Dr. Gordon

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

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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

DEPOSITION
EXHIBIT
LEVINSKAS 44
5-27-87 WK

WATER_PCB-SD0000012159

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

March 24, 1975

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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 Arocior 1254

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

Very truly yours,

J. C. Calandra
President

WATER_PCB-SD0000012160

[redacted]

Industrial BIO-TEST Laboratories, Inc.

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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

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 1254 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.

[redacted]

000173

WATER_PCB-SD0000012161

II. Summary

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. However, there were six benign liver tumors detected among six of the animals at the highest treatment level (100 ppm) of the 24-Month Sacrifice which were not previously reported. One liver tumor (a hepatoma) previously reported in a TE animal (No. 418) was re-classified as nodular hyperplasia. 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 ascribed to with biotransformation of the test material. The latter lesions were confined primarily to test animals of the 12 and 24 month sacrifices and they were dose-related in incidence and severity.

In conclusion, Aroclor 1254 appears to be slightly tumorigenic at levels of 100 ppm when fed continuously in the diet for two years.

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. Koplinger, Ph.D.
Manager, Toxicology

WATER_PCB-SD0000012162

IBT No. 622-07298
Monsanto

I have examined additional sections of liver from rats of Study Number 622-07298 and have re-evaluated them for evidence of carcinogenesis. I have tabulated my findings for Aroclor 1254 on the following pages.

There is evidence of a chemical effect on the liver which is most pronounced at time of the 12-Month and 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 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.

These lesions which I classified as hepatomas or cholangio-hepatomas 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; I chose to call these benign tumors rather than malignant (carcinomas). There was no evidence of metastasis or invasiveness of these tumors in this study.

WATER_PCB-SD0000012163

It should be pointed out that other pathologists might call these tumors carcinomas on the basis of other criteria but, this diagnosis could be debated. With exception of the vacuolar 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.

WATER_PCB-SD0000012164

Primary Liver Lesions - Aroclor 1254

3 Month Sacrifice - Rats

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

WATER_PCB-SD0000012165

Primary Liver Lesions - Aroclor 1254

6 Month Sacrifice - Rats

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

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Primary Liver Lesions - Aroclor 1254

14 Month Sacrifice - Rats

Lesion	Group I	Group II	Group III	Control
Vacuolar Change	1/10	4/10	1/10	1/10
Focal Hypertrophy	0/10	4/10	2/10	0/10
Nodular Hyperplasia	0/10	0/10	0/10	0/10
Hepatoma	0/10	0/10	0/10	0/10
Ductular Hyperplasia	1/10	1/10	0/10	1/10
Cholangio-Hepatoma	0/10	0/10	0/10	0/10
Hepatocellular Necrosis	0/10	0/10	1/10	0/10

WATER_PCB-SD0000012167

Primary Liver Lesions - Aroclor 1254

Terminal Sacrifice - Rats

Lesion	3	1	2	3	1	2	3	1	2	1	2
	Group										
	TI			TII			TIII			Control	
Vacuolar Change	8/31	3/31	5/25	10/26	4/26	4/25	13/27	13/27	7/25	1/23	[illegible]
Focal Hypertrophy	3/31	1/31	7/25	5/26	1/26	7/25	13/27	6/27	7/25	0/23	[illegible]
Nodular Hyperplasia	0/31		9/25	3/26	1/26	7/25	13/27	3/27	9/25	1/23	[illegible]
Hepatoma	0/31		7/25	0/26		7/25	4/27	1/27	7/25	0/23	[illegible]
Ductular Hyperplasia	6/31	3/31	4/25	3/26	1/26	7/25	4/27	1/27	7/25	5/23	[illegible]
Cholangio-Hepatoma	0/31		7/25	0/26		7/25	2/27	0/27	7/25	0/23	[illegible]
Hepatocellular Necrosis	3/31	2/31	7/25	1/26	1/26	7/25	2/27	1/27	7/25	1/23	[illegible]

* There were 5 animals in [illegible] at time of the 2nd [illegible], [illegible] present, [illegible]

