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

REPORT TO

MONSANTO COMPANY

TWO - YEAR CHRONIC ORAL TOXICITY STUDY WITH AROCLOR 1260 IN ALBINO RATS

HISTOPATHOLOGICAL EVALUATION OF ADDITIONAL LIVER SECTIONS

MARCH 24, 1975

IBT NO. 641 - 06672

DSW 036966

STLCOPCB4020790

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

July 1, 1975

George J. Levinskas, Ph.D.
Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, Missouri 63166

Dear Dr. Levinskas:

Re: IBT No. 641-06672 - Histopathological Evaluation of Additional Liver Sections From Rats of a Two - Year Chronic Oral Toxicity Study of Aroclor 1260.

We are submitting herewith our revised laboratory report dated March 24, 1975, prepared in connection with the above study.

Very truly yours,

J. C. Calandra

J. C. Calandra
President

JCC/fd

DSW 036967

STLCOPCB4020791

REPORT TO

MONSANTO COMPANY

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I. Introduction

At the request of Dr. Levinskas of the Monsanto Company, additional sections of liver from a two - year chronic oral toxicity study of Aroclor 1260 in rats (IBT No. 622-07298) were processed into H & E stained sections and evaluated by light microscopy. The following report presents the results of this study.

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II. Summary

In most instances, the spectrum of treatment-related histopathological findings in the liver from this re-evaluation did not differ significantly from that previously reported in our original report dated November 12, 1971. There were seven hepatomas detected among seven of the animals at the highest treatment level (100 ppm) of the 24-Month Sacrifice. No hepatocellular carcinomas were observed. The other treatment-related lesions reported are regarded as degenerative or hyperplastic in nature and they are morphologic manifestations of an adaptive response of the liver associated with biotransformation of the test material. In general, the latter findings were confined primarily to test animals of the 6-, 12- and 24-Month Sacrifices, and they were dose-related in incidence and severity.

In conclusion, Aroclor 1260 does not appear to be carcinogenic in rats fed for two years at levels up to and including 100 ppm.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report Prepared and Reviewed by:

D. E. Gordon, D. V. M., Ph. D.
Section Head, Pathology

Report Approved by:

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

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IBT No. 622-07298
Monsanto

I have examined additional sections of liver from rats of IBT No. 622-07298 and have re-evaluated them for evidence of carcinogenesis. I have tabulated my findings for Aroclor 1260 on the following pages:

There is evidence of a chemical effect on the liver which was most evident at time of the 12-Month and terminal (24-Month) sacrifices. This consists of a hepatocellular alteration beginning as focal hypertrophy which progresses to nodular hyperplasia, and in a few animals, to hepatoma or cholangiohepatoma. The hypertrophic cells contain large amounts of light staining cytoplasm which is probably rich in glycogen and endoplasmic reticulum. In some cases, ring-shaped structures, probably representing whorls of proliferative endoplasmic reticulum, were seen in the cytoplasm of these cells.

The hyperplastic nodules occupied larger areas and often compressed surrounding cells of the normal liver parenchyma. They also contained the same hypertrophic cells.

Those lesions classified as hepatomas or cholangiohepatomas were larger nodules which showed evidence of confluence or some variation in cell size, shape, staining or a ductular or adenomatous pattern of growth. In the absence of metastasis, invasiveness, severe basophilia, mitoses or other evidence of anaplasia, these are benign tumors rather than malignant carcinomas. There was no evidence of metastasis or invasiveness of these tumors in this study.

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With exception of the vacuolar changes in the cytoplasm of hepatocytes, the more severe hepatocellular alterations were confined to animals of the 12- and 24-Month Sacrifice periods.

Ward R. Richter

Ward R. Richter, D. V. M., M. S.
Diplomate, American College of
Veterinary Pathologists

Primary Liver Lesions - Aroclor 1260

3 Month Sacrifice - Rats

Lesion	Group			
	TI	TII	TIII	Control
Vacuolar Change	0/11	4/10	3/10	2/10
Focal Hypertrophy	0/11	0/10	2/10	0/10
Nodular Hyperplasia	0/11	0/10	0/10	0/10
Hepatoma	0/11	0/10	0/10	0/10
Ductular Hyperplasia	0/11	1/10	0/10	0/10
Cholangio-Hepatoma	0/11	0/10	0/10	0/10
Hepatocellular Necrosis	0/11	0/10	0/10	0/10

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Primary Liver Lesions - Aroclor 1260

6 Month Sacrifice - Rats

Lesion	Group			
	TI	TII	THI	Control
Vacuolar Change	1/6	2/5	5/9	1/10
Focal Hypertrophy	0/6	0/5	3/9	0/10
Nodular Hyperplasia	0/6	0/5	0/9	0/10
Hepatoma	0/6	0/5	0/9	0/10
Ductular Hyperplasia	0/6	0/5	0/9	0/10
Cholangio-Hepatoma	0/6	0/5	0/9	0/10
Hepatocellular Necrosis	0/6	1/5	0/9	1/10

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Primary Liver Lesions - Aroclor 1260

12 Month Sacrifice - Rats

Lesion	Group			
	TI	TII	TIII	Control
Vacuolar Change	2/9	5/10	3/9	1/10
Focal Hypertrophy	0/9	0/10	4/9	0/10
Nodular Hyperplasia	0/9	0/10	1/9	0/10
Hepatoma	0/9	0/10	0/9	0/10
Ductular Hyperplasia	1/9	0/10	2/9	1/10
Cholangio-Hepatoma	0/9	0/10	0/9	0/10
Hepatocellular Necrosis	0/9	0/10	0/9	0/10

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Primary Liver Lesions - Aroclor 1260

