



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON 98, DELAWARE
EMPLOYEE RELATIONS DEPARTMENT

HASKELL LABORATORY
FOR
TOXICOLOGY AND INDUSTRIAL MEDICINE

File
229-180

November 25, 1969

Dr. Schott
Hazleton Laboratories, Inc.
Falls Church, Virginia

Dear Dr. Schott:

I have examined the kidneys from rats on your two-year lead feeding study; slide numbers 42614 through 42656. There was a definite effect of lead ingestion in both sexes only at the 1,000 ppm level. These changes included intranuclear inclusions, cytomegaly, tubular dilatation, epithelial metaplasia and hyperplasia. Two out of six males had adenomas. Male rats, but not the females, fed 50 ppm had a more severe chronic nephritis than the controls, however, this degree of nephritis can be expected in two-year-old Chr-CD stock male rats. Epithelial metaplasia and hyperplasia is a prominent feature of spontaneous chronic nephritis and may simulate the effects due to lead. There was only one female rat at the 500 ppm level which was not sufficient for an evaluation. Rats fed 10 ppm did not appear significantly different from the controls.

I am returning your slides along with our rat kidney slides from the terminal sacrifice for your evaluation. The slides were stained in duplicate with H & E and our modified Masson procedure. Attached is the list of rat numbers with feeding level identification.

Sincerely yours,

E. F. Stula

E. F. Stula, D.V.M.
Chief, Pathology Section

EFS:sfs

Attachment

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BETTER THINGS FOR BETTER LIVING THROUGH CHEMISTRY

N 30678

DUP040013204

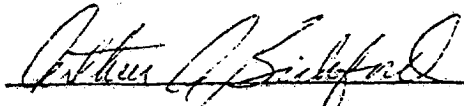
HAZLETON PROJECT NO. 229-100

RAT KIDNEY EVALUATION

CONCLUSIONS

Several rats in all 5 groups, including the controls, had typical lesions of chronic spontaneous nephrosis. In general it appeared that these lesions were somewhat more severe in males than in females and the incidence of these lesions was apparently unaffected by the various levels of the test compound.

Unique changes were detected in the kidneys of rats in the high-dose (Group No. 5 - 1000 PPM) group. Kidneys of 4 of the 6 males examined contained clearcut evidence of neoplastic involvement. Cytomegaly of the epithelial cells of the convoluted tubules was observed in 3 of the 6 males and in all of the 5 females, and intranuclear inclusion bodies were evident in these cells in 5 of the 6 males and in all of the 5 females. These alterations were not detected in any of the animals given the test compound at lower dose levels nor were they found in association with the spontaneous nephrotic changes. It is therefore concluded that these changes were induced by the test compound and that their occurrence was dose-related.



ARTHUR A. BICKFORD, V.M.D., Ph.D.
Veterinary Pathologist

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N 30678.01

DUP040013205
04-0005-0364

PATHOLOGY REPORT
PROJECT #229-100
LN #10,610

Prepared for Dr. L. Shatt

Sections of kidneys from 42 rats were submitted for histological evaluation. Although 43 are listed on the report form only 42 were presented.

Without prior knowledge of treatment or grouping this pathologist grouped these animals initially into six groups and finally into three affected groups and one not remarkable group. When tabbed according to treatment it was apparent that there was a dose-related response affecting the animals given 50 ppm and 1,000 ppm, but not those given 10 ppm. Inclusion bodies similar to those seen in lead poisoning were found in 10 of the 11 high level animals, but not in any animal at a lower dose following a moderate amount of time looking for them. With special acid fast staining procedures they may probably be seen in the next lower level. The dose relationship is recognized between the 10 and 50 ppm levels by the more severe renal reaction and incidence in the 50 ppm group, while the 10 ppm level was roughly similar to the controls.

In all levels the males appear to be the most severely affected, but this is only assumed by this pathologist.