** Similar to above involving 4 animals

WATER_PCB-SD0000012168

AROCLOR - 1254

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
3 Month	B-I 1ppm	356M	++										
		357"	+										
		358"											
		359"		+									
		360"	+										
		396F											
		397"											
		398"											
		399"											
		400"											
	B-II 10ppm	436M	+										
		437"											
		438"	+										
		439"											
		440"	+										
		476F		+									
		477"											
		478"											
		479"											
		480"											
	B-III 100ppm	516M											
		517"											
		518"	++	+-	++								
		519"											
		520"											
		555F											
		557"											
		558"											
		559"											
		560"											

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AROCLOR - 1254
Tabulation of Individual Liver Lesions in Rats

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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-hepatitis	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
6 Month	B-I 1ppm	921M		+									
		922"											
		923"		+									
		924"											
		925"											
		936F											
		937"											
		938"											
		939"											
		940"											
	B-II 10ppm	950M											
		951"											
		952"											
		953"											
		954"											
		966F											
		967"											
		968"											
		969"											
		970"											
	B-III 100ppm	981M		+ (-)	+ (-)								
		982"			+ (-)								
		983"											
		984"											
		985"											
		996F				+ (-)							
		997"				+ (-)							
		998"											
		999"		+ (-)		+ (-)							
		1000"				+ (-)							

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WATER_PCB-SD0000012170

AROCLOR - 1254
Tabulation of Individual Liver Lesions in Rats 233

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	Squamous Cell Carcinoma, metastatic	Mammary tumour, metastatic	Hepatitis/Cirrhosis
14 Month	B-I 1ppm	41M	+										
		42"											
		43"											
		44"											
		45"											
		46F											
		47"											
		48"						+					
		49"											
		50"											
	B-II 10ppm	51M											
		52"	++										
		53"	++										
		54"			+								
		55"	+										
		56F			+								
		57"	+			+							
		58"				+							
		59"				+							
		60"				+		+					
	B-III 100ppm	61M				++							
		62"											
		63"											
		64"											
		65"	++			++							
		66F											
		67"			++								
		68"											
		69"											
		70"		+(-)									

000183

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AROCLOR - 1254 234 12

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-I 1ppm	326M						(+) (+)					
		330"											
		335"											
10/9		338"											
		351"	(+)+ (+)	+ (+)	(+)								
		323"		(+)									
		325"											
		343"	(+)										
		346"*			+	+							
		342F											
		362"			(+)								
		368"						(+) + (+)					
		374"											
		375"				(P)		(+) +					
		376"				(+) +							
		475"	(+) +++										
22/22		366"						(+) + (+)					
		367"											
		372"						(+) + (+)					
		377"	(+) ++ (+)	(+) ++		(+) +		(+) +					
		378"*	(+) +		(P)								
		379"	(+) + (+)										
		380"											
		381"											
		384"	(+)										
		387"*											
		388"*											
		389"											
		391"	(+) +			(P)		(+) + (+)					
		394"	(+) +++ (+)										
		Ext"		(+) (P)	(+) ++			(+)					

Findings [illegible] of [illegible] slides in blue pencil

* No liver section on blade

\+ Slide missing

000184

WATER_PCB-SD0000012172

AROCLOR - 1254 13

Tabulation of Individual Liver Lesions in Rats 235

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-II	415M											
	10ppm	417"											
		418"											
		419"											
		423"											
		426"											
		427"											
		491"											
		402"											
		403"											
		405"											
		410"											
		434"											
		450F											
		451"											
		452"											
		456"											
		459"											
		463"											
		469"											
		470"											
		471"											
		478"											
		443"											
		445"											
		448"											

