ADME NTP Study K60344 Nickel sulfate hexahydrate

The contract laboratory abbreviation for the test article is NSHH. 
Sex/Species: adult male F344/N rats. 
Vehicles: intravenous, 0.9% saline; oral, 0.5 M H₂SO₄; inhalation, air.

CASRN 10101-97-0

Radiolabeled with ⁶³Ni as ⁶³NiCl₂ which was incorporated into the aerosols of nickel sulfate hexahydrate. 

Nickel sulfate hexahydrate Groups in Studies Performed:

- Subgroup A – Single 1-hour nose-only inhalation of 0.735, 1.96, or 11.7 ug/L NSHH with sacrifice immediately after exposure (respiratory tract deposition). (Tables 2 and 3; n= 3)

- Subgroup B – Single 1-hour nose-only inhalation of 0.735, 1.96, or 11.7 ug/L NSHH with sacrifice 10 to 13 days following exposure (excretion). (Tables 3 and 4; n= 3)

- Subgroup C – Single 1-hour nose-only inhalation of 0.735, 1.96, or 11.7 ug/L NSHH with serial sacrifice to up to 64 days following exposure (tissue distribution). (Tables 5-21; n= 3 per timepoint)

Separate groups of rats (n=3 per group) were administered NSHH (4 ug Ni/rat) by gavage or intravenous injection to determine the gastrointestinal absorption of nickel. The data was presented in figures and not shown here. The gastrointestinal absorption from the gavage and intravenous injection routes was approximately 1.7%.

The activity median aerodynamic diameter (AMAD) ranged from 2.1 to 2.7 um, with geometric standard deviations of 1.7 to 1.9 (Table 1).

Subgroup A rats were equipped with individual plethysmographic units during the 1-hour exposure to measure respiratory parameters during exposure. The concentration of the material in the atmosphere, the volume of air inspired during exposure and the amount of ⁶³Ni deposited and absorbed following inhalation were determined. Respiratory measurements were corrected for body temperature and pressure, saturated.

Subgroup B rats were sacrificed 10-13 days after the 1-hour inhalation exposures. Urine and feces were collected at approximately 4, 7, 10, 16, 24, 48, 72, and 96 hours after exposure and then daily until the daily urine sample had no more than 1% of the cumulative activity in the urine. The average data is presented in figures and not shown here. Cumulative individual animal data (total nmoles deposited) is shown in Table 4. After all three inhalation exposures, feces was the dominant route for excretion of


nickel, representing from 80-85% of the deposited nickel. Urinary excretion of nickel accounted for 12-18% of the dose.

Subgroup C rats were sacrificed at different times after the end of the inhalation exposure (n=3 per timepoint). Nickel deposition was determined for tissues associated with the respiratory tract (including the skull primarily to determine disposition associated with the bony structures of the upper respiratory tract; Tables 5-9), tissues associated with the gastrointestinal tract (Tables 10-14), and internal organs including blood (Tables 15-21).

Appendix tables referenced in footnotes are in the original report and not shown here except for table 4 which is a copy of the Appendix Table E-3d.

Toxicokinetics:

The data for the concentration of nickel in tissues taken at necropsy were fit to the single-component exponential function $F(t) = Ae^{-Bt}$ where $t$ is days after the end of exposure, $A$ is percentage of deposited nickel per gram tissues, and $B$ is the first order rate constant in 1/days. The associated half-time for clearance was calculated by using the following equation: $t_{1/2} = \ln 2/B$ where $B$ is the first order rate constant, as described above. The half-times of clearances from tissues are shown in Tables 22-24.

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Table 1

Summary of Nickel Sulfate Hexahydrate Exposure Atmosphere in $^{63}$Ni Toxicokinetic Studies

<table>
<thead>
<tr>
<th>Target Concentration (µg NiSO$_4$·6H$_2$O/L)</th>
<th>Actual Concentration$^a$ (µg NiSO$_4$·6H$_2$O/L)</th>
<th>AMAD$^b$ (µm)</th>
<th>Geometric Standard Deviation$^c$ (σ$_g$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.735</td>
<td>2.3</td>
<td>1.8</td>
</tr>
<tr>
<td>3</td>
<td>1.96</td>
<td>2.7</td>
<td>1.9</td>
</tr>
<tr>
<td>12</td>
<td>11.7</td>
<td>2.1</td>
<td>1.7</td>
</tr>
</tbody>
</table>

$^a$ Determined by radioanalysis of a 60-minute, continuous filter sample.