John M. King
JOHN M. KING, D.V.M., Ph.D.
Veterinary Pathologist

*Orig. to
Shatt*

File: 299-100



ECG

N 30678.02

DUP040013206
04-0005-0365

KEY TO DETAILED HISTOPATHOLOGY INCIDENCE TABLE

N = No Section

X = Not Remarkable

A = Autolysis

P or ✓ = Present or Taken

0 = Absent

1 = Minimal

2 = Slight

3 = Moderate

4 = Moderate to Severe

5 = Severe

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N 30678.03

DUP040013207

04-0005-0366

DETAILED HISTOPATHOLOGY INCIDENCE TABLE

		MALES																											
		GROUP NUMBER																											
		1																											
ORGANS	ANIMAL NUMBER	58-388	58-389	58-391	58-392	58-394	58-396	58-399	58-400	58-403	58-404	58-405	58-406	58-407	58-409	58-411	58-415	58-416	58-417	58-420	58-421	58-422	58-423	58-426	58-429	58-430	58-431	58-432	
KIDNEY		X																											
Artifact		1	1	1	4		2	1	5	4	3	2	3	1	1	5	4	3	2	2	4	3	3	2	1	3	3	1	
Nephropathy		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Tubular Casts		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Regenerative Epithelium		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Focal Lymphoid Infiltration																													
Pigment				1	2		1	1						2	2	2	2				2		1					1	
Mineral Deposition								1						1								2							
Interstitial Fibrosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Focal Tubular Ectasia				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
Tubular Nephrosis				P					P	P			P			P	P												
Congestion				P																						P			
Pelvic Epithelial Thickening								P							P														
Dilated Pelvis																													
Cyst																													
Tubular Adenoma																													
Infarction																													
Atypical Epithelial																													
Hyperplasia																													
Intranuclear Inclusion Cyst																													
Cytomegaly																													
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	MALES						
		GROUP NUMBER						
		1 (Continued)						
		58-433	58-435	58-436	58-439	58-440	58-441	58-444
KIDNEY								
Artifact								
Nephropathy								
Tubular Casts								
Regenerative Epithelium								
Focal Lymphoid Infiltration								
Pigment								
Mineral Deposition								
Interstitial Fibrosis								
Focal Tubular Ectasia								
Tubular Nephrosis								
Congestion								
Pelvic Epithelial Thickening								
Dilated Pelvis								
Cyst								
Tubular Adenoma								
Infarction								
Atypical Epithelial								
Hyperplasia								
Intraculear Inclusion Cyst								
Cytomegaly								
Glomerulosclerosis								

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	MALES											
		GROUP NUMBER											
		2											
		58-589	58-590	58-591	58-592	58-593	58-596	58-597	58-599	58-600	58-605	58-609	58-610
													58-613
													58-615
KIDNEY													
Artifact													X
Nephropathy													
Tubular Casts													
Regenerative Epithelium													
Focal Lymphoid Infiltration													
Pigment													
Mineral Deposition													
Interstitial Fibrosis													
Focal Tubular Ectasia													
Tubular Nephrosis													
Congestion													
Pelvic Epithelial Thickening													
Dilated Pelvis													
Cyst													
Tubular Adenoma													
Infarction													
Atypical Epithelial													
Hyperplasia													
Intranuclear Inclusion Cyst													
Cytomegaly													
Glomerulosclerosis													

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

		MALES									
		GROUP NUMBER									
		3									
ORGANS	ANIMAL NUMBER	58-688	58-690	58-697	58-699	58-700	58-704	58-705	58-710	58-714	58-715
KIDNEY											
Artifact								P		P	
Neprhopathy		2	3	2	3	3	3	2	2	3	4
Tubular Casts		P		P	P	P	P	P	P	P	P
Regenerative Epithelium		P	P	P	P	P	P	P	P	P	P
Focal Lymphoid Infiltration		P	P	P	P		P		P		
Pigment		2				2	2	2	1	2	2
Mineral Deposition					1						
Interstitial Fibrosis		P		P	P	P		P	P	P	
Focal Tubular Ectasia		P			P					P	
Tubular Nephrosis				P		P					
Congestion											
Pelvic Epithelial Thickening											
Dilated Pelvis				P							
Cyst											
Tubular Adenoma											
Infarction											
Atypical Epithelial											
Hyperplasia						P					
Intranuclear Inclusion Cyst											
Cytomegal											
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	MALES															
		GROUP NUMBER															
		4															
		58-788	58-790	58-791	58-792	58-793	58-795	58-798	58-801	58-802	58-803	58-804	58-806	58-811	58-813		
KIDNEY																	
Artifact				P		P	P										
Nephropathy		4	3	2	4	2	3	4	3	3	2	4	4	3	3		
Tubular Casts		P	P	P	P	P	P	P	P	P	P	P	P	P	P		
Regenerative Epithelium		P	P	P	P	P	P	P	P	P	P	P	P	P	P		
Focal Lymphoid Infiltration		P		P	P		P	P	P	P	P	P	P	P			
Pigment		2				1	2	2		1		3	2	2	2		
Mineral Deposition						1				1	1						
Interstitial Fibrosis		P	P		P	P	P	P	P	P		P	P	P	P		
Focal Tubular Ectasia		P		P			P	P	P	P	P	P	P	P	P		
Tubular Nephrosis		P		P	P			P			P	P	P	P	P		
Congestion																	
Pelvic Epithelial Thickening																	
Dilated Pelvis															P		
Cyst																	
Tubular Adenoma																	
Infarction																	
Atypical Epithelial																	
Hyperplasia				P		P					P	P					
Intranuclear Inclusion Cyst																	
Cytomegaly																	
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P		

