For Study: 02G16015

Title: Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat

Requested By: Dirk Schaudien

Job Number: 49857

Animal Reference: Animal Name

Animals Excluded: 1000, 1001, 1002, 1003, 1010, 1011, 1012, 1013, 1020, 1021, 1022, 1023, 1030, 1031, 1032, 1033, 1050, 1051, 1052, 1053, 1070, 1071, 1072, 1073, 1080, 1081,

1082, 1083, 1084, 1085, 1086, 1087, 1088, 1089, 1090, 1091, 1092, 1093, 1094, 1095, 1096, 1097, 1098, 2000, 2001, 2002, 2003, 2010, 2011, 2012, + others.

Day Numbers: All Groups: All

Observation Type: Histo - Neoplastic and Non-Neoplastic

Observation Summary: Incidence
Report Format: Group within Sex

Tissues: ΑII Rationalisation: 18M PE Removal Reasons: ΑII Completed Animals Only: No Animals with Observations Only: No Major Pathological Findings Only: No Split Observations by: GRADE Split Table by: Sex Use Alternative Descriptions: No Repeat First Group on Each Page:

Style: Landscape - 12 Columns

Include: NVL Tissues; NE Tissues; Neoplastic - QUALIFIERS; TUMOUR TYPE; ORIGIN; CLASSIFICATION; Non-neoplastic - QUALIFIERS; SIZE; DISTRIBUTION

Removal Reason: ALL		3 3 4 4 0 0 0 0 4 3 3 4 4 0 2 1 2 3 1 0 1 0 0 1 0 1 0 0 1 0 0 0 0 1 0 0 0 0 1 0 0 0 0 3 1 1 2 1 2 1 1 1 1					
	control					low	
Number of Animals:	4			4	4	4	
Number of Completed Animals:	0	0	0	0	0	0	
larynx							
Examined	4	3	3	4	4	4	
No Visible Lesions	0	2	1	2	3	2	
Dilatation, Submucosal Glands; focal	1	0	1	0	0	0	
very slight	1	0	1	0	0	0	
Infiltration, Inflammatory Cell; focal	1	0	0	0	0	0	
slight	1	0	0	0	0	0	
Infiltration, Mononuclear Cell; (multi)focal	3	1	1	2	1	2	
very slight	2	1	1	1	1	2	
slight	1	0	0	1	0	0	
liver							
Examined	0	1	0	0	0	0	
Adenoma, Hepatocellular; benign		1					
Focus Of Cellular Alteration, Basophilic Nos; focal	•	0		•			
moderate	•	0		•			
lung							
Examined	4	3	3	4	4	4	
Accumulation, Fibre-Laden Macrophages; multifocal	0	1 0	0	0	0	0	
very slight	0	0	0	0	0	0	

^{1 [}ccc - Group Factor Chi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001]

Removal Reason: ALL			Male	e		
	Clean air control	brake dust low	Brake dust E	Brake dust high	Titanium- dioxide	Chrysotile low
Number of Animals:	4	3	3	4	4	4
Number of Completed Animals:	0	0	0	0	0	0
lung (Continued)						
slight	0	1 0	0	0	0	0
Accumulation, Particle-Laden Macrophages; (multi)focal	0	1 1	2	4 f+	4 f+	4 f+
very slight	0	¹ 1	2	4 f+	4 f+	4 f+
Fibrosis; (multi)focal	0	0	0	0	0	0
very slight	0	0	0	0	0	0
Fibrosis; multifocal	0	1 0	0	0	0	0
slight	0	1 0	0	0	0	0
Giant Cells, Syncytial; (multi)focal	0	1 0	0	0	0	0
very slight	0	1 0	0	0	0	0
Giant Cells, Syncytial; multifocal	0 c	+ 0	0	0	0	0
slight	0 c	+ 0	0	0	0	0
Granuloma, Foreign-Body; multifocal	0	0	0	0	1	0
slight	0	0	0	0	1	0
Hyperplasia, Bronchiolo-Alveolar; (multi)focal	0	1	0	1	1	2
very slight	0	1	0	1	1	2
Hyperplasia, Bronchiolo-Alveolar; multifocal	0	1 0	0	0	0	0
slight	0	1 0	0	0	0	0
Hyperplasia, Bronchiolo-Alveolar; alveolar type, focal	1	0	0	0	0	0

^{+ [}Footnote is displayed in the Comments and Markers page]

