# Draft Report on Carcinogens Monograph for Cumene

# Data for Evaluating Alpha-2u Criteria

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**TABLE 6**
**Selected Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 3-Month Inhalation Study of Cumene[a]**

| | Chamber Control | 62.5 ppm | 125 ppm | 250 ppm | 500 ppm | 1,000 ppm |
|---|---|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| **Male** | | | | | | |
| Necropsy body wt | 312 ± 8 | 313 ± 6 | 322 ± 5 | 331 ± 4 | 314 ± 5 | 323 ± 5 |
| R. Kidney | | | | | | |
| Absolute | 0.923 ± 0.024 | 0.980 ± 0.025 | 1.010 ± 0.031*[b] | 1.059 ± 0.021** | 1.070 ± 0.017** | 1.152 ± 0.023** |
| Relative | 2.962 ± 0.032 | 3.128 ± 0.051** | 3.131 ± 0.056**[b] | 3.194 ± 0.036** | 3.411 ± 0.045** | 3.561 ± 0.029** |
| Liver | | | | | | |
| Absolute | 9.518 ± 0.327 | 10.123 ± 0.267 | 10.260 ± 0.264 | 11.170 ± 0.302** | 11.589 ± 0.282** | 12.637 ± 0.288** |
| Relative | 30.481 ± 0.348 | 32.279 ± 0.278* | 31.792 ± 0.430* | 33.660 ± 0.558** | 36.895 ± 0.563** | 39.068 ± 0.549** |
| **Female** | | | | | | |
| Necropsy body wt | 195 ± 2 | 190 ± 3 | 194 ± 4 | 190 ± 3 | 185 ± 3 | 187 ± 4 |
| R. Kidney | | | | | | |
| Absolute | 0.637 ± 0.016 | 0.636 ± 0.010 | 0.649 ± 0.018 | 0.655 ± 0.017 | 0.645 ± 0.011 | 0.675 ± 0.011 |
| Relative | 3.263 ± 0.061 | 3.355 ± 0.049 | 3.322 ± 0.057 | 3.439 ± 0.057* | 3.486 ± 0.044** | 3.612 ± 0.040** |
| Liver | | | | | | |
| Absolute | 5.553 ± 0.130 | 5.669 ± 0.148 | 5.885 ± 0.204 | 5.959 ± 0.137 | 5.979 ± 0.133 | 6.923 ± 0.227** |
| Relative | 28.442 ± 0.389 | 29.858 ± 0.458 | 30.094 ± 0.634* | 31.289 ± 0.412** | 32.286 ± 0.386** | 36.958 ± 0.724** |

* Significantly different ($P \leq 0.05$) from the chamber control group by Williams' test
** $P \leq 0.01$
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).
[b] n=9

**TABLE 7**
**Renal Toxicity Data for Male Rats in the 3-Month Inhalation Study of Cumene[a]**

| | Chamber Control | 62.5 ppm | 125 ppm | 250 ppm | 500 ppm | 1,000 ppm |
|---|---|---|---|---|---|---|
| n | 10 | 10 | 10 | 10 | 10 | 10 |
| Cells labeled | 60.60 ± 4.25 | 78.90 ± 5.60 | 63.80 ± 6.03 | 54.90 ± 4.50 | 43.70 ± 6.21 | 79.40 ± 6.65 |
| Cells counted | 2,095 ± 25 | 2,190 ± 28 | 2,100 ± 29 | 2,171 ± 31 | 2,268 ± 42 | 2,223 ± 45 |
| Labeling index (%)[b] | 2.894 ± 0.204 | 3.607 ± 0.266 | 3.051 ± 0.305 | 2.536 ± 0.219 | 1.944 ± 0.306 | 3.614 ± 0.346 |
| Soluble protein (mg/mL) | 21.22 ± 1.27 | 23.43 ± 0.51 | 23.93 ± 0.93[c] | 25.36 ± 0.69* | 25.51 ± 0.73** | 26.16 ± 1.09** |
| α2u-Globulin (nmol/g kidney) | 172.2 ± 22.3 | 328.1 ± 69.6 | 383.4 ± 46.3**[c] | 420.7 ± 50.1** | 363.2 ± 41.4** | 575.2 ± 74.8** |
| α2u-Globulin (ng/µg soluble protein) | 76.46 ± 9.24 | 130.98 ± 27.27 | 150.90 ± 19.23*[c] | 154.35 ± 16.98** | 133.01 ± 14.25** | 209.79 ± 31.34** |

