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

C+25AM

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

DSW 034270

STLCOPCB4018097

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.

STLCOPCB4018098

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

Report Approved by:

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

fd

DSW 034272

STLCOPCB4018099

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.

DSW 034273

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.

DSW 034274

STLCOPCB4018101

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

STLCOPCB4018102

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

STLCOPCB4018103

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

STLCOPCB4018104

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

DSW 034278

STLCOPCB4018105

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

DSW 034279

STLCOPCB4018106

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
1 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"											

DSW 034280

STLCOPCB4018107

AROCLOR - 1242
Tabulation of Individual Liver Lesions in Rats

acrifice nterval	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	71M											
	1ppm	72"	+										
		73"											
		74"											
		75"											
		76F	+										
		77"											
		78"											
		79"											
		80"											
	C-II	81M	+										
	10ppm	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"											

DSW 034281

STLCOPCB4018108

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
4 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"											

DSW 034282

STLCOPCB4018109

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
24 Month	C-II 10ppm	655M											
		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"				+							

DSW 034283

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	Telangiectasis, focal
24 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"											

DSW 034284

STLCOPCB4018111

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	Telangectasia, focal
4 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

DSW 034285

STLCOPCB4018112