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EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

PATHOLOGY REPORT ON THE BRAINS FROM MICE, HAMSTERS, AND RATS EXPOSED TO VINYL CHLORIDE IN IBT STUDY 663-03222

Submitted to:

Chemical Manufacturers Association
Washington, D. C. 20009

May 14, 1980

PATHOLOGY REPORT ON THE BRAINS FROM MICE, HAMSTERS, AND RATS EXPOSED TO VINYL CHLORIDE IN IBT STUDY 663-03222

I. INTRODUCTION

At the request of the Chemical Manufacturers Association, Experimental Pathology Laboratories, Inc. conducted a pathology evaluation of the available brains from mice, hamsters, and rats either exposed to vinyl chloride or used as controls in Industrial Bio-Test (IBT) Study 663-03222. This inhalation toxicology study was conducted in the IBT facilities at Decatur, Illinois, and was initiated on September 10, 1973.

The experimental design for this study is as follows:

Group	Number of Animals						Exposure Levels
	Mice		Rats		Hamsters		
	M	F	M	F	M	F	
Control	100	100	100	100	100	100	-
T1*	100	100	100	100	100	100	50 ppm Vinyl Chloride
T2*	100	100	100	100	100	100	200 ppm Vinyl Chloride
T3*	100	100	100	100	100	100	2500 ppm Vinyl Chloride
T4**	-	-	100#		-	-	2500 ppm Vinyl Chloride

*No food, water, or bedding in cages during exposure
**Food, water, and bedding to remain in cages during exposure
#All rats of same sex, either sex permitted

The protocol as amended called for the inhalation exposure of the above groups six hours per day, five days per week. Mice were to be exposed for nine months; rats and hamsters for twelve months. These groups were originally scheduled to be held for equal additional periods of time (nine or twelve months); but, subsequently it was agreed that

they would be kept for their lifetime or sacrificed if moribund. All animals were to be necropsied either at the time of death or sacrifice, and a relatively complete set of tissues was to be preserved in 10% neutral buffered formalin. These tissues were to be examined from all animals in the control, T2, and T3 groups. If exposure related lesions were detected in the organs of the T2 or T3 groups, these same organs from the T1 group were to be examined.

An EPL pathologist (Dr. William Busey) and four histology/pathology technicians traveled to IBT at Northbrook, Illinois, where the material from the study is archived. At IBT, facilities were provided for examination of the residual wet tissue, paraffin blocks, and microscope slides. In addition, facilities were provided for the histologic processing of brains recovered from the residual wet tissue.

II. MATERIALS AND METHODS

A. Residual Wet Tissue

All of the bags of residual fixed wet tissue from the mice, hamsters, and rats were examined for brain material. If brain material was discovered in the bag, it was recovered, examined grossly for any alterations, and trimmed into three to five sections for histologic processing.

B. Paraffin Blocks

All of the paraffin blocks from the mice, hamsters, and rats were examined for the presence of embedded brain material. If brains were discovered, the blocks were set aside for microtoming and staining.

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C. Microscope Slides (IBT Prepared)

All of the microscope slides from the mice, hamsters, and rats were examined for brains. All brain slides were examined microscopically at IBT by the EPL pathologist.

D. Pathology Sheets

The original pathology sheets from the mice, hamsters, and rats were examined for gross descriptions of brain abnormalities. The descriptions of any brain abnormalities were recorded along with the date of death of any animal with a recorded gross or microscopic brain lesion. In addition to the gross description of any brain abnormality, the microscopic findings of the IBT pathologist were also recorded.

In the animals for which brain material was recovered from either the residual wet tissue, paraffin blocks, or microscope slides, an attempt was made to verify the animal identification. This was done by comparing the animal number and date of death recorded on the pathology sheet with the animal numbers and date of death recorded on the bags of residual wet tissue and with the animal numbers embedded in the paraffin blocks or recorded on the microscope slides.

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The brains recovered from the residual wet tissue were processed, embedded, microtomed, and mounted on microscope slides at IBT. The paraffin blocks containing brain material, previously embedded by IBT, were microtomed and mounted on microscope slides. Duplicate slides were prepared from each paraffin block containing brain. One set of slides was left at IBT and the other set was returned to EPL, stained with hematoxylin and eosin, and evaluated by an EPL pathologist.

III. RESULTS

A. Number of Recovered Brains

The following table details the number of brains recovered from either the residual wet tissue or paraffin blocks previously prepared by IBT:

Number of Brains Recovered from Residual Wet Tissue or IBT Paraffin Embedded Blocks

Group	Mice		Hamsters		Rats	
	M	F	M	F	M	F
Untreated Control	5	4	4	3	18	20
T1	13	8	8	4	15	13
T2	3	7	14	10	23	11
T3	12	14	13	6	23	17
T4	-	-	-	-	-	12

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B. Pathology

1. Mice and Hamsters

With the exception of focal encephalitis in Group T3 male hamster No. 2208, no gross or microscopic alterations were seen in any of the brains examined from the mice and hamsters.