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	MALES													
		GROUP NUMBER													
		5													
		58-889	58-891	58-892	58-898	58-899	58-902	58-903	58-904	58-905	58-906	58-908	58-910	58-911	58-913
KIDNEY															
Artifact		3	2	5	1	2	3	3	3	4	4	3	4	3	5
Nephropathy		P	P	P		P	P	P	P	P	P	P	P	P	P
Tubular Casts		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Regenerative Epithelium		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Focal Lymphoid Infiltration		P	P		P	P	P	P	P	P		P	P	P	P
Pigment		1			2	2			3	2	2	2	2		
Mineral Deposition									1						
Interstitial Fibrosis		P	P		P	P	P	P	P	P		P	P	P	P
Focal Tubular Ectasia		P		P		P	P	P	P	P		P	P	P	P
Tubular Nephrosis		P	P			P	P		P	P	P	P		P	P
Congestion				P					P						
Pelvic Epithelial Thickening								P							
Dilated Pelvis															
Cyst										P	P			P	
Tubular Adenoma		P													
Infarction															
Atypical Epithelial															
Hyperplasia		P							P	P	P	P	P	P	P
Cytomegaly		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Intranuclear Inclusion Cyst		P	P	P	P	P	P	P	P	P	P	P	P	P	P

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	FEMALES																			
		GROUP NUMBER																			
		1																			
		58-488	58-490	58-491	58-492	58-493	58-494	58-498	58-505	58-506	58-507	58-508	58-510	58-511	58-513	58-514	58-516	58-517	58-520	58-521	58-522
KIDNEY		X																	X		X
Artifact																					
Nephropathy		1	1	1	2	2	2	2	1	2	2	2	2	2			1	1	2	1	3
Tubular Casts		P	P	P	P	P	P	P	P	P	P	P	P	P			P	P	P	P	P
Regenerative Epithelium		P	P	P	P	P	P	P	P	P	P	P	P	P	P			P	P	P	P
Focal Lymphoid Infiltration		P						P		P									P	P	P
Pigment		1	2	2	2	2							1	1	1	2				1	1
Mineral Deposition			1		2								2						1		
Interstitial Fibrosis								P												P	P
Focal Tubular Ectasia								P		P	P										P
Tubular Nephrosis							P			P	P	P	P				P		P		P
Congestion																				P	
Pelvic Epithelial Thickening																				P	
Dilated Pelvis								P													
Cyst																					
Tubular Adenoma																					
Infarction																					
Atypical Epithelial																					
Hyperplasia																					
Intranuclear Inclusion Cyst																					
Cytomegaly																					
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P			P	P	P	P

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	FEMALES															
		GROUP NUMBER															
		1 (Continued)															
		58-531	58-533	58-534	58-535	58-536	58-537	58-538	58-539	58-540	58-541	58-542	58-543	58-544	58-545	58-546	58-547
KIDNEY																	
Artifact											P		P	P	P	P	
Nephropathy	1	3	1	1	1	1	2	2				1	2	2	2	2	
Tubular Casts		P	P	P	P	P	P	P			P	P			P	P	
Regenerative Epithelium		P		P	P	P	P	P				P	P	P			
Focal Lymphoid Infiltration		P			P	P		P				P	P	P			
Pigment	1 1				2		1						1			1	2
Mineral Deposition					1	2	1			1			1				
Interstitial Fibrosis					P	P		P				P					
Focal Tubular Ectasia					P			P							P	P	
Tubular Nephrosis		P			P	P							P				
Congestion								P									
Pelvic Epithelial Thickening		P											P				
Dilated Pelvis																	
Cyst																	
Tubular Adenoma																	
Infarction																	
Atypical Epithelial																	
Hyperplasia																	
Intranuclear Inclusion Cyst																	
Cytomegaly																	
Glomerulosclerosis		P		P	P	P	P	P	P	P		P	P	P	P		P