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WATER_PCB-SD0000012173

AROCLOR - 1254

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-III	484M	(-)++					(+) (+++)					-/-
	100ppm	491"	[illegible]		(P)	(-)+	(-) P(P)		(-) P(-)				
		497"				(-)++	(-) P						
9/10		499"	(+)			(-)+	(-) P						
		507"					P						-/P
		509"											
		510"	(-)+										
		512"		(P)									
		483"	(-)++	(-)		(P)	(+)	(P) + (+)					
		489"	(-)+			(P) +	(P)	(P)					
		522F	(P)++			(-)++	(P)						
		524"	(P)++			(-)+	(-) P(P)						
		527"	(P)+++			(P)+	(-) P(P)					(-) P	
		541"	(P)			(-)+	(P) (P)		(-) P(-)				
17/17		547"	(P)++(+)			(P) (P)	(-) P						
		Ext1"	(P)++			(-)++++	(-) P(P)						
		Ext2"				(P)	(-) P	(P) +		(-) P(P)			
		Ext3"	(-)++	-		(-)+++							
		Ext4"	(P)			(-) (P)	(-) P		(-) P(-)				
		Ext5"		-+			(-) P						
		536"	(P)++			(P)+++	(-) P	(P)	(P)				
		537"	(P) (-)										
		539"	(P)++			(P)++	(P)	(-) +					
		441"											
		Ex1"				(P)	(P)		(-) P(-)				
		Ex2"	(P)++							(-) P(-)			
		Ex3"				(P)+	(P) P	+	(P) (P)				

Grading System

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

II. Summary

In most instances, 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. However, there were six benign liver tumors detected among six of the animals at the highest treatment level (100 ppm) of the 24-Month Sacrifice which were not previously reported. 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. The latter lesions were confined primarily to test animals of the 14 and 24 month sacrifices and they were dose-related in incidence and severity.

In conclusion, Aroclor 1254 appears to be slightly tumorigenic at levels of 100 ppm when fed continously in the diet for two years.

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. Koplinger, Ph.D.
Manager, Toxicology

WATER_PCB-SD0000012175

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. 64[illegible] - 06672

WATER_PCB-SD0000012176

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

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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 1254.

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
President

000133

WATER_PCB-SD0000012177

[redacted]

[redacted] BIO-TEST [redacted]

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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

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 1254 in rats (IBT No. 622-07296) were processed into H & E stained sections and evaluated by light microscopy. The following report presents the results of this study.

[redacted]

000190

WATER_PCB-SD0000012178

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. However, there were six benign liver tumors detected among six of the animals at the highest treatment level (100 ppm) of the 24-Month Sacrifice which were not previously reported. One liver tumor (a hepatoma) previously reported in a T-II animal (No. 445) was re-classified as nodular hyperplasia 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 ascribed to biotransformation of the test material. The latter lesions were confined primarily to test animals of the 12 and 24 month sacrifices and they were dose-related in incidence and severity.

In conclusion, Aroclor 1254 appears to be slightly tumorigenic at levels of 100 ppm when fed continously in the diet for two years.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

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-SD0000012179

[redacted]

Industrial BIO-TEST Laboratories, Inc.

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IBT No. 622-07298
Monsanto

I have examined additional sections of liver from rats of Study Number 622-07298 and have re-evaluated them for evidence of carcinogenesis. I have tabulated my findings for Aroclor 1254 on the following pages.

There is evidence of a chemical effect on the liver which is most pronounced at time of the 12-Month and 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 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.

These lesions which I classified as hepatomas or cholangio-hepatomas 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; I chose to call these benign tumors rather than malignant (carcinomas). There was no evidence of metastasis or invasiveness of these tumors in this study.

[redacted]

000192

WATER_PCB-SD0000012180

[redacted]

[redacted] BIO-TEST [redacted]

193

With exception of the vacuolar 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.

[redacted]

000193

WATER_PCB-SD0000012181

Primary Liver Lesions - [illegible]

[illegible]

Lesion	[illegible]	[illegible]	[illegible]	Control
Vacuolar Change	3/10	3/10	1/10	2/10
Focal Hypertrophy	0/10	0/10	1/10	0/10
Nodular Hyperplasia	0/10	0/10	0/10	0/10
Hepatoma	0/10	0/10	0/10	0/10
Ductular Hyperplasia	0/10	0/10	0/10	0/10
Cholangio-Hepatoma	0/10	0/10	0/10	0/10
Hepatocellular Necrosis	1/10	1/10	0/10	0/10