2. Rats

Grossly detected changes in the brain were described at the time of necropsy by IBT in four male rats from the T3 group. These gross observations are as follows:

Animal No.	Gross Observation
641	1 cm. mass located in front of brain in skull leaving a compression in brain.
664	A gelatinous-like focus beginning on the anterior frontal half of the brain beneath the meninges compressing the adjacent brain tissue. Mid sagittal section of the brain reveals an 8 mm white firm focus involving olfactory region and compression of adjacent cerebrum.
667	A soft tan mass was found in the right frontal region in the skull cap compressing the front quarter of the brain. Mass located between the meninges and the skull cap 1 cm. in diameter.
672	Front portion of brain was gelatinous and very soft.

In addition to the above four gross brain abnormalities, the following brain with a gross abnormality was detected by EPL personnel

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Animal No.	Gross Observation
649	0.2 x 0.5 tan mass attached to the left olfactory bulb.

The detailed histologic findings for the microscopic evaluation of the brains are presented in Table II. A summary of the findings is presented in Table I.

Microscopic evaluation of the brains from the control and vinyl chloride exposed male and female rats revealed olfactory neuroblastomas (esthesioneuroblastoma, esthesioneuroepithelioma, medulloepithelioma) in five T3 males (641, 649, 664, 667, and 672), one T3 female rat (761), and one T4 female rat (2413). A single glioblastoma multiforme was detected in the brain from T2 male rat No. 412, and a single astrocytoma was detected in the brain of T2 female rat No. 566.

The histological features of the seven olfactory neuroblastomas were remarkably similar. They were characterized by a proliferation of deeply basophilic cylindrical cells with abundant cytoplasm supported by small blood vessels. Characteristic pseudo-rosettes were present along with numerous mitotic figures. In most instances these neoplasms compressed the anterior portion of the cerebrum; and, in some cases, infiltration under the meninges was evident. The glioblastoma multiforme was characterized by a proliferation of a mixture of highly pleomorphic cells containing large nuclei. Numerous giant cells and mitotic figures were also evident. The astrocytoma was characterized by a proliferation of well differentiated astrocytes infiltrating the neuropile, forming no particular structural pattern. A few mitotic figures were eivdent.

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Scattered instances of meningoencephalitis, suppurative meningitis, encephalomalacia, and focal encephalitis were detected in a few rats from both the control and vinyl chloride exposed groups. The incidence of these inflammatory lesions was low and not related to any treatment group.

IV. DISCUSSION AND CONCLUSION

The presence of seven olfactory neuroblastomas in the brains from vinyl chloride exposed rats indicates a causal relationship between the exposure and the development of these neoplasms. Olfactory neuroblastomas rarely, if ever, occur spontaneously in the rat. Three of these neoplasms were initially diagnosed by IBT as neuroepitheliomas. Subsequent review of the slides indicates the classification of olfactory neuroblastoma to be appropriate for these neoplasms. The glioblastoma multiforme detected in T2 male rat No. 412 was also initially diagnosed as a neuroepithelioma by IBT. Subsequent evaluation of this neoplasm indicates that this lesion is more properly classified as a mixed glioma or glioblastoma multiforme.

The olfactory neuroblastomas detected in these vinyl chloride exposed rats are apparently identical to the neuroblastomas reported by Maltoni in 1975,[1] and again in 1977.[2] In 1975, Maltoni reported at the New York Academy of Sciences Symposium on the toxicity of vinyl chloride-

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[1]Carcinogenicity Bioassays of Vinyl Chloride: Current Results, Maltoni, C. and Lefemine, G., Annual New York Academy of Science, Vol. 246 (1975), 195-218.

[2]Vinyl Chloride Carcinogenicity: An Experimental Model for Carcinogenesis Studies, Maltoni, C., Origins of Human Cancer, Cold Spring Harbor Conferences on Cell Proliferation, Vol 4, 1977.

poly vinyl chloride. The results of his BT1 experiment revealed seven neuroblastomas in rats exposed to 10,000 ppm of vinyl chloride, three neuroblastomas in rats exposed to 6,000 ppm, and five neuroblastomas in rats exposed to 2,500 ppm of vinyl chloride. In 1977, at the Cold Spring Harbor Conference on Cell Proliferation, he again reported the results of his BT1 experiment in addition to the results of his BT3 and BT7 experiments where neuroblastomas were induced in rats exposed to vinyl chloride at 10,000, 6,000, and 2,500 ppm. The findings of olfactory neuroblastomas in the T3 male and female rats and a T4 female rat confirms the findings of Maltoni of an oncogenic effect on the rat brain from vinyl chloride exposure.