^{1 [}ccc - Group Factor Chi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001]

Removal Reason: ALL			Ma	le		
			Brake dust			
	control	low	mid	high	dioxide	low
Number of Animals:	4	3	3	4	4	4
Number of Completed Animals:	0	0	0	0	0	0
lung (Continued)						
very slight	1	0	0	0	0	0
Hyperplasia, Bronchiolo-Alveolar; alveolar type with atypia, focal	0	0	0	0	0	0
very severe	0	0	0	0	0	0
Hyperplasia, Neuroendocrine Cell; focal	0	0	0	0	1	0
slight	0	0	0	0	1	0
Infiltration, Inflammatory Cell; (mult)ifocal	0	1 0	0	0	0	0
very slight	0	1 0	0	0	0	0
Infiltration, Inflammatory Cell; (multi)focal	0	1 0	0	0	1	1
slight	0	1 0	0	0	0	0
very slight	0	1 0	0	0	1	1
Infiltration, Inflammatory Cell; multifocal	0	1 0	0	0	0	0
slight	0	1 0	0	0	0	0
Infiltration, Mononuclear Cell; (multi)focal	1	1	0	2	0	0
very slight	1	1	0	2	0	0
Infiltration, Mononuclear Cell; multifocal	0	0	0	0	0	1
slight	0	0	0	0	0	1
Inflammation, Chronic; (multi)focal	1	0	0	1	0	1
very slight	1	0	0	1	0	1

^{1 [}ccc - Group Factor Chi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001]

Removal Reason: ALL			Male Clean air brake dust Brake dust Brake dust Titanium- Chrysotile								
	Clean air control	brake dust low	Brake dust mid	Brake dust high	Titanium- dioxide	Chrysotile low					
Number of Animals:	4	3	3	4	4	4					
Number of Completed Animals:	0	0	0	0	0	0					
lung (Continued)											
Lipoproteinosis, Alveolar; multifocal	0	0	0	0	0	0					
slight	0	0	0	0	0	0					
Macrophage Aggregation, Alveolar; (multi)focal	3 c	1 3	1	1	0	1					
very slight	2	2	0	0	0	1					
slight	1	1	1	1	0	0					
Metaplasia, Chondro-Osseous; (multi)focal	1	0	1	1	0	1					
very slight	1	0	1	0	0	1					
slight	0	0	0	1	0	0					
Microgranuloma; (multi)focal	0	+ 0	0	0	0	0					
very slight	0	+ 0	0	0	0	0					
Microgranuloma; multifocal	0	+ 0	0	0	0	0					
slight	0	+ 0	0	0	0	0					
Wagner Grade 2	0	+ 1	2	4 f+	4 f	+ 4 f+					
Wagner Grade 4	0	+ 0	0	0	0	0					
Wagner Grade 1	4	+ 2	1	0 f+	0 f	+ 0 f+					
Accumulation, Particle-Laden Macrophages, Balt; (multi)focal	0	+ 0	1	3	4 f	† 1					
very slight	0	+ 0	1	3	4 f	+ 1					

^{+ [}Footnote is displayed in the Comments and Markers page]

^{1 [}c - Group Factor Chi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.05]

Removal Reason: ALL			Mal	е		
			Brake dust			
	control	low	mid	high	dioxide	low
Number of Animals:	4	3	3	4	4	4
Number of Completed Animals:	0	0	0	0	0	0
lung (Continued)						
Accumulation, Fibre-Laden Macrophages, Balt; (multi)focal	0	0	0	0	0	0
very slight	0 1	0	0	0	0	0
lung associated lymph nodes (laln)						
Examined	4	3	3	4	4	4
No Visible Lesions	4	3	1	0	1	4
Not Examined: No Significant Tissue Present In Section	0	0	0	0	0	0
Accumulation, Fibre-Laden Macrophages; (multi)focal	0	0	0	0	0	0
very slight	0	0	0	0	0	0
Accumulation, Fibre-Laden Macrophages; multifocal	0 c	0	0	0	0	0
slight	0 c	0	0	0	0	0
Accumulation, Particle-Laden Macrophages; (multi)focal	0	0	2	4 f+	2	0
very slight	0	0	2	4 f+	2	0
Accumulation, Particle-Laden Macrophages; multifocal	0	0	0	0	1	0
slight	0	0	0	0	1	0
skin/subcutaneous tissue						
Examined	3	0	0	0	0	0