WATER_PCB-SD0000012182

Primary Liver Lesions - Aroclor 1254

6 Month Sacrifice - Rats

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

WATER_PCB-SD0000012183

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Primary Liver Lesions - Aroclor 1254

12 Month Sacrifice - Rats

Lesion	Group			
	II	III	IIII	Control
Vacuolar Change	1/10	4/10	1/10	1/10
Focal Hypertrophy	0/10	4/10	2/10	0/10
Nodular Hyperplasia	0/10	0/10	0/10	0/10
Hepatoma	0/10	0/10	0/10	0/10
Ductular Hyperplasia	1/10	1/10	0/10	1/10
Cholangio-Hepatoma	0/10	0/10	0/10	0/10
Hepatocellular Necrosis	0/10	0/10	1/10	0/10

WATER_PCB-SD0000012184

Primary Liver Lesions - Aroclor 1254

Terminal Sacrifice - Rats

Lesion	Group			
	TI	TII	THI	Co.
Vacuolar Change	8/31	10/26	13/27	1/23
Focal Hypertrophy	3/31	5/26	13/27	0/23
Nodular Hyperplasia	0/31	3/26	13/27	1/23
Hepatoma	0/31	0/26	4/27	0/23
Ductular Hyperplasia	6/31	3/26	4/27	5/23
Cholangio-Hepatoma	0/31	0/26	2/27	0/23
Hepatocellular Necrosis	3/31	1/26	2/27	1/23

WATER_PCB-SD0000012185

AROCLOR - 1254

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic
3 Month	B-I 1ppm	356M	++									
		357"	+									
		358"										
		359"		+								
		360"	+									
		396F										
		397"										
		398"										
		399"										
		400"										
	B-II 10ppm	436M	+									
		437"										
		438"	+									
		439"										
		440"	+									
		476F		+								
		477"										
		478"										
		479"										
		480"										
	B-III 100ppm	516M										
		517"										
		518"	+	+								
		519"										
		520"										
		555F										
		557"										
		558"										
		559"										
		560"										

WATER_PCB-SD0000012186

AROCLOR - 1254 10

Tabulation of Individual Liver Lesions in Rats 199

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
6 Month	B-I 1ppm	921M		+									
		922"											
		923"		+									
		924"											
		925"											
		936F											
		937"											
		938"											
		939"											
		940"											
	B-II 10ppm	950M											
		951"											
		952"											
		953"											
		954"											
		966F											
		967"											
		968"											
		969"											
		970"											
	B-III 100ppm	981M		+	+								
		982"			+								
		983"											
		984"											
		985"											
		996F				+	+						
		997"											
		998"											
		999"		+									
		1000"				+	+						

WATER_PCB-SD0000012187

AROCLOR - 1254

Tabulation of Individual Liver Lesions in Rats

200

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	Squamous cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
12 Month	B-I 1ppm	41M	+										
		42"											
		43"											
		44"											
		45"											
		46F											
		47"											
		48"						+					
		49"											
		50"											
	B-II 10ppm	51M											
		52"	++										
		53"	++										
		54"			+								
		55"	+										
		56F			+								
		57"	+			+							
		58"				+							
		59"				+							
		60"				+		•					
	B-III 100ppm	61M				+							
		62"											
		63"											
		64"											
		65"	++			+							
		66F											
		67"			+								
		68"											
		69"											
		70"		+									

000200

WATER_PCB-SD0000012188

AROCLOR - 1254 12

Tabulation of Individual Liver Lesions in Rats 201

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-1 1ppm	326M											
		330"											
		335"											
		338"											
		351"	++	+									
		323"		+									
		325"											
		343"	+										
		346"			+	+							
		342F											
		362"											
		368"						+					
		374"											
		375"						+					
		376"				+							
		475"	+++										
		366"						+					
		367"											
		372"						+					
		377"	++	++		+		+					
		378"	+										
		379"	+										
		380"											
		381"											
		384"											
		387"											
		388"											
		389"											
		391"	+					+					
		394"	+++										
		Ext"			++								

