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

REPORT TO

MONSANTO COMPANY

TWO - YEAR CHRONIC ORAL TOXICITY STUDY WITH AROCLOR 1242 IN ALBINO RATS

HISTOPATHOLOGICAL EVALUATION OF ADDITIONAL LIVER SECTIONS

MARCH 24, 1975

IBT NO. 641 - 06672

DEPOSITION EXHIBIT
LEVINSKAS 43
5-27-87 WE

WATER_PCB-SD0000012142

REPORT TO

MONSANTO COMPANY

TWO - YEAR CHRONIC ORAL TOXICITY STUDY WITH AROCLOR 1242 IN ALBINO RATS

HISTOPATHOLOGICAL EVALUATION OF ADDITIONAL LIVER SECTIONS

MARCH 24, 1975

IBT NO. 641 - 06672

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 1242 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.

WATER_PCB-SD0000012143

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 three hepatomas detected among three 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 final sacrifice and they were dose-related in incidence and severity.

In conclusion, Aroclor 1242 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,

Report Prepared and Reviewed by: D. E. Gordon

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

Report Approved by: M. L. Keplinger

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

fd

WATER_PCB-SD0000012144

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 1242 on the following pages:

There is evidence of a chemical effect on the liver which is most pronounced at time of the terminal (24-Month) sacrifice. 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 volumes of light staining cytoplasm which is probably rich in glycogen and endoplasmic reticulum. In some sections, 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. These nodules 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 tumors (carcinomas). There was no evidence of metastasis or invasiveness of these tumors in this study.

WATER_PCB-SD0000012145

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

Ward R. Richter

Ward R. Richter, D.V.M., M.S.
Dipl., Am. College Vet. Path.

SCM 058153

030153

WATER_PCB-SD0000012146

Primary Liver Lesions - Aroclor 1242

3 Month Sacrifice - Rats

Lesion	Group			
	TI	TII	TIII	Control
Vacuolar Change	0/8	2/10	1/9	2/10
Focal Hypertrophy	0/8	0/10	0/9	0/10
Nodular Hyperplasia	0/8	0/10	0/9	0/10
Hepatoma	0/8	0/10	0/9	0/10
Ductular Hyperplasia	0/8	0/10	1/9	0/10
Cholangio- Hepatoma	0/8	0/10	0/9	0/10
Hepatocellular Necrosis	1/8	0/10	0/9	0/10

WATER_PCB-SD0000012147

Primary Liver Lesions - Aroclor 1242

6 Month Sacrifice - Rats

Lesion	Group			
	TI	TII	TIII	Control
Vacuolar Change	0/10	0/8	0/9	1/10
Focal Hypertrophy	0/10	0/8	0/9	0/10
Nodular Hyperplasia	0/10	0/8	0/9	0/10
Hepatoma	0/10	0/8	0/9	0/10
Ductular Hyperplasia	0/10	0/8	0/9	0/10
Cholangio-Hepatoma	0/10	0/8	0/9	0/10
Hepatocellular Necrosis	1/10	0/8	0/9	1/10

Primary Liver Lesions - Aroclor 1242

12 Month Sacrifice - Rats

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

WATER_PCB-SD0000012149

Primary Liver Lesions - Aroclor 1242

Terminal Sacrifice - Rats

Lesion	Group			
	TI	TII	TIII	Control
Vacuolar Change	7/31	8/30	9/20	1/23
Focal Hypertrophy	2/31	3/30	8/20	0/23
Nodular Hyperplasia	0/31	2/30	8/20	1/23
Hepatoma	0/31	0/30	2/20	0/23
Ductular Hyperplasia	3/31	3/30	3/20	5/23
Cholangio-Hepatoma	0/31	0/30	1/20	0/23
Hepatocellular Necrosis	1/31	1/30	0/20	1/23

WATER_PCB-SD0000012150

AROCLOR - 1242

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Animal 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	Telangiectasia, focal
3 Month	C-I 1ppm	596M											
		598"											
		599"											
		636F											
		637"											
		638"											
		639"		+									
		640"											
	C-II 10ppm	676M											
		677"	+										
		678"	+										
		679"											
		680"											
		716F											
		717"											
		718"											
		719"											
		720"											
	C-III 100ppm	756M											
		757"											
		758"	++										
		759"											
		760"						+					
		796F											
		797"											
		798"											
		800"											
	Control	36M	+										
		37"											
		38"											
		39"	+										
		40"											
		76F											
		77"											
		78"											
		79"											
		80"											

