TABLE 2:
SUMMARY INCIDENCE

**Table 2**

**Summary of Incidence and Severity for Lesions in the 14 Day Studies of Ethyltoluene Isomers and Cumene**

**INCIDENCES OF SELECTED LESIONS IN THE NOSE**

| **Chemical** | **Species** | **Diagnosis** | **0** **ppm** | **500** **ppm** | **1000 ppm** | **2000 ppm** |
| --- | --- | --- | --- | --- | --- | --- |
| Cumene | B6C3F1/N | Nose | 0 | 0 | 0 | *n/a* |
| Cumene | HSD  | Nose | 0 | 0 | 0 | *n/a* |
| 2-ET | B6C3F1/N  | Nose, Respiratory Epithelium – Squamous Metaplasia | 0 | *n/a* | 6 (2.0)\* | 0 |
|  |  | Nose, Respiratory Epithelium – Inflamm, neutrophil | 0 | *n/a* | 4 (1.5) | 0 |
|  |  | Nose, Olfactory Epithelium – Atrophy | 0 | *n/a* | 2 (2.5) | 0 |
|  |  | Nose, Olfactory Epithelium – Necrosis | 0 | *n/a* | 0 | 9 (3.7) |
| 2-ET | HSD  | Nose, Olfactory Epithelium – Atrophy | 0 | *n/a* | 5 (3.6) | 0 |
| 3-ET | B6C3F1/N  | Nose | 0 | *n/a* | 0 | 0 |
| 3-ET | HSD  | Nose, Respiratory Epithelium – Squamous Metaplasia | 1 (2.0) | *n/a* | 0 | 1 (1.0) |
| 4-ET | B6C3F1/N  | Nose | 0 | *n/a* | 0 | 0 |
| 4-ET | HSD  | Nose | 0 | *n/a* | 0 | 0 |

n/a = Exposure group not applicable; \* Incidence followed by average severity in parentheses

**Table 2**

**Summary of Incidence and Severity for Lesions in the 14 Day Studies of Ethyltoluene Isomers and Cumene**

**INCIDENCES OF SELECTED LESIONS IN THE LUNG**

| **Chemical** | **Species** | **Diagnosis** | **0** **ppm** | **500** **ppm** | **1000 ppm** | **2000 ppm** |
| --- | --- | --- | --- | --- | --- | --- |
| Cumene | B6C3F1/N | Lung, Bronchiolar Epithelium – Hyperplasia | 1 (3.0)\* | 2 (2.0) | 6 (1.5) | *n/a* |
|  |  | Lung, Bronchus Epithelium – Hyperplasia | 1 (3.0) | 2 (2.0) | 6 (1.5) | *n/a* |
| Cumene | HSD | Lung | 0 | 0 | 0 | *n/a* |
| 2-ET | B6C3F1/N  | Lung, Bronchiolar Epithelium – Hyperplasia | 2 (1.0) | *n/a* | 4 (1.5) | 6 (1.8) |
|  |  | Lung, Bronchus Epithelium – Hyperplasia | 2 (1.0) | *n/a* | 4 (1.5) | 6 (1.0) |
|  |  | Lung, Bronchiolar Epithelium – Vacuolation, Cytoplasmic | 0 | *n/a* | 0 | 6 (1.5) |
|  |  | Lung, Bronchus Epithelium – Vacuolation, Cytoplasmic | 0 | *n/a* | 0 | 6 (1.5) |
| 2-ET | HSD  | Lung | 0 | *n/a* | 0 | 0 |
| 3-ET | B6C3F1/N | Lung, Bronchiolar Epithelium – Hyperplasia | 1 (2.0) | *n/a* | 6 (1.3) | 4 (1.3) |
|  |  | Lung, Bronchus Epithelium – Hyperplasia | 1 (2.0) | *n/a* | 6 (1.3) | 4 (1.3) |
| 3-ET | HSD | Lung | 0 | *n/a* | 0 | 0 |
| 4-ET | B6C3F1/N | Lung, Bronchiolar Epithelium – Hyperplasia | 0 | *n/a* | 1 (1.0) | 0 |
|  |  | Lung, Bronchus Epithelium – Hyperplasia | 0 | *n/a* | 1 (1.0) | 0 |
| 4-ET | HSD | Lung | 0 | *n/a* | 0 | 0 |

n/a = Exposure group not applicable; \* Incidence followed by average severity in parentheses