$^b$ Activity median aerodynamic diameter, determined from samples taken during exposure from 2 Mercer cascade impactors.

$^c$ Geometric standard deviation of aerosol determined from Mercer cascade impactor measurements taken during the exposure.
Table 2
Total and Regional Fractional Deposition of 63Ni After Exposure to Aerosols of Nickel Sulfate Hexahydrate

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exposure Concentration (µg NiSO$_4$·6H$_2$O/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni Inhaled$^b$ (nmols)</td>
<td></td>
<td>21.0 ± 3.3</td>
<td>77 ± 14</td>
<td>395 ± 15</td>
</tr>
<tr>
<td>Total Ni Deposited$^c$ (nmols)</td>
<td></td>
<td>25.1 ± 5.3</td>
<td>29.34 ± 0.88</td>
<td>258.8 ± 9.4</td>
</tr>
<tr>
<td>(% of inhaled)</td>
<td></td>
<td>118.6 ± 6.7</td>
<td>42 ± 10</td>
<td>65.8 ± 3.8</td>
</tr>
<tr>
<td>Upper Respiratory Tract Deposition$^d$ (nmols)</td>
<td></td>
<td>13.05 ± 0.35</td>
<td>20.56 ± 0.39</td>
<td>117.6 ± 4.7</td>
</tr>
<tr>
<td>(% of total deposited)</td>
<td></td>
<td>54 ± 10</td>
<td>70.2 ± 3.0</td>
<td>45.5 ± 1.2</td>
</tr>
<tr>
<td>Lower Respiratory Tract Deposition$^e$ (nmols)</td>
<td></td>
<td>12.1 ± 5.0</td>
<td>8.7 ± 1.1</td>
<td>141.1 ± 6.7</td>
</tr>
<tr>
<td>(% of total deposited)</td>
<td></td>
<td>46 ± 10</td>
<td>29.7 ± 3.1</td>
<td>54.5 ± 1.2</td>
</tr>
</tbody>
</table>

$^a$Data represent means ± SEM. Data for individual animals are in Appendix E, Tables E-1 and E-2.
$^b$Ni inhaled is the product of the aerosol concentration (in nmols/L) and the total volume inhaled (in liters).
$^c$Total nickel deposited is the sum of nickel detected in the tissues represented in Figure 4, excluding pelt (i.e., nasal turbinates and skull, trachea and larynx, GI tract plus contents, lungs and bronchi, and carcass).
$^d$Upper respiratory tract deposition includes nickel detected in the nasal turbinates and skull, trachea and larynx, and GI tract plus contents.
$^e$Lower respiratory tract deposition includes nickel detected in lungs and bronchi and depelted carcass.
Table 3

Comparison of Total nmoles of Nickel Deposited in Rats After Exposure to Nickel Sulfate Hexahydrate Aerosols\textsuperscript{a}

<table>
<thead>
<tr>
<th>Exposure Concentration (μg/L)</th>
<th>Subgroup A Respiratory Tract Deposition\textsuperscript{b}</th>
<th>Subgroup B Pathways for Excretion\textsuperscript{c}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.735</td>
<td>31.0 ± 3.9</td>
<td>31.6 ± 1.2</td>
</tr>
<tr>
<td>1.96</td>
<td>33.31 ± 0.58</td>
<td>37.0 ± 1.4</td>
</tr>
<tr>
<td>11.7</td>
<td>298 ± 13</td>
<td>236 ± 12</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean ± SEM.

\textsuperscript{b}Represents nickel detected in all tissues shown in Figure 4 including the pelt. Data for individual animals are in Appendix E, Tables E-3a, E-3b, and E-3c.

