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

DEPOSITION EXHIBIT
LEVINSKAS 42
5-12-87 WK

SCM 058180

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WATER_PCB-SD0000012126

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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.
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Veterinary Pathologists

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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	TIII	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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Sacrifice Interval	Dose Level	Anima No. and Sex	Liver Lesions							
			Vacuolar Change	Focal Nucrosis	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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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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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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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 (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	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 (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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THE EPPLEY INSTITUTE
for
RESEARCH IN CANCER

October 31, 1975

Paul L. Wright, Ph.D.
Monsanto Company
800 North Lindbergh Boulevard
St. Louis, Missouri 63166

Dear Dr. Wright:

Enclosed please find the report on Histopathological Re-evaluation of Tissues from Female Sherman Rats Fed Aroclor 1260. As mentioned in this report, there were about 20 animals with lesions, which on a morphological basis alone, could be interpreted as neoplastic. However, the definite malignant nature of these lesions cannot be proved in the presented material because of the factors mentioned in the section entitled "discussion" in the enclosed report.

I am sorry that I was not able to contact you by telephone. I was very much tied up with several visitors last week.

If you have any questions concerning the report, please contact me.

Sincerely,

P. Pour, M.D.
Professor

rmj

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