**Table 2**

**Summary of Incidence and Severity for Lesions in the 14 Day Studies of Ethyltoluene Isomers and Cumene**

**INCIDENCES OF SELECTED LESIONS IN THE LIVER**

| **Chemical** | **Species** | **Diagnosis** | **0** **ppm** | **500** **ppm** | **1000 ppm** | **2000 ppm** |
| --- | --- | --- | --- | --- | --- | --- |
| Cumene | B6C3F1/N  | Liver | 0 | 0 | 0 | *n/a* |
| Cumene | HSD | Liver | 0 | 0 | 0 | *n/a* |
| 2-ET | B6C3F1/N  | Liver – Hypertrophy, Centrilobular | 0 | *n/a* | 0 | 5 (3.0)\* |
|  |  | Liver, Hepatocyte – Necrosis, Centrilobular | 0 | *n/a* | 0 | 5 (1.2) |
| 2-ET | HSD | Liver – Pigment, Centrilobular | 0 | *n/a* | 5 (1.2) | 0 |
|  |  | Liver, Hepatocyte – Glycogen Depletion | 0 | *n/a* | 8 (1.8) | 0 |
|  |  | Liver, Hepatocyte – Necrosis, Centrilobular | 0 | *n/a* | 8 (1.3) | 0 |
| 3-ET | B6C3F1/N  | Liver | 0 | *n/a* | 0 | 0 |
| 3-ET | HSD | Liver | 0 | *n/a* | 0 | 0 |
| 4-ET | B6C3F1/N  | Liver | 0 | *n/a* | 0 | 0 |
| 4-ET | HSD | Liver | 0 | *n/a* | 0 | 0 |

n/a = Exposure group not applicable; \* Incidence followed by average severity in parentheses

TABLE 3:
INDIVIDUAL ANIMAL DATA

Two-week Toxicogenomic Study of C9 Alkylbenzenes in Female B6C3F1/N Mice and Male Harlan Sprague Dawley Rats

Study Ref. No. 2015-306-328

Protocol: Comparison of C9 alkylbenzenes with cumene in B6C3F1/N Mice and HSD rats exposed for 3 hours/day for 12 exposures. Control (Group 1) animals received filtered conditioned air.

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **Air Control****HSD Rats** |
| 8 | n | n | n | n | n |
| 13 | n | n | n | n | n |
| 25 | n | n | n | n | n |
| 26 | n | n | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| 37 | n | n | n | n | n |
| 2 | - | - | Metaplasia, osseous, minimal | n | Chronic progressive nephropathy, minimal |
| 7 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 20 | - | - | n | n | n |
| 32 | - | - | n | n | n |
| 33 | - | - | n | n | n |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **1000 ppm****HSD Rats** |
| 5 | n | Olfactory epithelium – Atrophy, marked | n | Hepatocyte – Glycogen depletion, centrilobular, minimalHepatocyte – Necrosis, centrilobular, minimal | n |
| 17 | n | Olfactory epithelium – Atrophy, marked | n | Pigment, centrilobular, mildHepatocyte – Glycogen depletion, centrilobular, minimalHepatocyte – Necrosis, centrilobular, minimal | n |
| 19 | n | Olfactory epithelium – Atrophy, marked | n | Pigment, centrilobular, minimalHepatocyte – Glycogen depletion, centrilobular, mildHepatocyte – Necrosis, centrilobular, minimal | n |
| 30 | n | Olfactory epithelium – Atrophy, moderate | n | - | Chronic progressive nephropathy, minimal |
| 31 | n | Olfactory epithelium – Atrophy, moderate | n | Pigment, centrilobular, minimalHepatocyte – Glycogen depletion, centrilobular, mildHepatocyte – Necrosis, centrilobular, mild | n |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **1000 ppm****HSD Rats (Continued)** |
| 1 | - | - | n | Hepatocyte – Glycogen depletion, centrilobular, mildHepatocyte – Necrosis, centrilobular, minimal | n |
| 3 | - | - | n | n | n |
| 4 | - | - | n | Pigment, centrilobular, minimalHepatocyte – Glycogen depletion, centrilobular, mildHepatocyte – Necrosis, centrilobular, minimal | Chronic progressive nephropathy, minimal |
| 24 | - | - | n | Pigment, centrilobular, minimalHepatocyte – Glycogen depletion, centrilobular, mildHepatocyte – Necrosis, centrilobular, mild | n |
| 35 | - | - | n | Hepatocyte – Glycogen depletion, centrilobular, mildHepatocyte – Necrosis, centrilobular, minimal | n |
| **Incidence/****Average Severity** | - | OE - Atrophy 5 (3.6)\* | - | Pigment, centri 5 (1.2)Hepat – Glycogen depl 8 (1.8)Hepat – Necrosis, cetnri 8 (1.3) | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **2000 ppm****HSD Rats** |
| 18 MS | - | n | n | - | n |
| 29 MS | - | n | n | - | n |
| 36 MS | - | n | Alveolus – Hemorrhage, minimalAlveolus – Infiltration cell, histiocyte, minimalErythrophagocytosis, minimal | - | Renal tubule – Dilation, mildRenal tubule – Mineralization, minimal |
| 12 MS | - | n | n | - | Renal tubule – Dilation, mildRenal tubule – Mineralization, minimal |
| 9 MS | - | n | n | - | n |
| 11 MS | - | n | n | - | n |
| 14 MS | - | n | n | - | n |
| 15 FD | - | n | n | - | n |
| 21 MS | - | n | n | - | n |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present; MS = moribund sacrifice; FD = found dead