The shortcomings of this study have been previously documented. Regardless of these, the rarity of this neurological neoplasm coupled with the fact that it has only been reported in rats exposed to known carcinogens indicates a relationship between their presence in this study and exposure to vinyl chloride. As mentioned previously, the finding of these neoplasms confirms previously reported results from vinyl chloride exposures by Maltoni. Since the exposure conditions in this study have not been confirmed, the levels of vinyl chloride inducing these neoplasms cannot be stated at this time. Similarly, because of the large number of missing brains from the control and exposed rats, the true incidence of these neoplasms in IBT Study 663-03222, resulting from vinyl chloride exposure, cannot be determined.

WILLIAM M. BUSEY, D.V.M., Ph.D.
Pathologist

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WMB/sfh

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EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

IBT STUDY 663-03222

TABLE I

SUMMARY INCIDENCE TABLES

SUMMARY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Mice

	Untreated Control	T1	T2	T3		
BRAINS (NO. EXAMINED)	(5)	(13)	(3)	(12)		

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SUMMARY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Mice

	Untreated Control	T1	T2	T3		
BRAINS (NO. EXAMINED)	(4)	(8)	(7)	(14)		

SUMMARY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Hamsters

	Untreated Control	T1	T2	T3		
BRAINS (NO. EXAMINED)	(4)	(8)	(14)	(13)		
Focal Encephalitis				1		

SUMMARY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Hamsters

	Untreated Control	T1	T2	T3		
BRAINS (NO. EXAMINED)	(3)	(4)	(10)	(6)		

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SUMMARY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Rats

	Untreated Control	T1	T2	T3		
BRAINS (NO. EXAMINED)	(18)	(15)	(23)	(23)		
Meningoencephalitis	1					
Suppurative Meningitis	1	1				
Encephalomalacia			1			
Focal Encephalitis				1		
Olfactory Neuroblastoma				5		
Glioblastoma Multiforme			1			

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SUMMARY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

	Untreated Control	T1	T2	T3	T4	
BRAINS (NO. EXAMINED)	(30)	(13)	(11)	(17)	(12)	
Meningoencephalitis			1			
Astrocytoma			1			
Olfactory Neuroblastoma				1	1	
Pituitary Carcinoma	1					

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EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

IBT STUDY 663-03222

TABLE II

HISTOPATHOLOGY INCIDENCE TABLES

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Mice

Untreated Control

ANIMAL NUMBER	819	823	835	849	869
BRAIN	X	X	X	X	X

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Mice

T1

ANIMAL NUMBER	1009	1012*	1013	1024	1025	1030	1031	1049	1052	1065	1066	1082	1084
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X	X

CMA 006736

*Missexed

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EPL Experimental Pathology Laboratories, Inc

Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Mice

T2

ANIMAL NUMBER	1218	1223	1259
BRAIN	X	X	X

CMA 009737

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Mice

T3

ANIMAL NUMBER	1407	1412	1414	1433	1435	1438	1439	1443	1465	1477*	1488	1496
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X

CWA 006738

*Missexed

-18-

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Mice

Untreated Control

ANIMAL NUMBER	932	936	954	993*
BRAIN	X	A	X	X

CMA 006739

*Missexed

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Key P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; 1 = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Mice

T1

ANIMAL NUMBER	1105	1110	1112	1118	1139	1151	1156	1167
BRAIN	X	X	X	X	X	X	X	A

CMA 006740

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Mice

T2

ANIMAL NUMBER	1301	1308	1368	1382	1386	1390	1396
BRAIN	X	X	X	X	X	X	X

CMA 006741

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Mice

T3

ANIMAL NUMBER	1508	1516	1519	1522	1525	1526	1527	1534	1545	1556	1573A	1578	1592	1599
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X

CMA 006742

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Hamsters

Untreated Control

ANIMAL NUMBER	1608	1612	1621	1698
BRAIN	X	X	X	X
Focal Encephalitis				

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Hamsters

T1

ANIMAL NUMBER	1801	1839	1863	1870	1879	1881	1884	1895
BRAIN	X	X	X	X	X	X	X	X
Focal Encephalitis								

CMA 006744

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Hamsters

T2

ANIMAL NUMBER	2016	2033	2034	2037	2054	2068	2073	2076	2082	2084	2092	2093	2099	2100
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Focal Encephalitis														

CMA 006745

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Hamsters

T3

ANIMAL NUMBER	2208	2222	2226	2227	2237	2244	2259	2260	2261	2273	2275	2277	2295
BRAIN		X	X	A	X	A	X	X	X	X	X	X	X
Focal Encephalitis	3												