^{+ [}Footnote is displayed in the Comments and Markers page]

^{1 [}cc - Group Factor Chi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01]

Removal Reason: ALL			Ma	ale		
	Clean air control	brake dust low	Brake dust mid	Brake dust high	Titanium- dioxide	Chrysotile low
Number of Animals:	4	3	3	4	4	4
Number of Completed Animals:	0	0	0	0	0	0
skin/subcutaneous tissue (Continued)						
Hemorrhage; focal	1		•	•	•	•
moderate	1					
Hyperplasia, Epithelial; squamous, focal	1					
severe	1					
Inflammation, Chronic Active; ulcerated, focal	1					
severe	1					
Inflammation, Chronic Active; focal	1					
slight	1					
Laceration; focal	1					
slight	1					
trachea						
Examined	4	3	3	4	4	4
No Visible Lesions	2	3	2	4	3	3
Infiltration, Mononuclear Cell; (multi)focal	2	0	1	0	1	1
very slight	2	0	1	0	1	1
thymus						
Examined	0	0	0	0	0	1
Thymoma, [M]; malignant						1

Removal Reason: ALL		1 0 1 0 0 1 . 1						
	Clean air control					Chrysotile low		
Number of Animals:	4	3	3	4	4	4		
Number of Completed Animals:	0	0	0	0	0	0		
pituitary gland								
Examined	1	0	1	0	0	0		
Adenoma, Pars Distalis; benign	1		1					
kidney								
Examined	0	0	1	0	0	0		
Nephropathy, Chronic Progressive; multifocal			1					
slight			1					
testis								
Examined	0	0	1	0	0	0		
Adenoma, Interstitial (Leydig) Cell; benign			0					
Atrophy, Tubular; multifocal			0					
very slight			0					
Atrophy, Tubular; diffuse			1					
severe			1					
epididymis								
Examined	0	0	0	0	0	0		
Reduced Sperm, Luminal; diffuse			÷		·	•		
very severe					·			
seminal vesicles								
Examined	0	0	0	0	0	0		

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Pathology - Intergroup Comparison of Pathology Observations

Removal Reason: ALL			М	ale		
	Clean air control	brake dust low	Brake dust mid	Brake dust high	Titanium- dioxide	Chrysotile low
Number of Animals:	4	3	3	4	4	4
Number of Completed Animals:	0	0	0	0	0	0
seminal vesicles (Continued)						
Atrophy; diffuse			•	•	•	
slight		·		•	÷	•
thyroid gland						
Examined	0	0	0	1	0	0
Carcinoma, Follicular Cell; malignant	•			1		

Removal Reason: ALL			Male	
	Chrysotile		Amosite	
Number of Animals:	high	lite 4	3	
Number of Completed Animals:	1	4		
	0	U	0	
larynx	_		•	
Examined	1	4	3	
No Visible Lesions	1	1	3	
Dilatation, Submucosal Glands; focal	0	2	0	
very slight	0	2	0	
Infiltration, Inflammatory Cell; focal	0	0	0	
slight	0	0	0	
Infiltration, Mononuclear Cell; (multi)focal	0	1	0	
very slight	0	0	0	
slight	0	1	0	
liver				
Examined	0	1	0	
Adenoma, Hepatocellular; benign	•	0		
Focus Of Cellular Alteration, Basophilic Nos; focal	•	1		
moderate		1		
lung				
Examined	1	4	3	
Accumulation, Fibre-Laden Macrophages; multifocal	0	4 f1	3 f1	
very slight	0	1	0	

^{1 [}f - Test: Fisher's Exact 2 Sided p < 0.05]

Removal Reason: ALL			Male	
	Chrysotile high	Crocido- lite	Amosite	
Number of Animals:	1	4	3	
Number of Completed Animals:	0	0	0	
lung (Continued)				
slight	0	3	3 f1	
Accumulation, Particle-Laden Macrophages; (multi)focal	1	0	0	
very slight	1	0	0	
very slight Fibrosis; (multi)focal	0	1	0	
very slight	0	1	0	
Fibrosis; multifocal	0	3	3 f1	
slight	0	3	3 f1	
Giant Cells, Syncytial; (multi)focal	0	4 f ¹	1	
very slight	0	4 f ¹	1	
Giant Cells, Syncytial; multifocal	0	0	2	
slight	0	0	2	
Granuloma, Foreign-Body; multifocal	0	0	0	
slight	0	0	0	
Hyperplasia, Bronchiolo-Alveolar; (multi)focal	1	1	0	
very slight	1	1	0	
Hyperplasia, Bronchiolo-Alveolar; multifocal	0	3	3 f ¹	
slight	0	3	3 f ¹	
Hyperplasia, Bronchiolo-Alveolar; alveolar type, focal	0	0	0	