\textsuperscript{c}Represents nickel detected in all excreta samples and carcass, as shown in Figure 6. Data for individual animals are in Appendix E, Table E-3d (Table 4 below).
Table 4
Total nmoles deposited in rats after exposure to Nickel Sulfate Hexahydrate Aerosols
Subgroup B n=3

<table>
<thead>
<tr>
<th>Exp-Tissue</th>
<th>Animal No.</th>
<th>nmoles</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine 4776</td>
<td>8</td>
<td>4.321568</td>
<td>39.421007</td>
</tr>
<tr>
<td>Cagewash 4777</td>
<td>8</td>
<td>0.35584</td>
<td>39.421007</td>
</tr>
<tr>
<td>Feces 4777</td>
<td>8</td>
<td>33.520296</td>
<td></td>
</tr>
<tr>
<td>Pelt 4777</td>
<td>8</td>
<td>0.746949</td>
<td>39.421007</td>
</tr>
<tr>
<td>Carcass 4777</td>
<td>8</td>
<td>0.395928</td>
<td>39.421007</td>
</tr>
</tbody>
</table>

TOTAL 15 Rats x 3C

<table>
<thead>
<tr>
<th>Exp-Tissue</th>
<th>Animal No.</th>
<th>nmoles</th>
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<tr>
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<td>39.421007</td>
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<th>nmoles</th>
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</tr>
</thead>
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<tr>
<td>Feces 4777</td>
<td>8</td>
<td>33.520296</td>
<td></td>
</tr>
<tr>
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<td>8</td>
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</tr>
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</table>

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<tr>
<td>Feces 4777</td>
<td>8</td>
<td>33.520296</td>
<td></td>
</tr>
<tr>
<td>Pelt 4777</td>
<td>8</td>
<td>0.746949</td>
<td>39.421007</td>
</tr>
<tr>
<td>Carcass 4777</td>
<td>8</td>
<td>0.395928</td>
<td>39.421007</td>
</tr>
</tbody>
</table>

TOTAL 15 Rats x 3C
Table 5
Mean Percentage of Deposited Nickel Located in the Nasal Turbinates

<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>Exposure Concentration (μg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td></td>
<td>3.26 ± 0.26</td>
<td>0.56 ± 0.22</td>
<td>4.36 ± 1.4</td>
</tr>
<tr>
<td>0.19</td>
<td></td>
<td>2.56 ± 0.84</td>
<td>2.09 ± 0.50</td>
<td>6.8 ± 3.5</td>
</tr>
<tr>
<td>0.35</td>
<td></td>
<td>3.5 ± 1.1</td>
<td>1.25 ± 0.54</td>
<td>2.18 ± 0.79</td>
</tr>
<tr>
<td>1.01</td>
<td></td>
<td>2.08 ± 0.48</td>
<td>1.07 ± 0.31</td>
<td>1.6 ± 0.41</td>
</tr>
<tr>
<td>2.01</td>
<td></td>
<td>1.13 ± 0.24</td>
<td>0.87 ± 0.36</td>
<td>0.84 ± 0.36</td>
</tr>
<tr>
<td>4.67</td>
<td></td>
<td>0.52 ± 0.16</td>
<td>0.349 ± 0.083</td>
<td>0.511 ± 0.071</td>
</tr>
<tr>
<td>8.00</td>
<td></td>
<td>0.344 ± 0.045</td>
<td>0.177 ± 0.042</td>
<td>0.43 ± 0.11</td>
</tr>
<tr>
<td>13.00</td>
<td></td>
<td>0.129 ± 0.013</td>
<td>0.153 ± 0.026</td>
<td>0.121 ± 0.055</td>
</tr>
<tr>
<td>16.00</td>
<td></td>
<td>0.19 ± 0.11</td>
<td>0.042 ± 0.012</td>
<td>0.136 ± 0.036</td>
</tr>
<tr>
<td>24.00</td>
<td></td>
<td>0.016 ± 0.016</td>
<td>0.072 ± 0.010</td>
<td>0.057 ± 0.023</td>
</tr>
<tr>
<td>31.00</td>
<td></td>
<td>0.0227 ± 0.0035</td>
<td>0.0158 ± 0.0014</td>
<td>0.061 ± 0.025</td>
</tr>
<tr>
<td>64.00</td>
<td></td>
<td>0.051 ± 0.020</td>
<td>0.0120 ± 0.0015</td>
<td>0.0250 ± 0.0045</td>
</tr>
</tbody>
</table>

aData represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-4.

bSacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 6

Mean Percentage of Deposited Nickel Located in the Skull\textsuperscript{a}
(not including brain)

<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>Exposure Concentration (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
</tr>
<tr>
<td>0.07</td>
<td>0.12051 ± 0.00048</td>
</tr>
<tr>
<td>0.19</td>
<td>0.0701 ± 0.0048</td>
</tr>
<tr>
<td>0.35</td>
<td>0.097 ± 0.021</td>
</tr>
<tr>
<td>1.01</td>
<td>0.0596 ± 0.0080</td>
</tr>
<tr>
<td>2.01</td>
<td>0.0267 ± 0.0047</td>
</tr>
<tr>
<td>4.67</td>
<td>0.0094 ± 0.0030</td>
</tr>
<tr>
<td>8.00</td>
<td>0.00794 ± 0.00080</td>
</tr>
<tr>
<td>13.00</td>
<td>0.00276 ± 0.00059</td>
</tr>
<tr>
<td>16.00</td>
<td>0.00222 ± 0.00025</td>
</tr>
<tr>
<td>24.00</td>
<td>0.00059 ± 0.00045</td>
</tr>
<tr>
<td>31.00</td>
<td>0.00113 ± 0.00013</td>
</tr>
<tr>
<td>64.00</td>
<td>0.00270 ± 0.00069</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-5.

\textsuperscript{b}Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 7

Mean Percentage of Deposited Nickel Located in the Trachea and Larynx\textsuperscript{a}

<table>
<thead>
<tr>
<th>Days After End of Exposure \textsuperscript{b}</th>
<th>Exposure Concentration (\textmu g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
</tr>
<tr>
<td>0.07</td>
<td>4.3 ± 1.6</td>
</tr>
<tr>
<td>0.19</td>
<td>3.25 ± 0.38</td>
</tr>
<tr>
<td>0.35</td>
<td>2.92 ± 0.64</td>
</tr>
<tr>
<td>1.01</td>
<td>1.127 ± 0.012</td>
</tr>
<tr>
<td>2.01</td>
<td>0.54 ± 0.16</td>
</tr>
<tr>
<td>4.67</td>
<td>0.236 ± 0.028</td>
</tr>
<tr>
<td>8.00</td>
<td>0.1309 ± 0.0039</td>
</tr>
<tr>
<td>13.00</td>
<td>0.048 ± 0.012</td>
</tr>
<tr>
<td>16.00</td>
<td>0.0371 ± 0.0017</td>
</tr>
<tr>
<td>24.00</td>
<td>0.0259 ± 0.0018</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0227 ± 0.0026</td>
</tr>
<tr>
<td>64.00</td>
<td>0.0305 ± 0.0091</td>
</tr>
<tr>
<td></td>
<td>1.96</td>
</tr>
<tr>
<td>0.07</td>
<td>1.57 ± 0.65</td>
</tr>
<tr>
<td>0.19</td>
<td>1.261 ± 0.072</td>
</tr>
<tr>
<td>0.35</td>
<td>1.66 ± 0.46</td>
</tr>
<tr>
<td>1.01</td>
<td>1.18 ± 0.66</td>
</tr>
<tr>
<td>2.01</td>
<td>0.46 ± 0.12</td>
</tr>
<tr>
<td>4.67</td>
<td>0.1383 ± 0.0054</td>
</tr>
<tr>
<td>8.00</td>
<td>0.0752 ± 0.0038</td>
</tr>
<tr>
<td>13.00</td>
<td>0.112 ± 0.011</td>
</tr>
<tr>
<td>16.00</td>
<td>0.0239 ± 0.0016</td>
</tr>
<tr>
<td>24.00</td>
<td>0.0510 ± 0.0054</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0194 ± 0.0045</td>
</tr>
<tr>
<td>64.00</td>
<td>0.01231 ± 0.00027</td>
</tr>
<tr>
<td></td>
<td>11.7</td>
</tr>
<tr>
<td>0.07</td>
<td>8.07 ± 1.4</td>
</tr>
<tr>
<td>0.19</td>
<td>3.82 ± 0.56</td>
</tr>
<tr>
<td>0.35</td>
<td>2.51 ± 0.63</td>
</tr>
<tr>
<td>1.01</td>
<td>2.25 ± 0.47</td>
</tr>
<tr>
<td>2.01</td>
<td>0.46 ± 0.23</td>
</tr>
<tr>
<td>4.67</td>
<td>0.156 ± 0.013</td>
</tr>
<tr>
<td>8.00</td>
<td>0.123 ± 0.034</td>
</tr>
<tr>
<td>13.00</td>
<td>0.038 ± 0.014</td>
</tr>
<tr>
<td>16.00</td>
<td>0.062 ± 0.020</td>
</tr>
<tr>
<td>24.00</td>
<td>1.1 ± 1.1</td>
</tr>
<tr>
<td>31.00</td>
<td>0.022 ± 0.011</td>
</tr>
<tr>
<td>64.00</td>
<td>0.0240 ± 0.0043</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean percent/gram tissue \pm SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-6.