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Hamsters

Untreated Control

ANIMAL NUMBER	1701	1702	1716
BRAIN	X	X	X

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Hamsters

T1

ANIMAL NUMBER	1948	1959	1961	1996
BRAIN	X	X	X	X

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Hamsters

T2

ANIMAL NUMBER	2115	2118	2123	2153	2157	2170*	2187	2195	2198	2200*
BRAIN	X	X	X	X	X	X	X	X	X	X

CWA 006749

*Missexed

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Hamsters

T3

ANIMAL NUMBER	2304	2310	2324	2326	2332	2356
BRAIN	X	X	X	X	X	X

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Rats

Untreated Control

ANIMAL NUMBER	15	19	26	27	28	39	41	43	51	54	55	57	64	69	73	80	84	97
BRAIN	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Meningoencephalitis		3																
Suppurative Meningitis																		3
Encephalomalacia																		
Focal Encephalitis																		
Olfactory Neuroblastoma																		
Glioblastoma Multiforme																		

CMA 006751

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Key: P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Rats

T1

ANIMAL NUMBER	205	206	207	210	212	228	234	256	264	268	269	274	279	286	299
BRAIN	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Meningoencephalitis															
Suppurative Meningitis		3													
Encephalomalacia															
Focal Encephalitis															
Olfactory Neuroblastoma															
Glioblastoma Multiforme															

CMA 006752

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Rats

T2

ANIMAL NUMBER	404	412	413	418	426	428	430	433	435	436	440	445	452	453	456	459*	464	469	471	475	484	489	491
BRAIN	X		X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Meningoencephalitis																							
Suppurative Meningitis																							
Encephalomalacia									3														
Focal Encephalitis																							
Olfactory Neuroblastoma																							
Glioblastoma Multiforme		P																					

CWA 006753

*Missexed

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Male Rats

T3

ANIMAL NUMBER	601	609	616	618	625	632	639	641	644	649	651	655	663	664	667	668	671	672	676	677	682	687	694
BRAIN	X	X		X	X	X	X		X		X	X	X			X	X		X	X	X	X	X
Meningoencephalitis																							
Suppurative Meningitis																							
Encephalomalacia																							
Focal Encephalitis			2																				
Olfactory Neuroblastoma								P		P				P	P			P					
Glioblastoma Multiforme																							

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

Untreated Control

ANIMAL NUMBER	101	102	106	113	116	117	124	125	130	136	137	138	142	143	146	149	154	159	160	166	174	176	178	180	184	194	196	197
BRAIN	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Meningoencephalitis																												
Astrocytoma																												
Olfactory Neuroblastoma																												
Pituitary Carcinoma										P																		

CMA 006755

EPL Experimental Pathology Laboratories, Inc

Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

Untreated Control - Continued

	ANIMAL NUMBER	199	200																											
BRAIN		X	X																											
Meningoencephalitis																														
Astrocytoma																														
Olfactory Neuroblastoma																														
Pituitary Carcinoma																														

CMA 006756

EPL | Experimental Pathology Laboratories, Inc

Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

T1

ANIMAL NUMBER	302	303	326	331	335	342	349	363	369	376	381	382	397
BRAIN	X	X	X	X	X	X	X	X	X	X	X	X	X
Meningoencephalitis													
Astrocytoma													
Olfactory Neuroblastoma													
Pituitary Carcinoma													

CMA 009757

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

T2

ANIMAL NUMBER	511	520	522	524	550	557	566	569	570	594	599
BRAIN	X	X	X	X	X	X		X		X	X
Meningoencephalitis									4		
Astrocytoma							P				
Olfactory Neuroblastoma											
Pituitary Carcinoma											

CMA 006758

EPL Experimental Pathology Laboratories, Inc.

Key. P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

T3

ANIMAL NUMBER	709	710	717	722	728	732	733	735	740	742	746	761	762	765	767	778	783
BRAIN	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X
Meningoencephalitis																	
Astrocytoma																	
Olfactory Neuroblastoma												P					
Pituitary Carcinoma																	

CMA 006759

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Key P = Present N = No Section A = Autolysis X = Not Remarkable
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe/High
5 = Severe/High I = Incomplete Section

HISTOPATHOLOGY INCIDENCE TABLE

IBT Study 663-03222
Vinyl Chloride
Female Rats

T4

ANIMAL NUMBER	2413	2416	2421	2422	2425	2438	2461	2462	2485	2488	2494		3
BRAIN		X	X	X	X	X	X	X	X	X	X		X
Meningoencephalitis													
Astrocytoma													
Olfactory Neuroblastoma	P												
Pituitary Carcinoma													

CMA 006760

Key. P = Present; 1 = Minimal; 5 = Severe/High; N = No Section; 2 = Slight; I = Incomplete Section; A = Autolysis; 3 = Moderate; X = Not Remarkable; 4 = Moderately Severe/High