SCM 058158

090163

WATER_PCB-SD0000012151

AROCLOR - 1242

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Animal 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	Telangiectasia, focal
6 Month	C-I 1ppm	1011M		+	+								
		1012"											
		1013"			+								
		1014"											
		1015"											
		1026F											
		1027"											
		1028"											
		1029"											
		1030"			+								
	C-II 10ppm	1041M											
		1042"											
		1043"											
		1045"											
		1056F											
		1057"											
		1058"											
		1059"											
	C-III 100ppm	1071M											
		1072"											
		1073"											
		1075"											
		1086F											
		1087"											
		1088"											
		1089"											
		1090"											
	Control	801M	+	+									
		802"											
		803"											
		804"											
		805"											
		816F											
		817"											
		818"											
		819"											
		820"											

SCM 058159

000164

WATER_PCB-SD0000012152

Sacrifice terval	Dose Level	Animal 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	Telangiectasia, focal
2 Month	C-I 1ppm	71M											
		72"	+										
		73"											
		74"											
		75"											
		76F	+										
		77"											
		78"											
		79"											
		80"											
	C-II 10ppm	81M	+										
		82"											
		83"											
		84"	+					+					
		85"											
		86F											
		87"			+								
		88"											
		89"											
		90"	+										
	C-III	91M											
		92"											
		93"											
		94"											
		95"											
		96F											
		97"				+							
		98"											
		99"											
	Control	1M											
		2"	+										
		3"											
		4"											
		5"											
		6F											
		7"											
		8"											
		9"						+					

SCM 058160

000165

WATER_PCB-SD0000012153

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
24 Month	C-I 1ppm	564M										
		566"										
		591"										
		567"				+						
		569"									P	
		572"						+				
		576"										
		580"										
		588"										
		589"									P	
		595"	+									
		601F						+				
		604"										
		605"										
		582"	+									
		583"										
		607"				+		+				
		608"	+									
		609"										
		613"	+									
		621"										
		627"	+									
		628"	+									
		631"										
		634"										
		635"		+								
		606"										
		610"	+									
		620"										
		626"										
		633"										

SCM 058161

000166

WATER_PCB-SD0000012154

AROCLOR - 1242

Tabulation of Individual Liver Lesions in Rats

acrifice Interval	Dose Level	Animal 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	Cholanglo-hepatoma	Reticulum Cell Sarcoma metastatic	Mammary tumor, metastatic	Pulmonary fibrosis, focal
24 Month	C-II	655M											
	10ppm	657"	+										
		662"	++										
		667"											
		640"					P						
		641"											
		643"											
		644"						+++					
		645"											
		646"											
		649"											
		651"	+										
		673"	+			+							
		686F											
		687"						+					
		689"											
		685"											
		690"											
		695"										P	
		697"											
		700"				+							
		703"	++										
		707"					P						
		708"	++	+				+++					
		711"											
		712"	+										
		682"	+										
		683"											
		691"											
		702"				+							

SCM 058162

WATER_PCB-SD0000012155

Sacrifice Interval	Dose Level	Animal 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	Cholanglo-hepatoma	Reticulum Cell Sarcoma metastatic	Mammary tumor, metastatic
3 Month	C-III	740M										
	100ppm	722"										
		724"	+++				P					
		744"										
		746"				+						
		748"	++				P					
		768F				+	P					
		771"	+			++	P			P		
		775"				+++						
		Ext"	+++									
		733"										
		765"	+					+				
		766"	++			+	P	+				
		767"							P			
		776"				+	P	+				
		773"				+	P					
		786"	+++									
		789"							P			
		793"	++++									
		Ext"	++			+	P					
	Control	8M						+				
		11"										
		12"										
		21"										
		23"										
		33"						+				
		34"										
		35"										
		Ext"										
		46F			+							
		47"										
		49"						+				
		51"						++				
		52"										
		56"										
		59"										
		62"										

SCM 058163

WATER_PCB-SD0000012156

AROCLOR - 1242

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Animal 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	Telangiectasis, focal
1 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

SCM 058164

WATER_PCB-SD0000012157

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

REPORT TO

MONSANTO COMPANY

TWO - YEAR CHRONIC ORAL TOXICITY STUDY WITH AROCLOR 1254 IN ALBINO RATS

HISTOPATHOLOGICAL EVALUATION OF ADDITIONAL LIVER SECTIONS

MARCH 24, 1975

IBT NO. 641 - 06672

SCM 058165

000170

WATER_PCB-SD0000012158