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **Air Control****B6C3F1/N Mice** |
| 38 | n | n | n | n | - |
| 40 | n | n | n | n | - |
| 41 | n | n | n | n | - |
| 43 | n | n | n | n | - |
| 52 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 53 | n | n | n | Inflammation, chronic, minimal | - |
| 56 | n | - | n | n | - |
| 57 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 68 | n | n | n | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus hyper 2 (1.0)\*Bronchiole hyper 2 (1.0) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **1000 ppm,** **B6C3F1/N Mice** |
| 44 | n | Respiratory epithelium – Metaplasia, squamous, mild | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 46 | n | Respiratory epithelium – Metaplasia, squamous, mild | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 58 | n | Olfactory epithelium – Atrophy, markedRespiratory epithelium – Metaplasia, squamous, mildRespiratory epithelium – Inflammation, neutrophil, minimal | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 59 | n | Respiratory epithelium – Metaplasia, squamous, mildRespiratory epithelium – Inflammation, neutrophil, mild | n | n | - |
| 61 | n | Respiratory epithelium – Metaplasia, squamous, mildRespiratory epithelium – Inflammation, neutrophil, minimalOlfactory epithelium – Atrophy, minimal | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 72 | n | Respiratory epithelium – Metaplasia, squamous, mildRespiratory epithelium – Inflammation, neutrophil, mild | n | n | - |
| **Incidence/****Average Severity** | - | RE – Meta, squam 6 (2.0)\*OE - Atrophy 2 (2.5)RE – Inflamm, neut 4 (1.5) | Bronchus - Hyper 4 (1.5)Bronchiole- Hyper 4 (1.5) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **2000 ppm****B6C3F1/N Mice** |
| 51 | - | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, moderateBronchus, epithelium – Vacuolation, moderateBronchiole, epithelium – Vacuolation, moderate | n | - |
| 65 | - | Olfactory epithelium – Necrosis, moderate | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimalBronchus, epithelium – Vacuolation, mildBronchiole, epithelium – Vacuolation, mild | n | - |
| 42 | - | Olfactory epithelium – Necrosis, moderate | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, mildBronchus, epithelium – Vacuolation, minimalBronchiole, epithelium – Vacuolation, minimal | n | - |
| 47 | - | Olfactory epithelium – Necrosis, marked | n | Hepatocyte - Hypertrophy, centrilobular, moderateHepatocyte - Necrosis, centrilobular, mild | - |
| 50 | - | Olfactory epithelium – Necrosis, marked | n | Hepatocyte – Hypertrophy, centrilobular, mildHepatocyte - Necrosis, centrilobular, minimal | - |
| 54 | - | Olfactory epithelium – Necrosis, marked | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, moderate | Hepatocyte - Hypertrophy, centrilobular, moderateHepatocyte - Necrosis, centrilobular, minimal | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **2-ET** |  |  |  |  |  |
| **2000 ppm****B6C3F1/N Mice (Continued)** |
| 64 | - | Olfactory epithelium – Necrosis, marked | Bronchus, epithelium – Vacuolation, minimalBronchiole, epithelium – Vacuolation, minimal | n | - |
| 69 | - | Olfactory epithelium – Necrosis, marked | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimalBronchus, epithelium – Vacuolation, minimalBronchiole, epithelium – Vacuolation, minimal | Hepatocyte - Hypertrophy, centrilobular, markedHepatocyte - Necrosis, centrilobular, minimal | - |
| 70 | - | Olfactory epithelium – Necrosis, marked | n | Hepatocyte - Necrosis, centrilobular, minimal Hepatocyte - Hypertrophy, centrilobular, moderate | - |
| 71 | - | Olfactory epithelium – Necrosis, moderate | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimalBronchus, epithelium – Vacuolation, minimalBronchiole, epithelium – Vacuolation, minimal | n | - |
| **Incidence/****Average Severity** | - | OE – Necrosis 9 (3.7)\* | Bronchus - Hyper 6 (1.0)Bronchiole - Hyper 6 (1.8)Bronchus – Vacuolation 6 (1.5)Bronchiole - Vacuolation 6 (1.5) | Hypertrophy, centri 5 (3.0)Hepatocyte – Necrosis, centri 5 (1.2) | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **3-ET** |  |  |  |  |  |
| **Air Control****HSD Rats** |
| 9 | n | Respiratory epithelium – Metaplasia, squamous, mild | n | n | n |
| 18 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 19 | n | n | n | n | n |
| 24 | n | n | n | n | Chronic progressive nephropathy, minimalRenal tubule – Dilation, minimal |
| 29 | n | n | n | n | n |
| 20 | - | - | n | n | Renal tubule – Dilation, minimal |
| 21 | - | n | n | n | n |
| 23 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 34 | - | - | n | n | n |
| 37 | - | - | n | n | Chronic progressive nephropathy, minimal |
| **Incidence/****Average Severity** | - | RE – Meta, squam 1 (2.0)\* | - | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **3-ET** |  |  |  |  |  |
| **1000 ppm****HSD Rats** |
| 4 | - | n | n | n | Chronic progressive nephropathy, minimal |
| 16 | - | n | n | n | Chronic progressive nephropathy, minimal |
| 22 | - | n | n | n | Chronic progressive nephropathy, minimal |
| 25 | - | n | n | n | n |
| 36 | - | - | n | n | Renal tubule – Dilation, minimal |
| 2 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 6 | - | - | n | Inflammation, chronic, minimal | n |
| 8 | - | - | n | n | n |
| 31 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 33 | - | - | n | n | n |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **3-ET** |  |  |  |  |  |
| **2000 ppm****HSD Rats** |
| 1 | n | n | n | n | n |
| 11 | n | n | n | Inflammation, chronic, minimal | n |
| 27 | Ventricle – Dilation, mild | n | n | n | Chronic progressive nephropathy, minimal |
| 28 | n | Respiratory epithelium – Metaplasia, squamous, minimal | n | n | Chronic progressive nephropathy, minimal |
| 32 | n | n | n | n | n |
| 3 | - | - | n | n | n |
| 7 | - | - | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| 26 | - | - | n | n | n |
| 30 | - | - | n | n | n |
| 35 | - | - | n | n | Chronic progressive nephropathy, minimal |
| **Incidence/****Average Severity** | - | RE – Meta, squam 1 (1.0)\* | - | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **3-ET** |  |  |  |  |  |
| **Air Control****B6C3F1/N Mice** |
| 41 | n | n | n | Inflammation, chronic, minimal | - |
| 45 | n | n | n | n | - |
| 48 | n | n | n | Inflammation, chronic, minimal | - |
| 52 | n | n | n | n | - |
| 54 | n | n | n | n | - |
| 55 | n | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 66 | n | n | n | n | - |
| 68 | n | n | Inflammation, mixed cell, minimal | n | - |
| 69 | n | n | n | n | - |
| 70 | n | n | n | n | n |
| **Incidence/****Average Severity** | - | - | Bronchus - Hyper 1 (2.0)\*Bronchiole - Hyper 1 (2.0) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **3-ET** |  |  |  |  |  |
| **1000 ppm****B6C3F1/N Mice** |
| 39 | - | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 40 | - | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 44 | - | n | n | n | - |
| 50 | - | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 51 | - | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 53 | - | - | n | n | - |
| 61 | - | n | n | n | - |
| 64 | - | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 65 | - | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus hyper 6 (1.3)\*Bronchiole hyper 6 (1.3) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **3-ET** |  |  |  |  |  |
| **2000 ppm****B6C3F1/N Mice** |
| 38 | n | n | n | n | - |
| 42 | n | - | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 47 | n | n | n | n | - |
| 56 | n | n | n | Inflammation, chronic, minimal | - |
| 57 | n | n | n | n | - |
| 58 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 59 | n | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 62 | n | n | n | n | - |
| 67 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 71 | n | n | n | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus - Hyper 4 (1.3)\*Bronchiole - Hyper 4 (1.3) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **4-ET** |  |  |  |  |  |
| **Air Control****HSD Rats** |
| 4 | n | n | n | n | n |
| 26 | n | n | Alveolus – Inflammation, mixed cell, minimalErythrophagocytosis, minimal | n | - |
| 33 | n | n | n | n | n |
| 34 | n | n | n | Inflammation, chronic, minimal | Renal tubule – cast, minimal |
| 37 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 12 | - | - | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| 18 | - | - | Alveolus – Infiltration cell, histiocyte, minimal  | n | n |
| 19 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 22 | - | - | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| 35 | - | - | n | n | Chronic progressive nephropathy, minimal |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **4-ET** |  |  |  |  |  |
| **1000 ppm****HSD Rats** |
| 16 | - | n | n | n | n |
| 24 | - | n | n | n | Chronic progressive nephropathy, minimal  |
| 25 | n | n | Infiltration cell, perivascular, mixed, minimalAlveolus, epithelium – Hyperplasia, minimalAlveolus – Infiltration cell, histiocyte, minimal | Inflammation, chronic, minimal | Chronic progressive nephropathy, minimal |
| 27 | - | n | Alveolus, epithelium – Hyperplasia, minimalAlveolus – Infiltration cell, histiocyte, minimal | n | Chronic progressive nephropathy, minimal |
| 29 | n | n | n | n | n |
| 1 | - | - | n | n | n |
| 5 | - | - | n | n | n |
| 17 | - | - | n | n | n |
| 28 | - | - | Alveolus – Infiltration cell, histiocyte, minimal | n | Chronic progressive nephropathy, minimal |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **4-ET** |  |  |  |  |  |
| **2000 ppm****HSD Rats** |
| 7 | n | n | n | n | n |
| 8 | - | n | n | n | Chronic progressive nephropathy, minimal |
| 13 | n | n | Alveolus – Infiltration cell, histiocyte, minimalAlveolus, epithelium – Hyperplasia, minimal | n | Chronic progressive nephropathy, minimal |
| 31 | n | n | n | n | n |
| 9 | n | - | n | n | Chronic progressive nephropathy, minimal |
| 11 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 23 | - | - | n | n |  Chronic progressive nephropathy, minimal |
| 30 | - | - | Alveolus – Infiltration cell, histiocyte, minimalErythrophagocytosis, minimal | n | Chronic progressive nephropathy, minimal |
| 36 | n | - | n | n | Chronic progressive nephropathy, minimal |
| 32 FD | - | - | n | - | - |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present; FD = found dead