\textsuperscript{b}Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>Exposure Concentration (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
</tr>
<tr>
<td>0.07</td>
<td>8.9 ± 1.5</td>
</tr>
<tr>
<td>0.19</td>
<td>8.52 ± 0.37</td>
</tr>
<tr>
<td>0.35</td>
<td>5.44 ± 0.17</td>
</tr>
<tr>
<td>1.01</td>
<td>3.81 ± 0.94</td>
</tr>
<tr>
<td>2.01</td>
<td>1.503 ± 0.062</td>
</tr>
<tr>
<td>4.67</td>
<td>0.851 ± 0.082</td>
</tr>
<tr>
<td>8.00</td>
<td>0.345 ± 0.010</td>
</tr>
<tr>
<td>13.00</td>
<td>0.133 ± 0.018</td>
</tr>
<tr>
<td>16.00</td>
<td>0.082 ± 0.014</td>
</tr>
<tr>
<td>24.00</td>
<td>0.0222 ± 0.0031</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0300 ± 0.0074</td>
</tr>
<tr>
<td>64.00</td>
<td>0.0370 ± 0.0041</td>
</tr>
</tbody>
</table>

aData represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-7.

bSacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 9
Mean Percentage of Deposited Nickel Located in the Lung-Associated Lymph Nodes<sup>a</sup>

<table>
<thead>
<tr>
<th>Days After End of Exposure&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Exposure Concentration (µg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7-</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>0.30 ± 0.15</td>
<td>-0.040 ± 0.004</td>
<td>0.079 ± 0.048</td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>0.146 ± 0.075</td>
<td>0.070 ± 0.070</td>
<td>0.101 ± 0.092</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>0.153 ± 0.085</td>
<td>0.138 ± 0.073</td>
<td>0.037 ± 0.010</td>
<td></td>
</tr>
<tr>
<td>1.01</td>
<td>0.065 ± 0.023</td>
<td>0.081 ± 0.088</td>
<td>0.110 ± 0.088</td>
<td></td>
</tr>
<tr>
<td>2.01</td>
<td>0.069 ± 0.025</td>
<td>0.155 ± 0.061</td>
<td>0.039 ± 0.059</td>
<td></td>
</tr>
<tr>
<td>4.67</td>
<td>0.037 ± 0.032</td>
<td>0.075 ± 0.027</td>
<td>0.130 ± 0.044</td>
<td></td>
</tr>
<tr>
<td>8.00</td>
<td>-0.0113 ± 0.0072</td>
<td>0.067 ± 0.037</td>
<td>0.37 ± 0.12</td>
<td></td>
</tr>
<tr>
<td>13.00</td>
<td>-0.053 ± 0.014</td>
<td>0.167 ± 0.026</td>
<td>0.41 ± 0.29</td>
<td></td>
</tr>
<tr>
<td>16.00</td>
<td>0.057 ± 0.048</td>
<td>-0.023 ± 0.030</td>
<td>1.17 ± 0.92</td>
<td></td>
</tr>
<tr>
<td>24.00</td>
<td>-0.059 ± 0.014</td>
<td>0.137 ± 0.052</td>
<td>0.215 ± 0.070</td>
<td></td>
</tr>
<tr>
<td>31.00</td>
<td>0.30 ± 0.12</td>
<td>0.065 ± 0.015</td>
<td>0.051 ± 0.042</td>
<td></td>
</tr>
<tr>
<td>64.00</td>
<td>0.098 ± 0.052</td>
<td>0.167 ± 0.039</td>
<td>0.0256 ± 0.0085</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-8.

