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: 48778
Animal Reference: Animal Name

Animals Excluded: 1000, 1001, 1002, 1003, 1010, 1011, 1012, 1013, 1020, 1021, 1022, 1023, 1030, 1031, 1032, 1033, 1060, 1061, 1062, 1063, 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

ΑII Tissues: Rationalisation: None Removal Reasons: Αll Completed Animals Only: No Animals with Observations Only: No Major Pathological Findings Only: No GRADE Split Observations by: Split Table by: Sex Use Alternative Descriptions: No Repeat First Group on Each Page: No

Style: Landscape - 12 Columns

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

| 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 | 4 | 4 | 4 | 4 |
| Number of Completed Animals: | 0 | 0 | 0 | 0 | 0 | 0 |
| larynx | | | | | | |
| Examined | 4 | 3 | 4 | 4 | 4 | 4 |
| No Visible Lesions | 1 | 1 | 3 | 2 | 3 | 3 |
| Dilatation, Submucosal Glands | 1 | 1 | 1 | 1 | 0 | 1 |
| very slight | 0 | 0 | 1 | 0 | 0 | 1 |
| slight | 1 | 1 | 0 | 1 | 0 | 0 |
| Infiltration, Mononuclear Cell | 2 | 1 | 1 | 1 | 1 | 0 |
| very slight | 1 | 1 | 1 | 1 | 1 | 0 |
| slight | 1 | 0 | 0 | 0 | 0 | 0 |
| lung | | | | | | |
| Examined | 4 | 3 | 4 | 4 | 4 | 4 |
| Accumulation, Fibre-Laden Macrophages | 0 | 1 0 | 0 | 0 | 0 | 0 |
| slight | 0 | 1 0 | 0 | 0 | 0 | 0 |
| Accumulation, Particle-Laden Macrophages | 0 | 1 1 | 3 | 4 f+ | 4 f | 4 f+ |
| very slight | 0 | 1 1 | 3 | 4 f+ | 4 f | 4 f+ |
| Fibrosis | 0 | 1 0 | 0 | 0 | 0 | 1 |
| very slight | 0 | 0 | 0 | 0 | 0 | 1 |
| slight | 0 | 1 0 | 0 | 0 | 0 | 0 |
| Giant Cells, Syncytial | 0 | 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 | | |
|---|-------------------|-------------------|----------------|-----------------|----------------------|----------------|
| | Clean air control | brake dust low | Brake dust mid | Brake dust high | Titanium- dioxide | Chrysotile low |
| Number of Animals: | 4 | 3 | 4 | 4 | 4 | 4 |
| Number of Completed Animals: | 0 | 0 | 0 | 0 | 0 | 0 |
| lung (Continued) | | | | | | |
| very slight | 0 | 0 | 0 | 0 | 0 | 0 |
| slight | 0 | 0 | 0 | 0 | 0 | 0 |
| Hyperplasia, Bronchiolo-Alveolar | 0 | 0 | 1 | 2 | 0 | 4 f+ |
| very slight | 0 - | + 0 | 1 | 2 | 0 | 4 f+ |
| slight | 0 | 0 | 0 | 0 | 0 | 0 |
| Hyperplasia, Bronchiolo-Alveolar; alveolar type | 0 | 0 | 0 | 0 | 0 | 0 |
| slight | 0 | 0 | 0 | 0 | 0 | 0 |
| Hyperplasia, Neuroendocrine Cell | 0 | 1 | 0 | 0 | 0 | 0 |
| slight | 0 | 1 | 0 | 0 | 0 | 0 |
| Infiltration, Inflammatory Cell | 0 | 0 | 0 | 1 | 1 | 3 |
| very slight | 0 | 0 | 0 | 1 | 1 | 3 |
| slight | 0 - | + 0 | 0 | 0 | 0 | 0 |
| Infiltration, Mononuclear Cell | 1 | 1 | 0 | 2 | 0 | 0 |
| very slight | 1 | 1 | 0 | 2 | 0 | 0 |
