

1020_L_MWNT Tissue Burden Analysis in Male HD Rats at 0 days

| Parameter ^a | 0 mg/m3 | 0.1 mg/m3 | 0.3 mg/m3 | 1.0 mg/m3 | 3.0 mg/m3 | 10.0 mg/m3 | Trend ^b |
|--|--------------------|----------------------|----------------------|----------------------|----------------------|----------------------|--------------------|
| Sample Weight (g) ^b | 1.426 ± 0.047 [10] | 1.511 ± 0.064 [10] | 1.595 ± 0.105 [10] | 1.599 ± 0.112 [10] | 1.770 ± 0.054 [10]** | 1.782 ± 0.037 [10]** | <.001 |
| Sample Conc (ug Ni/g) ^c | 0.001 ± 0.000 [10] | 0.028 ± 0.001 [10]** | 0.095 ± 0.015 [10]** | 0.327 ± 0.019 [10]** | 0.818 ± 0.030 [10]** | 2.060 ± 0.102 [10]** | <.001 |
| Total Lung Burden (ug Ni/lung) ^c | 0.001 ± 0.000 [10] | 0.042 ± 0.002 [10]** | 0.141 ± 0.015 [10]** | 0.505 ± 0.018 [10]** | 1.439 ± 0.046 [10]** | 3.658 ± 0.163 [10]** | <.001 |
| Total Lung Burden (ug L-MWNT-1020/lung) ^c | 0.192 ± 0.006 [10] | 8.052 ± 0.405 [10]** | 27.10 ± 2.802 [10]** | 97.19 ± 3.421 [10]** | 276.8 ± 8.902 [10]** | 703.5 ± 31.28 [10]** | <.001 |
| Norm. Lung Burden (ug LMWNT/lung per mg/m3) ^c | | 80.52 ± 4.05 [10] | 90.33 ± 9.34 [10] | 97.19 ± 3.42 [10] | 92.27 ± 2.97 [10] | 70.35 ± 3.13 [10] | |

a: All values shown as mean ± standard error [number]

b: For sample weight, each dose was compared to the control with Williams' test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunnett's test was applied. [* = P<0.05, ** = P<0.01]

c: For endpoints other than sample weight, each dose was compared to the control with Shirley's test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunn's test was applied. [* = P<0.05, ** = P<0.01]

1020_L_MWNT Tissue Burden Analysis in Male HD Rats at 14 days

| Parameter ^a | 0 mg/m ³ | 0.1 mg/m ³ | 0.3 mg/m ³ | 1.0 mg/m ³ | 3.0 mg/m ³ | 10.0 mg/m ³ | Trend ^b |
|---|---------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------------------|--------------------|
| Sample Weight (g)^b | 1.675 ± 0.214 [5] | 1.807 ± 0.158 [5] | 1.825 ± 0.036 [5] | 1.752 ± 0.078 [5] | 2.106 ± 0.075 [5]* | 2.286 ± 0.139 [5]** | <.001 |
| Sample Conc (ug Ni/g) | 0.001 ± 0.000 [5] | 0.017 ± 0.001 [5]** | 0.052 ± 0.003 [5]** | 0.313 ± 0.019 [5]** | 0.721 ± 0.047 [5]** | 1.803 ± 0.082 [4]** | <.001 |
| Total Lung Burden (ug Ni/lung) | 0.002 ± 0.000 [5] | 0.030 ± 0.003 [5]** | 0.095 ± 0.005 [5]** | 0.543 ± 0.018 [5]** | 1.523 ± 0.129 [5]** | 3.868 ± 0.115 [4]** | <.001 |
| Total Lung Burden (ug L-MWNT-1020/lung) | 0.323 ± 0.096 [5] | 5.832 ± 0.641 [5]** | 18.24 ± 1.036 [5]** | 104.3 ± 3.377 [5]** | 292.9 ± 24.80 [5]** | 743.9 ± 22.07 [4]** | <.001 |
| Norm. Lung Burden (ug LMWNT/lung per mg/m³) | | 58.32 ± 6.41 [5] | 60.80 ± 3.45 [5] | 104.35 ± 3.38 [5] | 97.62 ± 8.27 [5] | 74.39 ± 2.21 [4] | |

a: All values shown as mean ± standard error [number]

b: For sample weight, each dose was compared to the control with Williams' test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunnett's test was applied. [* = P<0.05, ** = P<0.01]

c: For endpoints other than sample weight, each dose was compared to the control with Shirley's test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunn's test was applied. [* = P<0.05, ** = P<0.01]

