the groups.

TABLE III

TEST MATERIAL: Aroclor 1260

Teratogenic Study - Albino Rats

Reproductive Effects

Summary of Results

Group	Females Examined	Corpora Lutea Total	Corpora Lutea Mean/Female	Implantation Sites Total	Implantation Sites Mean/Female	Resorption Sites Total	Resorption Sites Mean/Female	Viable Fetuses Total	Viable Fetuses Mean/Female	Females With One or More Resorption Sites Total	Females With One or More Resorption Sites Percent
Control	26	305	11.7	267	10.3	13	0.5	254	9.8	6	23.1
T-I	17	210	12.4	191	11.2	8	0.5	183	10.8	5	29.4
T-II	19	222	11.7	203	10.7	23*	1.2	180	9.5	11	57.9

* Includes one female with twelve resorption sites.

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E. Fetal Development

1. Body Weight and Sex Ratio

Body weights of fetuses are presented in Table IV.

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

TABLE IV

TEST MATERIAL: Aroclor 1260

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	99	3.8	84	3.7	54.1
T-II	99	4.0	81	4.0	55.0

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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 1260 did not influence fetal skeletal development.

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TABLE V

TEST MATERIAL: Aroclor 1260

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	129	Supernumerary ribs	1	0.8
		Incomplete ossification of sternum section(s)	20	15.5
		Non-ossified sternum section(s)	9	7.0
		Total abnormal fetuses	27	20.9
		Total normal fetuses	102	79.1
T-II	113	Supernumerary ribs	1	0.9
		Incomplete ossification of sternum section(s)	21	18.6
		Non-ossified sternum section(s)	15	13.3
		Total abnormal fetuses	31	27.4
		Total normal fetuses	82	72.6

Submitted BIO-TEST Laboratories, Inc.

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4. Internal Development

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

Fetal examination revealed a small number of fetuses with large or small atria in each of the groups. The total incidence of these abnormalities did not differ markedly among the test or control groups.

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TABLE VI

TEST MATERIAL: Aroclor 1260

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
T-I	54	Small atria	1	1.9
		Large atria	11	20.4
		Total abnormal fetuses	12	22.2
		Total normal fetuses	42	77.8
T-II	67	Moderate internal hydrocephalus	1	1.5
		Small atria	11	16.4
		Large atria	5	7.5
		Total abnormal fetuses	17	25.4
		Total normal fetuses	50	74.6

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