| Macrophage Aggregation, Alveolar | 1 | 1 | 1 | 0 | 0 | 0 |
| very slight | 1 | 1 | 1 | 0 | 0 | 0 |
| Microgranuloma | 0 | 0 | 0 | 0 | 0 | 0 |
| very slight | 0 | 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 | | | Mal | e | • | |
|--|----------------------|-------------------|--------------|--------------------|----------------------|----------------|
| | Clean air control | brake dust low | Brake dust I | Brake dust high | Titanium- dioxide | Chrysotile low |
| Number of Animals: | 4 | 3 | 4 | 4 | 4 | 4 |
| Number of Completed Animals: | 0 | 0 | 0 | 0 | 0 | 0 |
| lung (Continued) | | | | | | |
| slight | ۱ 0 | 0 | 0 | 0 | 0 | 0 |
| Wagner Grade 2 | 0 + | 1 | 3 | 4 f+ | 4 f+ | 2 |
| Wagner Grade 3 | 0 c⁺ | 0 | 0 | 0 | 0 | 2 |
| Wagner Grade 4 | 0 1 | 0 | 0 | 0 | 0 | 0 |
| Wagner Grade 1 | 4 1 | 2 | 1 | 0 f+ | 0 f+ | 0 f+ |
| Accumulation, Particle-Laden Macrophages, Balt | 0 1 | 2 | 4 f+ | 3 | 4 f+ | 2 |
| very slight | 0 1 | 2 | 4 f+ | 3 | 4 f+ | 2 |
| Accumulation, Fibre-Laden Macrophages, Balt | 0 + | 0 | 0 | 0 | 0 | 0 |
| very slight | 0 + | 0 | 0 | 0 | 0 | 0 |
| lung associated lymph nodes (laln) | | | | | | |
| Examined | 4 | 3 | 4 | 4 | 4 | 4 |
| No Visible Lesions | 4 | 3 | 1 | 0 | 0 | 4 |
| Accumulation, Fibre-Laden Macrophages | 0 1 | 0 | 0 | 0 | 0 | 0 |
| very slight | 0 + | 0 | 0 | 0 | 0 | 0 |
| slight | 0 | 0 | 0 | 0 | 0 | 0 |
| Accumulation, Particle-Laden Macrophages | 0 1 | 0 | 3 | 4 f+ | 4 f+ | 0 |
| very slight | 0 1 | 0 | 3 | 4 f+ | 3 | 0 |
| slight | 0 | 0 | 0 | 0 | 1 | 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 | ale | | |
|--|---------|-------------------|----------------|-----------------|----------------------|----------------|
| | control | brake dust low | Brake dust mid | Brake dust high | Titanium- dioxide | Chrysotile low |
| Number of Animals: | 4 | 3 | 4 | 4 | 4 | 4 |
| Number of Completed Animals: | 0 | 0 | 0 | 0 | 0 | 0 |
| lung associated lymph nodes (laln) (Continued) | | | | | | |
| Hyperplasia, Lymphoid | 0 | 0 | 0 | 0 | 2 | 0 |
| slight | 0 | 0 | 0 | 0 | 2 | 0 |
| nasal cavity | | | | | | |
| Examined | 4 | 3 | 4 | 4 | 4 | 4 |
| No Visible Lesions | 0 | 0 | 2 | 0 | 2 | 2 |
| Corpora Amylacea | 0 | 0 | 0 | 0 | 0 | 0 |
| very slight | 0 | 0 | 0 | 0 | 0 | 0 |
| Droplets, Hyaline | 2 | 3 | 2 | 4 | 2 | 1 |
| very slight | 2 | 0 | 1 | 2 | 2 | 1 |
| slight | 1 | 2 | 1 | 2 | 0 | 0 |
| moderate | 0 | 1 | 0 | 0 | 0 | 0 |
| Hyperplasia, Mucous Cell | 0 | 1 | 0 | 1 | 0 | 1 |
| very slight | 0 | 1 | 0 | 1 | 0 | 1 |
| Infiltration, Inflammatory Cell | 1 | 0 | 0 | 1 | 0 | 0 |
| very slight | 1 | 0 | 0 | 0 | 0 | 0 |
| slight | 0 | 0 | 0 | 1 | 0 | 0 |
| Hyperplasia, Nalt | 1 | 0 | 1 | 1 | 0 | 0 |
| slight | 1 | 0 | 1 | 1 | 0 | 0 |