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

		FEMALES																		
		GROUP NUMBER																		
		2																		
ORGANS	ANIMAL NUMBER	58-639	58-640	58-641	58-643	58-644	58-648	58-649	58-650	58-652	58-653	58-654	58-655	58-658	58-659	58-660	58-661	58-662	58-663	58-665
KIDNEY																				
Artifact		P										P		P	P				P	
Nephropathy		3	1		1	3	3	2	3	2		1	2	2	2	1		2	4	
Tubular Casts		P	P		P	P	P	P	P			P		P	P				P	
Regenerative Epithelium		P	P			P	P		P	P		P	P	P		P			P	
Focal Lymphoid Infiltration						P	P							P					P	P
Pigment		2	1	2		2	2		2	1	2	1		2		2				
Mineral Deposition				1						1				2		1	1			
Interstitial Fibrosis							P	P	P					P					P	P
Focal Tubular Ectasia		P				P	P		P										P	
Tubular Nephrosis								P				P								
Congestion																				
Pelvic Epithelial Thickening							P													
Dilated Pelvis							P												P	
Cyst																				
Tubular Adenoma														P						
Infarction																				
Atypical Epithelial																				
Hyperplasia																				
Intranuclear Inclusion Cyst																				
Cytomegaly																				
Glomerulosclerosis		P	P		P	P	P	P	P	P		P	P	P	P	P		P	P	

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

		FEMALES												
		GROUP NUMBER												
		3												
ORGANS	ANIMAL NUMBER	58-738	58-741	58-742	58-745	58-746	58-748	58-749	58-755	58-757	58-761	58-762	58-763	58-764
KIDNEY														
Artifact			P	P		P								
Nephropathy		5		2		2	2	2	2			1	3	
Tubular Casts		P			P	P		P	P				P	
Regenerative Epithelium		P		P		P		P	P				P	
Focal Lymphoid infiltration		P				P	P		P					
Pigment				2	2		2		2	1		1	2	
Mineral Deposition		2				2			2	2	2		2	
Interstitial Fibrosis		P							P				P	
Focal Tubular Ectasia		P											P	
Tubular Nephrosis		P						P						
Congestion														
Pelvic Epithelial Thickening														
Dilated Pelvis														
Cyst														
Tubular Adenoma														
Infarction														
Atypical Epithelial														
Hyperplasia														
Intranuclear Inclusion Cyst														
Cytomegaly														
Glomerulosclerosis		P		P		P	P	P	P			P	P	

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	FEMALES															
		GROUP NUMBER															
		4															
		58-839	58-840	58-843	58-845	58-847	58-848	58-850	58-851	58-852	58-853	58-854	58-856	58-857	58-858	58-860	58-862
KIDNEY																	
Artifact				P	P												
Nephropathy		4	2	2	3	2	2	2	2	2	1	3	3	2	4	2	1
Tubular Casts		P		P	P	P	P	P	P	P	P	P	P		P	P	
Regenerative Epithelium		P		P			P	P	P	P	P	P	P	P	P	P	
Focal Lymphoid Infiltration		P				P	P	P						P	P	P	
Pigment		2	2	2	2	1	2	2		1	3	2		2		1	
Mineral Deposition		1	1	1					2							1	
Interstitial Fibrosis		P					P	P				P	P		P	P	
Focal Tubular Ectasia		P		P			P					P	P		P	P	
Tubular Nephrosis		P	P			P			P			P			P		
Congestion											P						
Pelvic Epithelial Thickening													P				
Dilated Pelvis													P				
Cyst																	
Tubular Adenoma																	
Infarction																	
Atypical Epithelial																	
Hyperplasia																	
Intranuclear Inclusion Cyst																	
Cytomegaly																	
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

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DETAILED HISTOPATHOLOGY INCIDENCE TABLE

ORGANS	ANIMAL NUMBER	FEMALES													
		GROUP NUMBER													
		5													
		58-938	58-944	58-946	58-948	58-949	58-950	58-951	58-952	58-955	58-957	58-958	58-959	58-962	58-965
KIDNEY															
Artifact		2	1	4	3	2	3	3	3	4	4	5	2	4	3
Nephropathy		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Tubular Casts		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Regenerative Epithelium		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Focal Lymphoid Infiltration		P	P			P	P	P	P	P	P	P	P	P	P
Pigment		2	1	3	2	2		2	2	2	3	3	2	2	3
Mineral Deposition											2	2			2
Interstitial Fibrosis		P		P	P	P	P	P	P	P	P	P	P	P	P
Focal Tubular Ectasia				P	P			P	P	P	P	P	P	P	P
Tubular Nephrosis				P	P	P	P	P	P	P	P	P	P	P	P
Congestion				P	P	P	P	P	P	P	P	P	P	P	P
Pelvic Epithelial Thickening											P				P
Dilated Pelvis															
Cyst															
Tubular Adenoma															
Infarction															
Atypical Epithelial															
Hyperplasia											P	P		P	
Cytomegaly		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Glomerulosclerosis		P	P	P	P	P	P	P	P	P	P	P	P	P	P
Intranuclear Inclusion Cyst		P	P	P	P	P	P	P	P	P	P	P	P	P	P

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