<sup>b</sup>Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 10
Mean Percentage of Deposited Nickel Located in the Esophagus\textsuperscript{a}

<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>Exposure Concentration (µg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.07</td>
<td></td>
<td>1.30 ± 0.29</td>
<td>0.89 ± 0.50</td>
<td>1.78 ± 0.87</td>
</tr>
<tr>
<td>0.19</td>
<td></td>
<td>0.412 ± 0.067</td>
<td>0.436 ± 0.044</td>
<td>0.67 ± 0.12</td>
</tr>
<tr>
<td>0.35</td>
<td></td>
<td>0.450 ± 0.074</td>
<td>0.297 ± 0.058</td>
<td>0.25 ± 0.10</td>
</tr>
<tr>
<td>1.01</td>
<td></td>
<td>0.0234 ± 0.0031</td>
<td>0.036 ± 0.011</td>
<td>0.122 ± 0.090</td>
</tr>
<tr>
<td>2.01</td>
<td></td>
<td>0.0163 ± 0.0025</td>
<td>0.0184 ± 0.0056</td>
<td>0.0081 ± 0.0018</td>
</tr>
<tr>
<td>4.67</td>
<td></td>
<td>0.00379 ± 0.00091</td>
<td>0.00588 ± 0.00049</td>
<td>0.0204 ± 0.0060</td>
</tr>
<tr>
<td>8.00</td>
<td></td>
<td>0.0040 ± 0.0020</td>
<td>0.0075 ± 0.0024</td>
<td>0.19 ± 0.10</td>
</tr>
<tr>
<td>13.00</td>
<td></td>
<td>0.0043 ± 0.0043</td>
<td>0.0271 ± 0.0035</td>
<td>0.0226 ± 0.0037</td>
</tr>
<tr>
<td>16.00</td>
<td></td>
<td>0.0075 ± 0.0030</td>
<td>0.0040 ± 0.0023</td>
<td>0.039 ± 0.012</td>
</tr>
<tr>
<td>24.00</td>
<td></td>
<td>0.0009 ± 0.0026</td>
<td>0.0201 ± 0.0021</td>
<td>0.0130 ± 0.0071</td>
</tr>
<tr>
<td>31.00</td>
<td></td>
<td>0.0150 ± 0.0036</td>
<td>0.0075 ± 0.0018</td>
<td>0.0077 ± 0.0048</td>
</tr>
<tr>
<td>64.00</td>
<td></td>
<td>0.0163 ± 0.0066</td>
<td>0.0176 ± 0.0029</td>
<td>0.0071 ± 0.0024</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (originally, Table 3 here) (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-9. 

\textsuperscript{b}Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
### Table 11

Mean Percentage of Deposited Nickel Located in the Stomach
(without contents)