| Removal Reason: ALL | | | Ма | le | | |
|-----------------------------------|-------------------|-------------------|----------------|-----------------|----------------------|----------------|
| | Clean air control | brake dust low | Brake dust mid | Brake dust high | Titanium- dioxide | Chrysotile low |
| Number of Animals: | | 3 | 4 | 4 | 4 | 4 |
| Number of Completed Animals: | 0 | 0 | 0 | 0 | 0 | 0 |
| nasopharynx | | | | | | |
| Examined | 4 | 3 | 4 | 4 | 4 | 4 |
| No Visible Lesions | 4 | 3 | 4 | 4 | 4 | 4 |
| skin/subcutaneous tissue | | | | | | |
| Examined | 0 | 0 | 0 | 0 | 1 | 1 |
| Tumor, Hair Follicle, [B]; benign | | | | | 0 | 1 |
| Abscess(Es) | | | | | 1 | 0 |
| Severe | | | | | 1 | 0 |
| trachea | | | | | | |
| Examined | 4 | 3 | 4 | 4 | 4 | 4 |
| No Visible Lesions | 3 | 3 | 3 | 3 | 4 | 4 |
| Infiltration, Mononuclear Cell | 1 | 0 | 1 | 1 | 0 | 0 |
| very slight | 0 | 0 | 1 | 1 | 0 | 0 |
| slight | 1 | 0 | 0 | 0 | 0 | 0 |
| thymus | | | | | | |
| Examined | 0 | 0 | 0 | 0 | 0 | 1 |
| Thymoma, [M]; malignant | | | | | | 1 |

| Removal Reason: ALL | | | Male | |
|--|------------------|------------------|---------|--|
| | Chrysotile high | Crocido- lite | Amosite | |
| Number of Animals: | | 4 | 4 | |
| Number of Completed Animals: | 0 | 0 | 0 | |
| larynx | | | | |
| Examined | 3 | 4 | 4 | |
| No Visible Lesions | 1 | 3 | 3 | |
| Dilatation, Submucosal Glands | 0 | 1 | 0 | |
| very slight | 0 | 1 | 0 | |
| slight | 0 | 0 | 0 | |
| Infiltration, Mononuclear Cell | 2 | 0 | 1 | |
| very slight | 2 | 0 | 1 | |
| slight | 0 | 0 | 0 | |
| lung | | | | |
| Examined | 3 | 4 | 4 | |
| Accumulation, Fibre-Laden Macrophages | 0 | 4 f1 | 4 f1 | |
| slight | 0 | 4 f1 | 4 f1 | |
| Accumulation, Particle-Laden Macrophages | 3 f ¹ | 0 | 0 | |
| very slight | 3 f ¹ | 0 | 0 | |
| Fibrosis | 1 | 4 f1 | 4 f1 | |
| very slight | 1 | 1 | 1 | |
| slight | 0 | 3 | 4 f1 | |
| Giant Cells, Syncytial | 0 | 4 f ¹ | 4 f1 | |
| | | | | |

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

| Removal Reason: ALL | | | Male | | |
|---|-----------------|------------------|---------|--|--|
| | Chrysotile high | Crocido- lite | Amosite | | |
| Number of Animals: | 3 | 4 | 4 | | |
| Number of Completed Animals: | 0 | 0 | 0 | | |
| lung (Continued) | | | | | |
| very slight | 0 | 4 f ¹ | 0 | | |
| slight | 0 | 0 | 4 f1 | | |
| Hyperplasia, Bronchiolo-Alveolar | 2 | 4 f1 | 4 f1 | | |
| very slight | 2 | 1 | 0 | | |
| slight | 0 | 3 | 4 f1 | | |
| Hyperplasia, Bronchiolo-Alveolar; alveolar type | 0 | 1 | 0 | | |
| slight | 0 | 1 | 0 | | |
| Hyperplasia, Neuroendocrine Cell | 0 | 0 | 0 | | |
| slight | 0 | 0 | 0 | | |
| Infiltration, Inflammatory Cell | 2 | 4 f ¹ | 4 f1 | | |
| very slight | 2 | 4 f1 | 4 f1 | | |
| slight | 0 | 3 | 2 | | |
| Infiltration, Mononuclear Cell | 0 | 1 | 0 | | |
| very slight | 0 | 1 | 0 | | |
| Macrophage Aggregation, Alveolar | 0 | 0 | 0 | | |
| very slight | 0 | 0 | 0 | | |
| Microgranuloma | 1 | 4 f1 | 4 f1 | | |
| very slight | 1 | 2 | 0 | | |
| | | | | | |