1020_L_MWNT Tissue Burden Analysis in Male HD Rats at 42 days

| Parameter ^a | 0 mg/m3 | 0.1 mg/m3 | 0.3 mg/m3 | 1.0 mg/m3 | 3.0 mg/m3 | 10.0 mg/m3 | Trend ^b |
|--|-------------------|---------------------|---------------------|---------------------|---------------------|---------------------|--------------------|
| Sample Weight (g) ^b | 2.029 ± 0.180 [5] | 1.772 ± 0.101 [5] | 1.749 ± 0.076 [5] | 2.123 ± 0.135 [5] | 2.135 ± 0.147 [5] | 1.973 ± 0.112 [5] | 0.337 |
| Sample Conc (ug Ni/g) ^c | 0.001 ± 0.000 [5] | 0.012 ± 0.002 [5]** | 0.041 ± 0.004 [5]** | 0.204 ± 0.020 [5]** | 0.576 ± 0.060 [5]** | 1.657 ± 0.057 [5]** | <.001 |
| Total Lung Burden (ug Ni/lung) ^c | 0.002 ± 0.001 [5] | 0.020 ± 0.002 [5]** | 0.071 ± 0.006 [5]** | 0.430 ± 0.042 [5]** | 1.203 ± 0.092 [5]** | 3.258 ± 0.168 [5]** | <.001 |
| Total Lung Burden (ug L-MWNT-1020/lung) ^c | 0.444 ± 0.180 [5] | 3.858 ± 0.410 [5]** | 13.72 ± 1.248 [5]** | 82.64 ± 8.158 [5]** | 231.4 ± 17.66 [5]** | 626.5 ± 32.40 [5]** | <.001 |
| Norm. Lung Burden (ug LMWNT/lung per mg/m3) ^c | | 38.58 ± 4.10 [5] | 45.73 ± 4.16 [5] | 82.64 ± 8.16 [5] | 77.13 ± 5.89 [5] | 62.65 ± 3.24 [5] | |

a: All values shown as mean ± standard error [number]

b: For sample weight, each dose was compared to the control with Williams' test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunnett's test was applied. [* = P<0.05, ** = P<0.01]

c: For endpoints other than sample weight, each dose was compared to the control with Shirley's test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunn's test was applied. [* = P<0.05, ** = P<0.01]

1020_L_MWNT Tissue Burden Analysis in Male HD Rats at 126 days

| Parameter ^a | 0 mg/m ³ | 0.1 mg/m ³ | 0.3 mg/m ³ | 1.0 mg/m ³ | 3.0 mg/m ³ | 10.0 mg/m ³ | Trend ^b |
|---|---------------------|-----------------------|-----------------------|-----------------------|-----------------------|------------------------|--------------------|
| Sample Weight (g) ^b | 1.996 ± 0.178 [5] | 1.885 ± 0.056 [5] | 2.009 ± 0.199 [5] | 2.153 ± 0.208 [5] | 2.191 ± 0.258 [5] | 2.175 ± 0.068 [5] | 0.163 |
| Sample Conc (ug Ni/g) ^c | 0.001 ± 0.000 [5] | 0.005 ± 0.001 [5]** | 0.020 ± 0.005 [5]** | 0.097 ± 0.016 [5]** | 0.428 ± 0.062 [5]** | 1.426 ± 0.084 [5]** | <.001 |
| Total Lung Burden (ug Ni/lung) ^c | 0.001 ± 0.000 [5] | 0.010 ± 0.002 [5]** | 0.038 ± 0.006 [5]** | 0.201 ± 0.027 [5]** | 0.891 ± 0.091 [5]** | 3.095 ± 0.179 [5]** | <.001 |
| Total Lung Burden (ug L-MWNT-1020/lung) ^c | 0.269 ± 0.024 [5] | 1.907 ± 0.331 [5]** | 7.262 ± 1.074 [5]** | 38.74 ± 5.273 [5]** | 171.3 ± 17.49 [5]** | 595.3 ± 34.34 [5]** | <.001 |
| Norm. Lung Burden (ug LMWNT/lung per mg/m ³) ^c | | 19.07 ± 3.31 [5] | 24.21 ± 3.58 [5] | 38.74 ± 5.27 [5] | 57.09 ± 5.83 [5] | 59.53 ± 3.43 [5] | |

a: All values shown as mean ± standard error [number]

b: For sample weight, each dose was compared to the control with Williams' test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunnett's test was applied. [* = P<0.05, ** = P<0.01]

c: For endpoints other than sample weight, each dose was compared to the control with Shirley's test when a trend was present (P <0.01 from Jonckheere's trend test).

Otherwise, Dunn's test was applied. [* = P<0.05, ** = P<0.01]