000201

WATER_PCB-SD0000012189

AROCLOR - 1254

Tabulation of Individual Liver Lesions in Rats

202

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-II 10ppm	415M											
		417"				++		+					
		418"											
		419"											
		423"											
		426"	++										
		427"	+										
		491"									P		
		402"	+										
		403"	++										
		405"											
		410"											
		434"	+										
		450F											
		451"	+				P						
		452"	+	+			P						
		456"				+							
		459"				++		++					
		463"	++										
		469"				+							
		470"											
		471"											
		475"						+					
		443"											
		445"					P						
		448"											

000202

WATER_PCB-SD0000012190

AROCLOR - 1254 14

Tabulation of Individual Liver Lesions in Rats 203

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hep-atitis/Cirrhosis
24 Month	B-III	484M	++										-/+
	100ppm	491"				+	P		P				
		497"				++	P						
		499"				+	P						
		507"					P						
		509"											
		510"	+										
		512"											
		483"	++					+					
		489"	+			+							
		522F	++			+							
		524"	++			+	P						
		527"	+++			+	P					P	
		541"				+			P				
		547"	++				P						
		Ext1"	++			++++	P						
		Ext2"					P	+		P			
		Ext3"	++			+++							
		Ext4"					P		P				
		Ext5"		+			P						
		536"	++			++	P						
		537"											
		539"	++			++		+					
		441"											
		Ex1"							P				
		Ex2"	++							P			
		Ex3"				+	P	+					

Grading System

- - minimal in severity
- ++ - mild in severity
- +++ - moderate in severity
- ++++ - marked in severity
- P - Present, no grade
- . - Absent

000203

WATER_PCB-SD0000012191

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

056

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

Final Report

WATER_PCB-SD0000012192

[redacted]

Industrial BIO-TEST Laboratories, Inc.
2010 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

057

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 1254.

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/ld

[redacted]

000205

WATER_PCB-SD0000012193

[redacted]

[redacted] BIO-TEST [redacted]

058

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

BBT 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 1254 in rats (BBT No. 622-07298) were processed into H & E stained sections and evaluated by light microscopy. The following report presents the results of this study.

[redacted]

000206

WATER_PCB-SD0000012194

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 six hepatomas detected among six of the animals at the highest treatment level (100 ppm) of the 24-Month Sacrifice. No hepatocellular carcinomas were observed. One liver tumor (a hepatoma) previously reported in a T-H animal (No. 445) was re-classified as nodular hyperplasia. 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 ascribed to biotransformation of the test material. The latter lesions were confined primarily to test animals of the 12 and 24 month sacrifices and they were dose-related in incidence and severity.

In conclusion, Aroclor 1254 appears to be slightly tumorigenic at levels of 100 ppm when fed continously in the diet for two years.

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, M.D.
Manager, Toxicology

sew

WATER_PCB-SD0000012195

[redacted] 3

[redacted] 060

I have examined additional sections of liver from [redacted] and have re-evaluated them for evidence of carcinogenesis. I have modified my findings for October 1984 as the following pages:

There is evidence of a chemical effect on the liver which is most pronounced at time of the 12-month and 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 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.

These 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.

000003

WATER_PCB-SD0000012196

Submitted BIO-TEST Laboratories, Inc. 881

With exception of the vacuolar 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.

000203

WATER_PCB-SD0000012197

062

Primary Liver Lesions - Aroclor 1254

3 Month Sacrifice - Rats

Lesion	Group			
	II	III	IIII	Control
Vacuolar Change	3/10	3/10	1/10	2/10
Focal Hypertrophy	0/10	0/10	1/10 C	0/10
Nodular Hyperplasia	0/10	0/10	0/10	0/10
Hepatoma	0/10	0/10	0/10	0/10
Ductular Hyperplasia	0/10	0/10	0/10	0/10
Cholangio-Hepatoma	0/10	0/10	0/10	0/10
Hepatocellular Necrosis	1/10	1/10	1/10	0/10