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

| Removal Reason: ALL | | | Male | |
|--|--------------------|------------------|------------------|--|
| | Chrysotile high | Crocido- lite | Amosite | |
| Number of Animals: | | 4 | 4 | |
| Number of Completed Animals: | 0 | 0 | 0 | |
| lung (Continued) | | | | |
| slight | 0 | 2 | 4 f ¹ | |
| Wagner Grade 2 | 1 | 0 | 0 | |
| Wagner Grade 3 | 2 | 0 | 0 | |
| Wagner Grade 4 | 0 | 4 f1 | 4 f1 | |
| Wagner Grade 1 | 0 f1 | 0 f1 | 0 f1 | |
| Accumulation, Particle-Laden Macrophages, Balt | 3 f1 | 0 | 0 | |
| very slight | 3 f ¹ | 0 | 0 | |
| Accumulation, Fibre-Laden Macrophages, Balt | 0 | 2 | 3 | |
| very slight | 0 | 2 | 3 | |
| lung associated lymph nodes (laln) | | | | |
| Examined | 3 | 4 | 4 | |
| No Visible Lesions | 0 | 0 | 0 | |
| Accumulation, Fibre-Laden Macrophages | 0 | 4 f1 | 4 f1 | |
| very slight | 0 | 2 | 3 | |
| slight | 0 | 2 | 1 | |
| Accumulation, Particle-Laden Macrophages | 3 fi | 0 | 0 | |
| very slight | 3 fi | 0 | 0 | |
| 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: | 3 | 4 | 4 | |
| Number of Completed Animals: | 0 | 0 | 0 | |
| lung associated lymph nodes (laln) (Continued) | | | | |
| Hyperplasia, Lymphoid | 0 | 1 | 1 | |
| slight | 0 | 1 | 1 | |
| nasal cavity | | | | |
| Examined | 3 | 4 | 4 | |
| No Visible Lesions | 2 | 0 | 0 | |
| Corpora Amylacea | 0 | 0 | 1 | |
| very slight | 0 | 0 | 1 | |
| Droplets, Hyaline | 1 | 3 | 2 | |
| very slight | 1 | 2 | 1 | |
| slight | 0 | 1 | 1 | |
| moderate | 0 | 1 | 1 | |
| Hyperplasia, Mucous Cell | 0 | 0 | 1 | |
| very slight | 0 | 0 | 1 | |
| Infiltration, Inflammatory Cell | 0 | 1 | 2 | |
| very slight | 0 | 1 | 2 | |
| slight | 0 | 0 | 0 | |
| Hyperplasia, Nalt | 0 | 0 | 2 | |
| slight | 0 | 0 | 2 | |

Pathology - Intergroup Comparison of Pathology Observations

| Removal Reason: ALL | | | Male | | |
|-----------------------------------|-----------------|------------------|---------|--|--|
| | Chrysotile high | Crocido- lite | Amosite | | |
| Number of Animals: | | 4 | 4 | | |
| Number of Completed Animals: | 0 | 0 | 0 | | |
| nasopharynx | | | | | |
| Examined | 3 | 4 | 4 | | |
| No Visible Lesions | 3 | 4 | 4 | | |
| skin/subcutaneous tissue | | | | | |
| Examined | 0 | 0 | 0 | | |
| Tumor, Hair Follicle, [B]; benign | | | | | |
| Abscess(Es) | | | | | |
| severe | | | | | |
| trachea | | | | | |
| Examined | 3 | 4 | 4 | | |
| No Visible Lesions | 3 | 3 | 3 | | |
| Infiltration, Mononuclear Cell | 0 | 1 | 1 | | |
| very slight | 0 | 1 | 1 | | |
| slight | 0 | 0 | 0 | | |
| thymus | | | | | |
| Examined | 0 | 0 | 0 | | |
| Thymoma, [M]; malignant | | | | | |