^{1 [}f - Test: Fisher's Exact 2 Sided p < 0.05]

Removal Reason: ALL			Male		
	Chrysotile high	Crocido- lite	Amosite		
Number of Animals:	1	4	3		
Number of Completed Animals:	0	0	0		
ung (Continued)					
very slight	0	0	0		
Hyperplasia, Bronchiolo-Alveolar; alveolar type with atypia, focal	0	1	1		
very severe	0	1	1		
Hyperplasia, Neuroendocrine Cell; focal	0	0	0		
slight	0	0	0		
Infiltration, Inflammatory Cell; (mult)ifocal	0	4 f1	0		
very slight	0	4 f1	0		
Infiltration, Inflammatory Cell; (multi)focal	0	4 f1	3 f1		
slight	0	0	3 f1		
very slight	0	4 f ¹	3 f1		
Infiltration, Inflammatory Cell; multifocal	0	0	3 f1		
slight	0	0	3 f1		
Infiltration, Mononuclear Cell; (multi)focal	0	0	0		
very slight	0	0	0		
Infiltration, Mononuclear Cell; multifocal	0	0	0		
slight	0	0	0		
Inflammation, Chronic; (multi)focal	0	0	0		
very slight	0	0	0		

^{1 [}f - Test: Fisher's Exact 2 Sided p < 0.05]

Removal Reason: ALL			Male	
	Chrysotile high	Crocido- lite	Amosite	
Number of Animals:	1	4	3	
Number of Completed Animals:	0	0	0	
lung (Continued)				
Lipoproteinosis, Alveolar; multifocal	0	0	1	
slight	0	0	1	
Macrophage Aggregation, Alveolar; (multi)focal	0	0	0	
very slight	0	0	0	
slight	0	0	0	
Metaplasia, Chondro-Osseous; (multi)focal	0	0	1	
very slight	0	0	1	
slight	0	0	0	
Microgranuloma; (multi)focal	0	3	0	
very slight	0	3	0	
Microgranuloma; multifocal	0	0	3 f1	
slight	0	0	3 f1	
Wagner Grade 2	1	0	0	
Wagner Grade 4	0	4 f ¹	3 f1	
Wagner Grade 1	0	0 f ¹	0 f1	
Accumulation, Particle-Laden Macrophages, Balt; (multi)focal	1	0	0	
very slight	1	0	0	

^{1 [}f - Test: Fisher's Exact 2 Sided p < 0.05]

Removal Reason: ALL			Male	
	Chrysotile high	Crocido- lite	Amosite	
Number of Animals:	1	4	3	
Number of Completed Animals:	0	0	0	
lung (Continued)				
Accumulation, Fibre-Laden Macrophages, Balt; (multi)focal	0	3	2	
very slight	0	3	2	
lung associated lymph nodes (laln)				
Examined	0	4	3	
No Visible Lesions	ė	1	0	
Not Examined: No Significant Tissue Present In Section	1	0	0	
Accumulation, Fibre-Laden Macrophages; (multi)focal		1	1	
very slight		1	1	
Accumulation, Fibre-Laden Macrophages; multifocal		2	2	
slight		2	2	
Accumulation, Particle-Laden Macrophages; (multi)focal	•	0	0	
very slight		0	0	
Accumulation, Particle-Laden Macrophages; multifocal		0	0	
slight		0	0	
skin/subcutaneous tissue				
Examined	0	0	0	

Removal Reason: ALL			Male	
	Chrysotile high	Crocido- lite	Amosite	
Number of Animals:	1	4	3	
Number of Completed Animals:	0	0	0	
skin/subcutaneous tissue (Continued)				
Hemorrhage; focal				
moderate				
Hyperplasia, Epithelial; squamous, focal	•			
severe				
Inflammation, Chronic Active; ulcerated, focal				
severe				
Inflammation, Chronic Active; focal				
slight	•			
Laceration; focal				
slight				
trachea				
Examined	1	4	3	
No Visible Lesions	0	3	2	
Infiltration, Mononuclear Cell; (multi)focal	1	1	1	
very slight	1	1	1	
thymus				
Examined	0	0	0	
Thymoma, [M]; malignant				