* Significantly different ($P \leq 0.05$) from the chamber control group by Shirley's test
** $P \leq 0.01$
[a] Data are presented as mean ± standard error.
[b] Labeling index was calculated as the number of labeled cells divided by the total number of cells counted times 100. A minimum of 2,000 cells were counted.
[c] n=9

**TABLE 8**
**Incidences of Nonneoplastic Lesions in the Kidney of Male Rats in the 3-Month Inhalation Study of Cumene**

| | Chamber Control | | 62.5 ppm | | 125 ppm | | 250 ppm | | 500 ppm | | 1,000 ppm | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number Examined Microscopically | 10 | | 10 | | 10 | | 10 | | 10 | | 10 | |
| Cortex Renal Tubule, Accumulation, Hyaline Droplet[a] | 10 | (1.1)[b] | 10 | (1.4) | 10 | (1.9) | 10 | (2.4) | 10 | (3.0) | 10 | (2.9) |
| Cortex Renal Tubule, Regeneration | 8 | (1.0) | 6 | (1.2) | 8 | (1.5) | 10 | (1.8) | 10 | (2.1) | 10 | (2.1) |
| Medulla, Casts Granular | 0 | | 0 | | 2 | (1.0) | 8** | (1.5) | 10** | (2.5) | 9** | (2.2) |

** Significantly different ($P \leq 0.01$) from the chamber control group by the Fisher exact test
[a] Number of animals with lesion
[b] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

**Table 5-3. Renal toxicity data for rats exposed to cumene vapor for 2 years**

| Sex | Conc. (ppm) | Renal tubule hyperplasia | Renal papilla mineralization | Renal pelvis transitional epithelium hyperplasia | Nephropathy |
|---|---|---|---|---|---|
| Male | 0 | 0 | 5 (1.0) | 3 (1.7) | 47 (2.3) |
| | 250 | 3[a] (3.3)[b] | 35** (1.7) | 5 (1.8) | 47 (2.6) |
| | 500 | 8** (2.6) | 44** (2.1) | 14** (2.4) | 47 (2.9) |
| | 1,000 | 6* (2.2) | 41** (2.1) | 15** (2.0) | 50 (2.7) |
| Female | 0 | NR | 6 (NR) | 1 (NR) | 38 (1.4) |
| | 250 | | 3 | 1 | 37 (1.5) |
| | 500 | | 4 | 6 | 41 (1.9) |
| | 1,000 | | 6 | 1 | 44 (1.9) |

Source: NTP 2009.
NR = Not reported.
*$P \leq 0.05$ (compared with chamber controls).
**$P \leq 0.01$.
[a]Number of animals with lesion (50 animals examined per group).
[b]Average severity grade: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked.

**Table B4**
**Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 2-Year Inhalation Study of Cumene**

| | Chamber Control | 250 ppm | 500 ppm | 1,000 ppm |
|---|---|---|---|---|
| **Special Senses System** | | | | |
| Eye | (50) | (49) | (50) | (50) |
| Bilateral, lens, cataract | 1 (2%) | | | |
| Bilateral, retina, atrophy | 1 (2%) | 1 (2%) | 1 (2%) | |
| Cornea, epithelium, hyperplasia | | | | 1 (2%) |
| Cornea, inflammation | | | | 1 (2%) |
| Cornea, inflammation, suppurative | 1 (2%) | | | |
| Lens, cataract | 5 (10%) | 2 (4%) | 5 (10%) | 3 (6%) |
| Retina, atrophy | 3 (6%) | 5 (10%) | 8 (16%) | 2 (4%) |
| Harderian gland | (50) | (49) | (50) | (50) |
| Inflammation, chronic | 1 (2%) | | 1 (2%) | 1 (2%) |
| Zymbal's gland | (1) | | (1) | (1) |
| **Urinary System** | | | | |
| Kidney | (50) | (50) | (50) | (50) |
| Infarct, multiple | | | 1 (2%) | |
| Nephropathy | 38 (76%) | 37 (74%) | 41 (82%) | 44 (88%) |
| Artery, inflammation, chronic active | | | | 1 (2%) |
| Papilla, mineralization | 6 (12%) | 3 (6%) | 4 (8%) | 6 (12%) |
| Pelvis, transitional epithelium, hyperplasia | 1 (2%) | 1 (2%) | 6 (12%) | 1 (2%) |
| Pelvis, transitional epithelium, mineralization | 23 (46%) | 27 (54%) | 27 (54%) | 22 (44%) |
| Pelvis, dilatation | 1 (2%) | | | |
| Renal tubule, accumulation, hyaline droplet | 1 (2%) | | 1 (2%) | |
| Renal tubule, cyst | 1 (2%) | | 1 (2%) | 1 (2%) |
| Renal tubule, pigmentation | 1 (2%) | | | |
| Urinary bladder | (50) | (49) | (50) | (50) |
| Transitional epithelium, hyperplasia | 1 (2%) | 2 (4%) | 2 (4%) | 1 (2%) |