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **4-ET** |  |  |  |  |  |
| **Air Control****B6C3F1/N Mice** |
| 39 | n | n | n | n | - |
| 51 | n | - | n | n | - |
| 53 | n | n | n | n | - |
| 54 | n | n | n | n | - |
| 57 | n | n | n | Inflammation, chronic, minimal | - |
| 65 | n | - | n | Inflammation, chronic, minimal | - |
| 72 | n | n | n | Inflammation, chronic, minimal | - |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **4-ET** |  |  |  |  |  |
| **1000 ppm****B6C3F1/N Mice** |
| 44 | n | n | n | Inflammation, chronic, minimal | - |
| 46 | n | n | n | n | - |
| 50 | n | n | n | n | - |
| 58 | n | n | n | n | - |
| 60 | n | n | Alveolus – Infiltration cell, histiocyte, minimalBronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 61 | n | - | n | n | - |
| 62 | n | - | n | n | - |
| 64 | n | n | - | Fibrosis, minimalPigment, minimal | - |
| 71 | n | n | n | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus - Hyper 1 (1.0)\*Bronchiole - Hyper 1 (1.0) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN**  | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **4-ET** |  |  |  |  |  |
| **2000 ppm****B6C3F1/N Mice** |
| 38 MS | - | n | n | Inflammation, chronic, minimal | - |
| 41 | n | n | n | n | - |
| 42 | n | n | n | n | - |
| 48 MS | n | - | n | n | - |
| 49 MS | - | n | n | n | - |
| 66 | n | n | Alveolus – Infiltration cell, histiocyte, minimal | n | - |
| 69 MS | - | - | n | n | - |
| 70 MS | - | n | n | Necrosis, moderateFibrosis, moderateInfiltration cell, histiocyte, mildHemorrhage, minimal | - |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present; MS = moribund sacrifice