Removal Reason: ALL			Male	
	Chrysotile high	Crocido- lite	Amosite	
Number of Animals:	1	4	3	
Number of Completed Animals:	0	0	0	
pituitary gland				
Examined	0	0	0	
Adenoma, Pars Distalis; benign				
kidney				
Examined	0	0	0	
Nephropathy, Chronic Progressive; multifocal				
slight				
testis				
Examined	0	1	0	
Adenoma, Interstitial (Leydig) Cell; benign		1		
Atrophy, Tubular; multifocal		1		
very slight		1		
Atrophy, Tubular; diffuse		0		
severe		0		
epididymis				
Examined	0	1	0	
Reduced Sperm, Luminal; diffuse		1		
very severe		1		
seminal vesicles				
Examined	0	1	0	

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Pathology - Intergroup Comparison of Pathology Observations

Removal Reason: ALL			Male	
	Chrysotile high	Crocido- lite	Amosite	
Number of Animals:	1	4	3	
Number of Completed Animals:	0	0	0	
seminal vesicles (Continued)				
Atrophy; diffuse		1	•	
slight		1		
thyroid gland				
Examined	0	0	0	
Carcinoma, Follicular Cell; malignant				

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	1	lung : Accumulation, Fibre-Laden Macrophages; multifocal	ccc
	Comment:	Group Factor Cl	hi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Accumulation, Fibre-Laden Macrophages; multifocal, slight	ccc
	Comment:	Group Factor Cl	hi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Accumulation, Particle-Laden Macrophages; (multi)focal	ccc
	Comment:	Group Factor Cl	hi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	4	lung : Accumulation, Particle-Laden Macrophages; (multi)focal	f
	Comment:	Test: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	5	lung : Accumulation, Particle-Laden Macrophages; (multi)focal	f
	Comment:	Test: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	6	lung : Accumulation, Particle-Laden Macrophages; (multi)focal	f
	Comment:	Test: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	1	lung : Accumulation, Particle-Laden Macrophages; (multi)focal, very slight	ccc
	Comment:	Group Factor Cl	hi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	4	lung : Accumulation, Particle-Laden Macrophages; (multi)focal, very slight	f
	Comment:	Test: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	5	lung : Accumulation, Particle-Laden Macrophages; (multi)focal, very slight	f
	Comment:	Test: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	6	lung : Accumulation, Particle-Laden Macrophages; (multi)focal, very slight	f
	Comment:	Test: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	1	lung : Fibrosis; multifocal	ccc
	Comment:	Group Factor Cl	hi-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	1	lung: Fibrosis; multifocal, slight	CCC
	Comment: G	roup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Giant Cells, Syncytial; (multi)focal	CCC
	Comment: G	roup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Giant Cells, Syncytial; (multi)focal, very slight	CCC
	Comment: G	roup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Giant Cells, Syncytial; multifocal	С
	Comment: G	roup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.05	
ALL	Male	1	lung : Giant Cells, Syncytial; multifocal, slight	С
	Comment: G	roup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.05	
ALL	Male	1	lung : Hyperplasia, Bronchiolo-Alveolar; multifocal	CCC
	Comment: G	roup Factor Ch	ii-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Hyperplasia, Bronchiolo-Alveolar; multifocal, slight	CCC
	Comment: G	roup Factor Ch	ii-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Infiltration, Inflammatory Cell; (mult)ifocal	ccc
	Comment: G	roup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Infiltration, Inflammatory Cell; (mult)ifocal, very slight	CCC
	Comment: G	roup Factor Ch	ii-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Infiltration, Inflammatory Cell; (multi)focal	CCC
	Comment: G	roup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Infiltration, Inflammatory Cell; (multi)focal, slight	CCC
	Comment: G	roup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	1	lung : Infiltration, Inflammatory Cell; (multi)focal, very slight	CCC
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Infiltration, Inflammatory Cell; multifocal	ccc
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Infiltration, Inflammatory Cell; multifocal, slight	ccc
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Macrophage Aggregation, Alveolar; (multi)focal	С
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.05	
ALL	Male	1	lung : Microgranuloma; (multi)focal	cc
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	1	lung: Microgranuloma; (multi)focal, very slight	cc
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	1	lung : Microgranuloma; multifocal	CCC
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Microgranuloma; multifocal, slight	ccc
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Wagner Grade 2	ccc
	Comment: G	oup Factor Ch	i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	4	lung : Wagner Grade 2	f
	Comment: Te	st: Fisher's Ex	act 2 Sided p < 0.05	
ALL	Male	5	lung : Wagner Grade 2	f
	Comment: Te	st: Fisher's Ex	act 2 Sided p < 0.05	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	6	lung : Wagner Grade 2	f