Pathology - Intergroup Comparison of Pathology Observations

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|------------|------------------|--|--------|
| ALL | Male | 1 | lung : Accumulation, Fibre-Laden Macrophages | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung: Accumulation, Fibre-Laden Macrophages, slight | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Accumulation, Particle-Laden Macrophages | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 4 | lung : Accumulation, Particle-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung : Accumulation, Particle-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 6 | lung : Accumulation, Particle-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Accumulation, Particle-Laden Macrophages, very slight | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 4 | lung : Accumulation, Particle-Laden Macrophages, very slight | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung : Accumulation, Particle-Laden Macrophages, very slight | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 6 | lung : Accumulation, Particle-Laden Macrophages, very slight | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung: Fibrosis | ccc |
| | Comment: G | roup Factor Ch | i-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, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|------------|------------------|--|--------|
| ALL | Male | 1 | lung: Fibrosis, slight | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Giant Cells, Syncytial | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Giant Cells, Syncytial, very slight | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Giant Cells, Syncytial, slight | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Hyperplasia, Bronchiolo-Alveolar | CCC |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 6 | lung : Hyperplasia, Bronchiolo-Alveolar | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Hyperplasia, Bronchiolo-Alveolar, very slight | cc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01 | |
| ALL | Male | 6 | lung : Hyperplasia, Bronchiolo-Alveolar, very slight | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Hyperplasia, Bronchiolo-Alveolar, slight | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Infiltration, Inflammatory Cell | ccc |
| | Comment: G | roup Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Infiltration, Inflammatory Cell, very slight | ccc |
| | Comment: G | roup Factor Ch | ii-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |

Pathology - Intergroup Comparison of Pathology Observations

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|-------------|-------------------|--|--------|
| ALL | Male | 1 | lung : Infiltration, Inflammatory Cell, slight | CC |
| | Comment: G | roup Factor Chi | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.01 | |
| ALL | Male | 1 | lung : Microgranuloma | CCC |
| | Comment: G | roup Factor Chi | -Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Microgranuloma, slight | CCC |
| | Comment: G | roup Factor Chi | -Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Wagner Grade 2 | CC |
| | Comment: G | roup Factor Chi | -Squared & Fisher's Exact: Test: Chi-Squared p < 0.01 | |
| ALL | Male | 4 | lung : Wagner Grade 2 | f |
| | Comment: To | est: Fisher's Exa | act 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung : Wagner Grade 2 | f |
| | Comment: To | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Wagner Grade 3 | С |
| | Comment: G | roup Factor Chi | -Squared & Fisher's Exact: Test: Chi-Squared p < 0.05 | |
| ALL | Male | 1 | lung : Wagner Grade 4 | CCC |
| | Comment: G | roup Factor Chi | -Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung : Wagner Grade 1 | CCC |
| | Comment: G | roup Factor Chi | -Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 4 | lung : Wagner Grade 1 | f |
| | Comment: To | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung : Wagner Grade 1 | f |
| | Comment: To | est: Fisher's Exa | act 2 Sided p < 0.05 | |