WATER_PCB-SD0000012198

Primary Liver Lesions - Aroclor 1254

6 Month Sacrifice - Rats

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

WATER_PCB-SD0000012199

Primary Liver Lesions - Aroclor 1254

12 Month Sacrifice - Rats

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

WATER_PCB-SD0000012200

Primary Liver Lesions - Aroclor 1254

Terminal Sacrifice - Rats

Focal Hypertrophy	3/31	1/26	13/27	0/23
Nodular Hyperplasia	0/31	3/26	13/27	1/23
Hepatoma	0/31	0/26	4/27	0/23
Ductular Hyperplasia	6/31	3/26	4/27	3/23
Cholangio-Hepatoma	0/31	0/26	2/27	0/23
Hepatocellular Necrosis	3/31	1/26	2/27	1/23

WATER_PCB-SD0000012201

AROCLOR - 1254

Tabulation of Individual Liver Lesions in Rats 066

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
3 Month	B-I 1ppm	356M	++										
		357"	+										
		358"											
		359"		+									
		360"	+										
		396F											
		397"											
		398"											
		399"											
		400"											
	B-II 10ppm	436M	+										
		437"											
		438"	+										
		439"											
		440"	+										
		476F		+									
		477"											
		478"											
		479"											
		480"											
	B-III 100ppm	516M											
		517"											
		518"	+	+	+								
		519"											
		556"											
		560"											

000214

WATER_PCB-SD0000012202

AROCLOR - 1254 10

Tabulation of individual Liver Lesions in Rats 067

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
6 Month	B-I 1ppm	921M		+									
		922"											
		923"		+									
		924"											
		925"											
		936F											
		937"											
		938"											
		939"											
		940"											
	B-II 10ppm	950M											
		951"											
		952"											
		953"											
		954"											
		966F											
		967"											
		968"											
		969"											
		970"											
	B-III 100ppm	981M		+		+							
		982"				+							
		983"											
		984"											
		985"											
		996F				+							
		997"				+							
		998"											
		999"		+		+							
		1000"				+							

000215

WATER_PCB-SD0000012203

AROCLOR - 1254
Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Animal No. Sex	Liver Lesions: Cytoplasmic Accumulation of Lymphocytes	Focal necrosis of hepatocytes	Focal lymphoid infiltrations	Focal hypertrophy of hepatocytes	Nodular hyperplasia of hepatocytes	Focal bile duct hyperplasia	Hepatoma	Cholangio-hepatoma	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
12 Month	B-I 1ppm	41M	+										
		42"											
		43"											
		44"											
		45"											
		46F											
		47"											
		48"						+					
		49"											
		50"											
	B-II 10ppm	51M											
		52"	+										
		53"	+										
		54"			+								
		55"	+										
		56F			+								
		57"	+			+							
		58"				+							
		59"				+							
		60"				+		+					
	B-III 100ppm	61M				+							
		62"											
		63"											
		64"											
		65"	+			+							
		66F											
		67"			+								
		68"											
		69"											
		70"		+									

WATER_PCB-SD0000012204

AROCLOR - 1254

Tabulation of Individual Liver Lesions in Rats 069

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-1 1ppm	326M											
		330"											
		335"											
		338"											
		351"	++	+									
		323"		+									
		325"											
		343"	+										
		346"			+	+							
		342F											
		362"											
		368"						+					
		374"											
		375"						+					
		376"				+							
		475"	+++										
		366"						+					
		367"											
		372"						+					
		377"	++	-		+		+					
		378"	+										
		379"	+										
		380"											
		381"											
		384"											
		387"											
		388"											
		389"											
		391"	+					+					
		394"	+-										
		Ext"			++								

WATER_PCB-SD0000012205

AROCLOR - 1254 070 13

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-II 10ppm	415M											
		417"				++		+					
		418"											
		419"											
		423"											
		426"	++										
		427"	+										
		491"									P		
		402"	+										
		403"	++										
		405"											
		410"											
		434"	+										
		450F											
		451"	+				P						
		452"	+	+			P						
		456"				+							
		459"				++		++					
		463"	++										
		469"				+							
		470"											
		471"											
		478"						+					
		443"											
		445"					P						
		448"											