	Comment: Te	st: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	1	lung : Wagner Grade 4	ccc
	Comment: Gi	oup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	1	lung : Wagner Grade 1	ccc
	Comment: Gi	oup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001	
ALL	Male	4	lung : Wagner Grade 1	f
	Comment: Te	st: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	5	lung : Wagner Grade 1	f
	Comment: Te	st: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	6	lung : Wagner Grade 1	f
	Comment: Te	st: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	1	lung: Accumulation, Particle-Laden Macrophages, Balt; (multi)focal	cc
	Comment: Gi	oup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	5	lung: Accumulation, Particle-Laden Macrophages, Balt; (multi)focal	f
	Comment: Te	st: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	1	lung: Accumulation, Particle-Laden Macrophages, Balt; (multi)focal, very slight	cc
	Comment: Gi	oup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	5	lung: Accumulation, Particle-Laden Macrophages, Balt; (multi)focal, very slight	f
	Comment: Te	st: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	1	lung : Accumulation, Fibre-Laden Macrophages, Balt; (multi)focal	CC
	Comment: Gi	oup Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	1	lung: Accumulation, Fibre-Laden Macrophages, Balt; (multi)focal, very slight	CC
	Comment: C	Group Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	1	lung associated lymph nodes (laln): Accumulation, Fibre-Laden Macrophages; multifocal	С
	Comment: C	Group Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.05	
ALL	Male	1	lung associated lymph nodes (laln): Accumulation, Fibre-Laden Macrophages; multifocal, slight	С
	Comment: C	Group Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.05	
ALL	Male	1	lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages; (multi)focal	CC
	Comment: C	Group Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	4	lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages; (multi)focal	f
	Comment: T	est: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	1	lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages; (multi)focal, very slight	CC
	Comment: C	Group Factor Ch	ni-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01	
ALL	Male	4	lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages; (multi)focal, very slight	f
	Comment: T	est: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	8	lung : Accumulation, Fibre-Laden Macrophages; multifocal	f
	Comment: T	est: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Accumulation, Fibre-Laden Macrophages; multifocal	f
	Comment: T	est: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	9	lung: Accumulation, Fibre-Laden Macrophages; multifocal, slight	f
	Comment: T	est: Fisher's Ex	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Fibrosis; multifocal	f
	Comment: T	est: Fisher's Ex	xact 2 Sided p < 0.05	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	9	lung : Fibrosis; multifocal, slight	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	8	lung : Giant Cells, Syncytial; (multi)focal	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	8	lung : Giant Cells, Syncytial; (multi)focal, very slight	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	9	lung : Hyperplasia, Bronchiolo-Alveolar; multifocal	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	9	lung : Hyperplasia, Bronchiolo-Alveolar; multifocal, slight	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	8	lung : Infiltration, Inflammatory Cell; (mult)ifocal	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	8	lung : Infiltration, Inflammatory Cell; (mult)ifocal, very slight	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	8	lung : Infiltration, Inflammatory Cell; (multi)focal	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	9	lung : Infiltration, Inflammatory Cell; (multi)focal	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	9	lung : Infiltration, Inflammatory Cell; (multi)focal, slight	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	
ALL	Male	8	lung : Infiltration, Inflammatory Cell; (multi)focal, very slight	f
	Comment: Te	st: Fisher's Exa	ct 2 Sided p < 0.05	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Removal Reason	Sex	Group	Measurement	Marker
ALL	Male	9	lung : Infiltration, Inflammatory Cell; (multi)focal, very slight	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Infiltration, Inflammatory Cell; multifocal	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Infiltration, Inflammatory Cell; multifocal, slight	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Microgranuloma; multifocal	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Microgranuloma; multifocal, slight	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	8	lung : Wagner Grade 4	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Wagner Grade 4	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	8	lung : Wagner Grade 1	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	
ALL	Male	9	lung : Wagner Grade 1	f
	Comment: Te	st: Fisher's E	xact 2 Sided p < 0.05	