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **Cumene** |  |  |  |  |  |
| **Air Control****HSD Rats** |
| 2 | n | n | Alveolus – Infiltration cell, histiocyte, minimal | n | Renal tubule – Cast, minimal |
| 5 | n | n | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| 8 | n | n | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| 11 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 30 | n | n | n | n | n |
| 6 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 27 | - | - | n | Inflammation, chronic, minimal | n |
| 28 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 32 | - | - | n | n | Chronic progressive nephropathy, minimal |
| 34 | - | - | n | n | n |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **Cumene** |  |  |  |  |  |
| **500 ppm****HSD Rats** |
| 1 | n | n | n | Capsule – fibrosis, minimal | n |
| 21 | n | n | n | Inflammation, chronic, minimal | n |
| 22 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 24 | n | n | n | n | n |
| 33 | n | n | n | n | n |
| 7 | - | - | Alveolus – Infiltration cell, histiocyte, minimal | n | Chronic progressive nephropathy, minimal |
| 10 | - | - | n | n | Renal tubule – Dilation, minimal |
| 20 | - | - | n | n | n |
| 35 | - | - | n | n | n |
| 36 | - | - | n | n | n |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **Cumene** |  |  |  |  |  |
| **1000 ppm****HSD Rats** |
| 4 | n | - | n | Inflammation, chronic, minimal | Renal tubule – Dilation, minimalChronic progressive nephropathy, minimal |
| 9 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 23 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 26 | n | n | n | n | Chronic progressive nephropathy, minimal |
| 37 | n | n | n | Inflammation, chronic, minimal | n |
| 12 | - | - | n | n | n |
| 13 | - | - | n | n | Renal tubule – Dilation, minimal |
| 16 | n | n | n | n | n |
| 17 | n | n | n | n | n |
| 18 | n | n | Alveolus – Infiltration cell, histiocyte, minimal | n | n |
| **Incidence/****Average Severity** | - | - | - | - | - |