**Table 5-3. Renal toxicity data for rats exposed to cumene vapor for 2 years**

| Sex | Conc. (ppm) | Renal tubule hyperplasia | Renal papilla mineralization | Renal pelvis transitional epithelium hyperplasia | Nephropathy |
|---|---|---|---|---|---|
| Male | 0 | 0 | 5 (1.0) | 3 (1.7) | 47 (2.3) |
| | 250 | 3[a] (3.3)[b] | 35** (1.7) | 5 (1.8) | 47 (2.6) |
| | 500 | 8** (2.6) | 44** (2.1) | 14** (2.4) | 47 (2.9) |
| | 1,000 | 6* (2.2) | 41** (2.1) | 15** (2.0) | 50 (2.7) |
| Female | 0 | NR | 6 (NR) | 1 (NR) | 38 (1.4) |
| | 250 | | 3 | 1 | 37 (1.5) |
| | 500 | | 4 | 6 | 41 (1.9) |
| | 1,000 | | 6 | 1 | 44 (1.9) |

Source: NTP 2009.
NR = Not reported.
*$P \leq 0.05$ (compared with chamber controls).
**$P \leq 0.01$.
[a]Number of animals with lesion (50 animals examined per group).
[b]Average severity grade: 1 = minimal, 2 = mild, 3 = moderate, 4 = marked.

**TABLE A4**
**Summary of the Incidence of Nonneoplastic Lesions in Male Rats in the 2-Year Inhalation Study of Cumene**

| | Chamber Control | 250 ppm | 500 ppm | 1,000 ppm |
|---|---|---|---|---|
| **Urinary System** | | | | |
| Kidney | (50) | (50) | (50) | (50) |
| Atrophy | | | | 1 (2%) |
| Infarct | | 1 (2%) | 2 (4%) | 1 (2%) |
| Infarct, multiple | | 1 (2%) | | |
| Nephropathy | 47 (94%) | 47 (94%) | 47 (94%) | 50 (100%) |
| Bilateral, renal tubule, cyst | | | 1 (2%) | |
| **Urinary System** (continued) | | | | |
| Kidney (continued) | (50) | (50) | (50) | (50) |
| Bilateral, infarct | | 1 (2%) | | |
| Capsule, dilatation | | | 1 (2%) | |
| Glomerulus, inflammation, suppurative | | 1 (2%) | | |
| Papilla, mineralization | 5 (10%) | 35 (70%) | 44 (88%) | 41 (82%) |
| Pelvis, transitional epithelium, hyperplasia | 3 (6%) | 5 (10%) | 14 (28%) | 15 (30%) |
| Pelvis, dilatation | | | 1 (2%) | 1 (2%) |
| Renal tubule, accumulation, hyaline droplet | | | 1 (2%) | 1 (2%) |
| Renal tubule, cyst | | 1 (2%) | 3 (6%) | 2 (4%) |
| Renal tubule, hyperplasia | | 3 (6%) | 8 (16%) | 6 (12%) |
| Renal tubule, hypertrophy | | | | 1 (2%) |
| Renal tubule, mineralization | 1 (2%) | | | |