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Key Page

Measurement/Statistics

MeasurementDescriptiveComparativeArithmetic/AdjustedTransformationPathology ObservationCount PositivesChi-Squared & Fisher's Exact

Group Information

Short Name	Long Name	Report Headings	
1	Clean air	Clean air	control
2	brake dust low	brake dust	low
3	brake dust mid	Brake dust	mid
4	brake dust high	Brake dust	high
5	Particel Control	Titanium-	dioxide
6	Chrysotile low	Chrysotile	low
7	Chrysotile high	Chrysotile	high
8	Crocidolite	Crocido-	lite
9	Amosite	Amosite	

Removal Reason Grouping

Grouping Name	<u>Abbreviation</u>	Removal Reasons
Killed - Terminal Kill	TeKi	Killed - Terminal Kill
Killed - Moribund	US	Killed - Moribund
Found Dead	FD	Found Dead

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Key Page

Rationalisation Details

Rationalisation: 18M_PE

Merges

larynx, Hemorrhage, subepithelial, (multi)focal, very slight

Is used to report the following findings:

larynx, Hemorrhage, subepithelial, focal, very slight

larynx, Hemorrhage, subepithelial, multifocal, very slight

larynx, Infiltration, Mononuclear Cell, subepithelial, (multi)focal, very slight

Is used to report the following findings:

larynx, Infiltration, Mononuclear Cell, subepithelial, focal, very slight

larynx, Infiltration, Mononuclear Cell, subepithelial, multifocal, very slight

larynx, Infiltration, Mononuclear Cell, subepithelial, (multi)focal, slight

Is used to report the following findings:

larynx, Infiltration, Mononuclear Cell, subepithelial, focal, slight

larynx, Infiltration, Mononuclear Cell, subepithelial, multifocal, slight

lung, Accumulation, Particle-Laden Macrophages, alveolar/interstitial, (multi)focal, very slight

Is used to report the following findings:

lung, Accumulation, Particle-Laden Macrophages, alveolar/interstitial, focal, very slight

lung, Accumulation, Particle-Laden Macrophages, alveolar/interstitial, multifocal, very slight

lung, Fibrosis, interstitial, (multi)focal, very slight

Is used to report the following findings:

lung, Fibrosis, interstitial, focal, very slight

lung, Fibrosis, interstitial, multifocal, very slight

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Key Page

Merges (Continued)

lung, Giant Cells, Syncytial, (multi)focal, very slight

Is used to report the following findings:

lung, Giant Cells, Syncytial, focal, very slight

lung, Giant Cells, Syncytial, multifocal, very slight

lung, Hyperplasia, Bronchiolo-Alveolar, (multi)focal, very slight

Is used to report the following findings:

lung, Hyperplasia, Bronchiolo-Alveolar, focal, very slight

lung, Hyperplasia, Bronchiolo-Alveolar, multifocal, very slight

lung, Infiltration, Inflammatory Cell, peribronchiolar, (mult)ifocal, very slight

Is used to report the following findings:

lung, Infiltration, Inflammatory Cell, peribronchiolar, focal, very slight

 $lung, Infiltration, Inflammatory \ Cell, peribronchiolar, multifocal, very \ slight$

lung, Infiltration, Inflammatory Cell, peribronchiolar, (multi)focal, slight

Is used to report the following findings:

 $lung,\,Infiltration,\,Inflammatory\,\,Cell,\,peribronchiolar,\,focal,\,slight$

lung, Infiltration, Inflammatory Cell, peribronchiolar, multifocal, slight

lung, Infiltration, Inflammatory Cell, perivascular, (multi)focal, very slight

Is used to report the following findings:

 $lung, Infiltration, Inflammatory \, Cell, \, perivascular, \, focal, \, very \, slight$

lung, Infiltration, Inflammatory Cell, perivascular, multifocal, very slight

lung, Infiltration, Inflammatory Cell, perivascular, (multi)focal, slight

Is used to report the following findings:

lung, Infiltration, Inflammatory Cell, perivascular, focal, slight

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Key Page

Merges (Continued)

lung, Infiltration, Inflammatory Cell, perivascular, multifocal, slight

lung, Infiltration, Inflammatory Cell, alveolar/interstitial, (multi)focal, very slight