WATER_PCB-SD0000012206

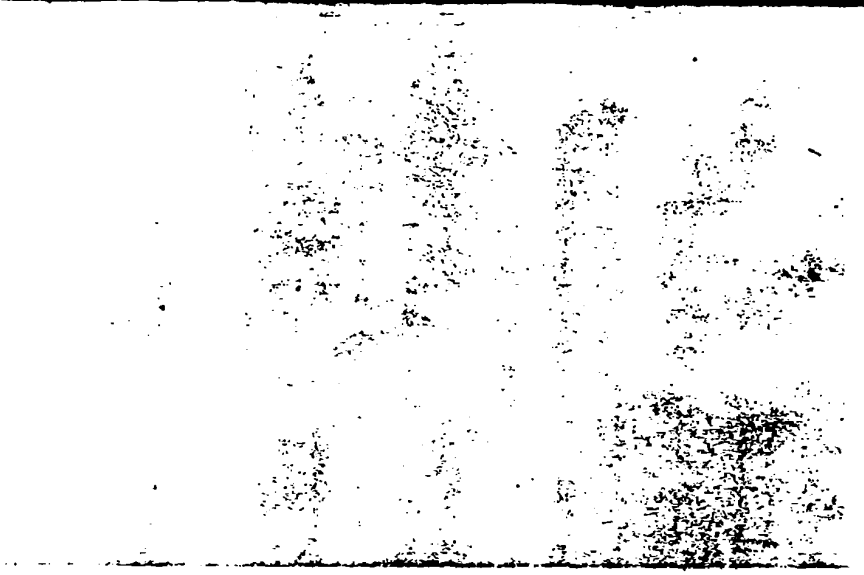
AROCLOR - 1254
Tabulation of Individual Liver Lesions in Rats 071

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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-III	484M	++			+	P		P				
	100ppm	491"				++	P						
		497"				+	P						
		499"					P						
		507"											
		509"	+										
		510"											
		512"	++					+					
		483"	+			+							
		489"	++			++							
		522F	++			+	P						
		524"	+++			+	P					P	
		527"				+			P				
		541"	++				P						
		547"	++			++++	P						
		Ext1"	++				P	+		P			
		Ext2"	++			+++	P						
		Ext3"					P		P				
		Ext4"		+			P						
		Ext5"	++			+++	P						
		536"											
		537"	++			++		+					
		539"							P				
		441"	++			+	P	+		P			
		Ex1"											
		Ex2"											
		Ex3"											

Grading System
- = minimal in severity
— = mild in severity
--- = moderate in severity
---- = marked in severity
P = Present, no grade
. = Absent