n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **Cumene** |  |  |  |  |  |
| **Air Control****B6C3F1/N Mice** |
| 40 | n | n | n | n | - |
| 41 | n | n | n | n | - |
| 43 | n | n | n | n | - |
| 47 | n | n | n | n | - |
| 50 | n | n | n | n | - |
| 65 | n | n | Bronchus, epithelium - Hyperplasia, moderateBronchiole, epithelium – Hyperplasia, moderate | n | - |
| 66 | n | n | n | Inflammation, chronic, mild | - |
| 67 | n | - | Alveolus, epithelium – Hyperplasia, minimalAlveolus – Infiltration cell, histiocyte, minimal | n | - |
| 71 | n | n | n | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus - Hyper 1 (3.0)Bronchiole - Hyper 1 (3.0) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **Cumene** |  |  |  |  |  |
| **500 ppm****B6C3F1/N Mice** |
| 42 | - | n | n | n | - |
| 46 | - | n | n | n | - |
| 49 | - | n | n | n | - |
| 51 | - | n | Alveolus - Infiltration cell, histiocyte, minimal | n | - |
| 54 | - | n | n | n | - |
| 55 | - | n | n | n | - |
| 56 | - | n | n | Inflammation, focal, minimal | - |
| 61 | - | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 64 | - | n | n | n | - |
| 69 | - | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus - Hyper 2 (2.0)\*Bronchiole - Hyper 2 (2.0) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present

|  | **BRAIN** | **NOSE** | **LUNG** | **LIVER** | **KIDNEY** |
| --- | --- | --- | --- | --- | --- |
| **Exp/An #** **Cumene** |  |  |  |  |  |
| **1000 ppm****B6C3F1/N Mice** |
| 39 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 45 | n | n | Bronchus, epithelium – Hyperplasia, mildBronchiole, epithelium – Hyperplasia, mild | n | - |
| 53 | n | n | Bronchus, epithelium – Hyperplasia, moderateBronchiole, epithelium – Hyperplasia, moderate | n | - |
| 57 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 58 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 59 | n | n | n | n | - |
| 60 | n | n | n | n | - |
| 62 | n | n | Bronchus, epithelium – Hyperplasia, minimalBronchiole, epithelium – Hyperplasia, minimal | n | - |
| 70 | n | n | n | n | - |
| 72 | n | n | n | n | - |
| **Incidence/****Average Severity** | - | - | Bronchus - Hyper 6 (1.5)\*Bronchiole - Hyper 6 (1.5) | - | - |

\* Incidence followed by average severity in parentheses; n = no remarkable lesion; - = not present