Pathology - Intergroup Comparison of Pathology Observations

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|---------------|----------------|--|--------|
| ALL | Male | 6 | lung : Wagner Grade 1 | f |
| | Comment: Test | : Fisher's Exa | ct 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Accumulation, Particle-Laden Macrophages, Balt | CCC |
| | Comment: Grou | ıp Factor Chi- | Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 3 | lung : Accumulation, Particle-Laden Macrophages, Balt | f |
| | Comment: Test | : Fisher's Exa | ct 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung : Accumulation, Particle-Laden Macrophages, Balt | f |
| | Comment: Test | : Fisher's Exa | ct 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Accumulation, Particle-Laden Macrophages, Balt, very slight | CCC |
| | Comment: Grou | up Factor Chi- | Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 3 | lung : Accumulation, Particle-Laden Macrophages, Balt, very slight | f |
| | Comment: Test | : Fisher's Exa | ct 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung : Accumulation, Particle-Laden Macrophages, Balt, very slight | f |
| | Comment: Test | : Fisher's Exa | ct 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung : Accumulation, Fibre-Laden Macrophages, Balt | CC |
| | Comment: Grou | ıp Factor Chi | Squared & Fisher's Exact: Test: Chi-Squared p < 0.01 | |
| ALL | Male | 1 | lung : Accumulation, Fibre-Laden Macrophages, Balt, very slight | CC |
| | Comment: Grou | ıp Factor Chi | Squared & Fisher's Exact: Test: Chi-Squared p < 0.01 | |
| ALL | Male | 1 | lung associated lymph nodes (laln): Accumulation, Fibre-Laden Macrophages | CCC |
| | Comment: Grou | ıp Factor Chi | Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 1 | lung associated lymph nodes (laln): Accumulation, Fibre-Laden Macrophages, very slight | CC |
| | Comment: Grou | ıp Factor Chi | 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, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|------------|------------------|---|--------|
| ALL | Male | 1 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages | CCC |
| | Comment: C | Group Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 4 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 5 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 1 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages, very slight | CCC |
| | Comment: C | Group Factor Ch | i-Squared & Fisher's Exact: Test: Chi-Squared p < 0.001 | |
| ALL | Male | 4 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages, very slight | f |
| | Comment: T | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Accumulation, Fibre-Laden Macrophages | f |
| | Comment: 1 | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Accumulation, Fibre-Laden Macrophages | f |
| | Comment: 1 | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Accumulation, Fibre-Laden Macrophages, slight | f |
| | Comment: 1 | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Accumulation, Fibre-Laden Macrophages, slight | f |
| | Comment: 1 | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 7 | lung : Accumulation, Particle-Laden Macrophages | f |
| | Comment: 1 | est: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 7 | lung : Accumulation, Particle-Laden Macrophages, very slight | f |
| | Comment: T | est: 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, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|-------------|-----------------|---|--------|
| ALL | Male | 8 | lung : Fibrosis | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung: Fibrosis | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung: Fibrosis, slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Giant Cells, Syncytial | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Giant Cells, Syncytial | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Giant Cells, Syncytial, very slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Giant Cells, Syncytial, slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Hyperplasia, Bronchiolo-Alveolar | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Hyperplasia, Bronchiolo-Alveolar | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Hyperplasia, Bronchiolo-Alveolar, slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Infiltration, Inflammatory Cell | 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, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|-------------|-----------------|---|--------|
| ALL | Male | 9 | lung : Infiltration, Inflammatory Cell | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Infiltration, Inflammatory Cell, very slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Infiltration, Inflammatory Cell, very slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Microgranuloma | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Microgranuloma | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Microgranuloma, slight | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Wagner Grade 4 | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Wagner Grade 4 | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 7 | lung : Wagner Grade 1 | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung : Wagner Grade 1 | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung : Wagner Grade 1 | f |
| | Comment: Te | st: Fisher's Ex | act 2 Sided p < 0.05 | |

Pathology - Intergroup Comparison of Pathology Observations

02G16015 - Subchronic (13 week) brake dust inhalation toxicology study (nose-only) with lifelong follow-up in the rat, 3 months post exposure

| Removal Reason | Sex | Group | Measurement | Marker |
|----------------|------------|------------------|---|--------|
| ALL | Male | 7 | lung : Accumulation, Particle-Laden Macrophages, Balt | f |
| | Comment: T | est: Fisher's Ex | xact 2 Sided p < 0.05 | |
| ALL | Male | 7 | lung : Accumulation, Particle-Laden Macrophages, Balt, very slight | f |
| | Comment: T | est: Fisher's Ex | xact 2 Sided p < 0.05 | |
| ALL | Male | 8 | lung associated lymph nodes (laln): Accumulation, Fibre-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | xact 2 Sided p < 0.05 | |
| ALL | Male | 9 | lung associated lymph nodes (laln): Accumulation, Fibre-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | xact 2 Sided p < 0.05 | |
| ALL | Male | 7 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages | f |
| | Comment: T | est: Fisher's Ex | xact 2 Sided p < 0.05 | |
| ALL | Male | 7 | lung associated lymph nodes (laln): Accumulation, Particle-Laden Macrophages, very slight | 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, 3 months post exposure

Key Page

Measurement/Statistics

| <u>Measurement</u> | <u>Descriptive</u> | <u>Comparative</u> | Arithmetic/Adjusted | Transformation |
|-----------------------|--------------------|------------------------------|---------------------|----------------|
| Pathology Observation | Count Positives | Chi-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, 3 months post exposure

End Of Print