000213

WATER_PCB-SD0000012207



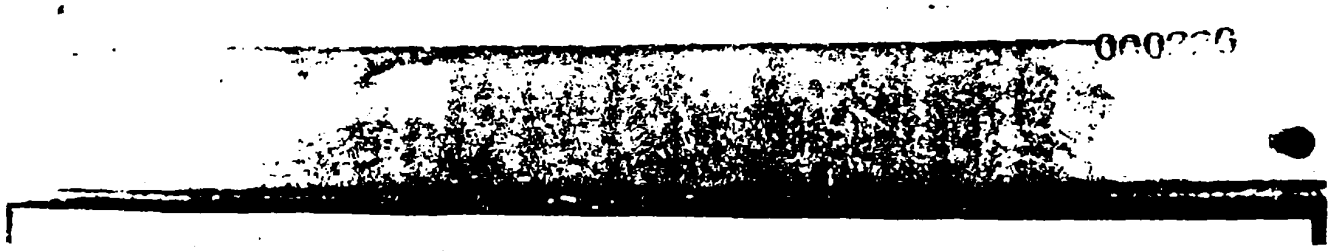
Primary Liver Lesions - Aroclor 1254

Terminal Sacrifice - Rats

Lesion	Group TI 1	TI 2	TI 3	TII 1	TII 2	TII 3	TIII 1	TIII 2	TIII 3	Control 1	Control 2
Vacuolar Change	3/31	5/28	8/31	4/26	4/25	10/26	13/27	3/25	13/27	1/23	0/24
Focal Hypertrophy	1/31	2/28	3/31	1/26	1/25	5/26	6/27	3/25	13/27	0/23	0/24
Nodular Hyperplasia		0/28	0/31	1/26	3/25	3/26	3/27	9/25	13/27	1/23	0/24
Hepatoma		0/28	0/31	½	0/25	0/26	1/27	2/25	4/27	0/23	0/24
Ductular Hyperplasia	3/31	6/28	6/31	3/26	4/25	3/26	5/27	2/25	4/27	5/23	6/24
Cholangio-Hepatoma		9/28	0/31		0/25	0/26	0/27	1/25	2/27	0/23	0/24
Hepatocellular Necrosis	2/31	2/28	3/31	1/26	2/25	1/26	1/27	1/25	2/27	1/23	0/24

1 = First evaluation of original slides
2 - Re-evaluation of original slides
3 - Evaluation of additional tissue sections

There were 5 animals in which this lesion was not seen at time of the second evaluation but was present on the first.
Similar to above involving 4 animals.



WATER_PCB-SD0000012208

Industrial BIO-TEST Laboratories Inc

073

Primary Liver Lesions - AROCLOR 1254

Terminal Sacrifice - Rats

Re-evaluation of Original Slides

	B-1	B-2	B-3	Control
Vacuolar Change	5/28	4/25	3/25	0/24
Focal Hypertrophy	2/28	1/25	3/25	0/24
Nodular Hyperplasia	0/28	3/25	9/25	0/24
Ductular Hyperplasia	6/28	4/25	2/25	6/24
Cholangio-hepatoma	2/28	0/25	1/25	0/24
Hepatoma	0/28	0/25	2/25	0/24

WATER_PCB-SD0000012209

AROCLOR - 1254

Tabulation of Individual Liver Lesions in Rats

Sacrifice Interval	Dose Level	Animal No. and Sex	Liver Lesions: Cytoplasmic vacuolation of hepatocytes	Focal neurosis of hepatocytes	Focal hyperplasia bilirubinosis	Focal hypertrophy of hepatocytes	Nodular hyperplasia of hepatocytes	Focal bile duct hyperplasia	Hepatoma	Cholangio hepatoma	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-1 1 ppm	326 M						•					
		330 "											
		335 "											
		338 "											
		351 "	—	——									
		323 "											
		325 "											
		342 "											
		346 "	no liver section on slide										
		342 F											
		362 "											
		368 "						•					
		374 "											
		375 "				P							
		376 "											
		475 "											
		366 "						•					
		367 "											
		372 "						•					
		377 "	—										
		378 "											
		379 "	•										
		380 "											
		381 "											
		384 "	•										
		387 "											
		389 "											
		391 "				P		•					
		394 "	——										
		Exc "		P				•					

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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	Hepatitis	Cholangio-hepatitis	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-E 10 ppm	415 M	→										
		417 "											
		418 "											
		419 "	•										
		423 "											
		427 "											
		491 "		→									
		402 "				•							
		403 "											
		406 "						•					
		410 "											
		434 "											
		450 F											
		451 "						•					
		452 "			•		P						
		456 "											
		459 "											
		463 "	•										
		469 "											
		470 "		→									
		471 "											
		478 "						•					
		443 "					P						
		446 "					P	•					
		448 "											

WATER_PCB-SD0000012211

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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	Squamous Cell Carcinoma, metastatic	Mammary tumor, metastatic	Hepatitis/Cirrhosis
24 Month	B-III 100 ppm	424 M						---					
		491 "					P						
		497 "											
		499 "											
		507 "											
		509 "											
		510 "											
		512 "	necrosis										
		483 "	+			P							
		489 "					P						
		522 F					P						
		524 "					P						
		527 "					P						
		541 "					P						
		547 "	--			P							
		Ex1 "					P						
		Ex2 "								P			
		Ex3 "											
		Ex4 "				P							
		Ex5 "											
		536 "							P				
		537 "	+										
		539 "					P						
		441 "											
		Ex1 "					P						
		Ex2 "											
		Ex3 "							P				

Grading System

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

WATER_PCB-SD0000012212