Is used to report the following findings:

lung, Infiltration, Inflammatory Cell, alveolar/interstitial, focal, very slight

lung, Infiltration, Inflammatory Cell, alveolar/interstitial, multifocal, very slight

lung, Infiltration, Mononuclear Cell, interstitial, (multi)focal, very slight

Is used to report the following findings:

lung, Infiltration, Mononuclear Cell, interstitial, focal, very slight

lung, Infiltration, Mononuclear Cell, interstitial, multifocal, very slight

lung, Infiltration, Mononuclear Cell, pleural, (multi)focal, very slight

Is used to report the following findings:

lung, Infiltration, Mononuclear Cell, pleural, focal, very slight

lung, Infiltration, Mononuclear Cell, pleural, multifocal, very slight

lung, Inflammation, Chronic, (multi)focal, very slight

Is used to report the following findings:

lung, Inflammation, Chronic, focal, very slight

lung, Inflammation, Chronic, multifocal, very slight

lung, Macrophage Aggregation, Alveolar, (multi)focal, very slight

Is used to report the following findings:

lung, Macrophage Aggregation, Alveolar, focal, very slight

lung, Macrophage Aggregation, Alveolar, multifocal, very slight

lung, Macrophage Aggregation, Alveolar, (multi)focal, slight

Is used to report the following findings:

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Key Page

Merges (Continued)

lung, Macrophage Aggregation, Alveolar, focal, slight lung, Macrophage Aggregation, Alveolar, multifocal, slight

lung, Metaplasia, Chondro-Osseous, (multi)focal, very slight

Is used to report the following findings:

lung, Metaplasia, Chondro-Osseous, focal, very slight lung, Metaplasia, Chondro-Osseous, multifocal, very slight

lung, Metaplasia, Chondro-Osseous, (multi)focal, slight

Is used to report the following findings:

lung, Metaplasia, Chondro-Osseous, focal, slight

lung, Metaplasia, Chondro-Osseous, multifocal, slight

lung, Microgranuloma, (multi)focal, very slight

Is used to report the following findings:

lung, Microgranuloma, focal, very slight

lung, Microgranuloma, multifocal, very slight

lung, Accumulation, Particle-Laden Macrophages, Balt, (multi)focal, very slight

Is used to report the following findings:

lung, Accumulation, Particle-Laden Macrophages, Balt, focal, very slight

lung, Accumulation, Particle-Laden Macrophages, Balt, multifocal, very slight

lung, Accumulation, Fibre-Laden Macrophages, Balt, (multi)focal, very slight

Is used to report the following findings:

lung, Accumulation, Fibre-Laden Macrophages, Balt, focal, very slight

lung, Accumulation, Fibre-Laden Macrophages, Balt, multifocal, very slight

lung associated lymph nodes (laln), Accumulation, Fibre-Laden Macrophages, (multi)focal, very slight

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

Key Page

Merges (Continued)

Is used to report the following findings:

lung associated lymph nodes (laln), Accumulation, Fibre-Laden Macrophages, focal, very slight lung associated lymph nodes (laln), Accumulation, Fibre-Laden Macrophages, multifocal, very slight

lung associated lymph nodes (laln), Accumulation, Particle-Laden Macrophages, (multi)focal, very slight Is used to report the following findings:

lung associated lymph nodes (laln), Accumulation, Particle-Laden Macrophages, focal, very slight lung associated lymph nodes (laln), Accumulation, Particle-Laden Macrophages, multifocal, very slight

nasal cavity, Hyperplasia, Mucous Cell, (multi)focal, very slight

Is used to report the following findings:

nasal cavity, Hyperplasia, Mucous Cell, focal, very slight nasal cavity, Hyperplasia, Mucous Cell, multifocal, very slight

nasal cavity, Infiltration, Inflammatory Cell, subepithelial, (multi)focal, very slight

Is used to report the following findings:

nasal cavity, Infiltration, Inflammatory Cell, subepithelial, focal, very slight nasal cavity, Infiltration, Inflammatory Cell, subepithelial, multifocal, very slight

 $trachea,\,Infiltration,\,Mononuclear\,\,Cell,\,subepithelial,\,(multi)focal,\,very\,\,slight$

Is used to report the following findings:

trachea, Infiltration, Mononuclear Cell, subepithelial, focal, very slight trachea, Infiltration, Mononuclear Cell, subepithelial, multifocal, very slight

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 18 months post exposure

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