Terminal Sacrifice - Rats

Lesion	Group			
	TI	TII	TIII	Control
Vacuolar Change	5/25	6/23	10/27	1/23
Focal Hypertrophy	3/25	10/23	11/27	0/23
Nodular Hyperplasia	0/25	9/23	7/27	1/23
Hepatoma	0/25	0/23	5/27	0/23
Ductular Hyperplasia	6/25	5/23	14/27	5/23
Cholangio-Hepatoma	0/25	0/23	2/27	0/23
Hepatocellular Necrosis	4/25	2/23	6/27	1/23

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Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Anima No. and Sex	Liver Lesions								
			Vacuolar Change	Focal Necrosis	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hypertrophy of hepatocytes	Focal Bile Duct Hyperplasia	Hepatoma	Cholangio-hepatoma	
3 Month	AI	116M									
		117"									
		118"									
		119"									
		120"									
		147F									
		156"									
		157"									
		158"									
		159"									
		160"									
	AII	195M	++								
		196"	++								
		198"	+								
		200"	++								
		Extra"									
		236F									
		237"									
		238"									
		239"									
		240"									
	AIII	276M									
		277"	++								
		278"	++			+					
		279"				++					
		280"	++								
		315F									
		317"									
		318"									
		319"									
		320"									

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AROCLOR 1260

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Anima No. and Sex	Liver Lesions								
			Vacuolar Change	Focal Necrosis	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hypertrophy of hepatocytes	Focal Bile Duct Hyperplasia	Hepatoma	Cholangio-hepatoma	
6 Month	AI	832M									
		834"			+						
		835"									
		846F									
		848"	+								
		849"			+						
	AII	864M	+		+						
		865"	+		+						
		873"		+							
		878F									
		879"									
	AIII	891M	+			++					
		893"	++			+					
		894"	+			+					
		895"	+								
		906F	+								
		907"									
		908"									
		909"									
		910"									

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Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Anima No. and Sex	Liver Lesions								
			Vacuolar Change	Focal Necrosis	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hypertrophy of hepatocytes	Focal Bile Duct Hyperplasia	Hepatoma	Cholangio-hepatoma	
12 Month	AI	11M									
		12"	+					+			
		13"	+								
		14"									
		15"									
		16F									
		17"									
		18"									
		19"									
	AII	21M	+								
		22"									
		23"	+								
		24"	+								
		25"	++								
		26F									
		27"	+								
		28"									
		29"									
		30"									
	AIII	31M	++								
		32"									
		33"	++								
		34"	+								
		36F				+					
		37"				+					
		38"				+		+			
		39"					P				
		40"				+		+			

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AROCLOR 1260

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Anima No. and Sex	Liver Lesions								
			Vacuolar Change	Focal Necrosis	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hypertrophy of hepatocytes	Focal Bile Duct Hyperplasia	Hepatoma	Cholangio-hepatoma	
Final	AI	85M		+							
		86"	++	+		+					
		87"		++							
		101"									
		106"						+			
		112"									
		114"									
		105"	+								
		107"									
		109"		+		+		+			
		122F									
		125"						+			
		127"						+			
		129"						+			
		130"									
		138"	+++								
		141"									
		147"									
		151"									
		155"	+								
		144"									
		131"	+								
		132"									
		135"				+		+			
		139"									
	AII	167M			+						
		168"	+			+					
		179"				+		+			
		182"					P				
		184"	++								
		187"									
		Extra"				+		+			
		205F					P	+			
		208"									
		210"									

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AROCLOR 1260

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Animal No. and Sex	Liver Lesions								
			Vacuolar Change	Focal Necrosis	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hypertrophy of hepatocytes	Focal Bile Duct Hyperplasia	Hepatoma	Cholangio-hepatoma	
Final (continued)	AII	212F					P	+			
		213"	+			+					
		220"				+					
		221"									
		224"					P				
		233"									
		234"				++		+			
		219"	++	+		+					
		230"		++							
		203"				++					
		204"									
		206"	+								
		207"	+			++					
	AIII	241M		+			P	+			
		253"									
		261"				+		+			
		264"	+	+		++					
		270"				+		+			
		271"	++			+					
		272"	+++								
		275"	++				P				
		243"	+					++		P	
		244"		+							
		312"				+		+			
		231F				++	P	+			
		274"	+			+++					
		275"	+++	++		+++		++			
		294"							P		
		297"	++	+					P		
		302"					P				
		306"				+		+			
		308"					P	+			
		311"	++						P		
		314"							P		
		240"	++			+		+			

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Sacrifice Interval	Dose Level	Animal No. and Sex	Liver Lesions								
			Vacuolar Change	Focal Necrosis	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hypertrophy of hepatocytes	Focal Bile Duct Hyperplasia	Hepatoma	Cholangio-hepatoma	
Final (continued)	AIII	245F				++		+			
		281"					P	+			
		287"					P	+			
		291"						++	P		
		309"		+						P	

Grading System

+ = minimal in severity
++ = mild in severity
+++ = moderate in severity
++++ = marked in severity
P = Present, no grade

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AROCLOR - 1242

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Anima No. and Sex	Liver Lesions											
			Cytoplasmic vacuolation of hepatocytes	Focal necrosis of hepatocytes	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hyperplasia of hepatocytes	Focal bile duct hyperplasia	Hepatoma	Cholangio-hepatoma	Reticulum Cell Sarcoma metastatic	Mammary tumor, metastatic	Telangectasia, focal
24 Month	Control	63F											
		64"		+			P						
		66"											
		70"											
		71"											
		Ext"	+					+					

Grading System

\+ = Minimal in severity
++ = Mild in severity
+++ = Moderate in severity
++++ = Marked in severity
P = Present, no grade

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