<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>0.735 (µg/L)</th>
<th>1.96 (µg/L)</th>
<th>11.7 (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>0.1060 ± 0.0088</td>
<td>0.0158 ± 0.0079</td>
<td>0.0471 ± 0.0094</td>
</tr>
<tr>
<td>0.19</td>
<td>0.040 ± 0.012</td>
<td>0.042 ± 0.034</td>
<td>0.0343 ± 0.0046</td>
</tr>
<tr>
<td>0.35</td>
<td>0.0258 ± 0.0044</td>
<td>0.0214 ± 0.0048</td>
<td>0.029 ± 0.011</td>
</tr>
<tr>
<td>1.01</td>
<td>0.0091 ± 0.0028</td>
<td>0.0043 ± 0.0044</td>
<td>0.039 ± 0.022</td>
</tr>
<tr>
<td>2.01</td>
<td>0.0064 ± 0.0027</td>
<td>0.0179 ± 0.0036</td>
<td>0.032 ± 0.028</td>
</tr>
<tr>
<td>4.67</td>
<td>0.0115 ± 0.0073</td>
<td>0.0090 ± 0.0011</td>
<td>0.032 ± 0.017</td>
</tr>
<tr>
<td>8.00</td>
<td>0.00189 ± 0.00070</td>
<td>0.00433 ± 0.00027</td>
<td>0.041 ± 0.027</td>
</tr>
<tr>
<td>13.00</td>
<td>-0.0005 ± 0.0013</td>
<td>0.0264 ± 0.0042</td>
<td>0.041 ± 0.034</td>
</tr>
<tr>
<td>16.00</td>
<td>0.00206 ± 0.00092</td>
<td>0.0023 ± 0.0036</td>
<td>0.028 ± 0.012</td>
</tr>
<tr>
<td>24.00</td>
<td>-0.00303 ± 0.00044</td>
<td>0.0273 ± 0.0024</td>
<td>0.0073 ± 0.0017</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0199 ± 0.0036</td>
<td>0.0123 ± 0.0037</td>
<td>0.0090 ± 0.0062</td>
</tr>
<tr>
<td>64.00</td>
<td>0.0124 ± 0.0033</td>
<td>0.0165 ± 0.0034</td>
<td>0.00578 ± 0.00085</td>
</tr>
</tbody>
</table>

aData represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-10.

bSacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 12

Mean Percentage of Deposited Nickel Located in the Small Intestine\textsuperscript{a} (without contents)

<table>
<thead>
<tr>
<th>Days After End of Exposure\textsuperscript{b}</th>
<th>Exposure Concentration (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
</tr>
<tr>
<td>0.07</td>
<td>0.010 ± 0.033</td>
</tr>
<tr>
<td>0.19</td>
<td>0.0398 ± 0.0079</td>
</tr>
<tr>
<td>0.35</td>
<td>0.0176 ± 0.0040</td>
</tr>
<tr>
<td>1.01</td>
<td>0.0083 ± 0.0024</td>
</tr>
<tr>
<td>2.01</td>
<td>0.0049 ± 0.0029</td>
</tr>
<tr>
<td>4.67</td>
<td>0.0039 ± 0.0027</td>
</tr>
<tr>
<td>8.00</td>
<td>0.0019 ± 0.0022</td>
</tr>
<tr>
<td>13.00</td>
<td>-0.0017 ± 0.0018</td>
</tr>
<tr>
<td>16.00</td>
<td>0.0041 ± 0.0012</td>
</tr>
<tr>
<td>24.00</td>
<td>-0.00329 ± 0.00089</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0201 ± 0.0034</td>
</tr>
<tr>
<td>64.00</td>
<td>0.0168 ± 0.0028</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-11.

\textsuperscript{b}Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 13

Mean Percentage of Deposited Nickel Located in the Large Intestinea
(without contents)

<table>
<thead>
<tr>
<th>Days After End of Exposure b</th>
<th>Exposure Concentration (μg/L)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
<td>1.96</td>
<td>11.7</td>
</tr>
<tr>
<td>0.07</td>
<td>0.0370 ± 0.0019</td>
<td>0.0094 ± 0.0020</td>
<td>0.0266 ± 0.0046</td>
</tr>
<tr>
<td>0.19</td>
<td>1.12 ± 0.58</td>
<td>0.18 ± 0.17</td>
<td>0.29 ± 0.20</td>
</tr>
<tr>
<td>0.35</td>
<td>0.333 ± 0.064</td>
<td>0.065 ± 0.031</td>
<td>0.57 ± 0.16</td>
</tr>
<tr>
<td>1.01</td>
<td>0.150 ± 0.045</td>
<td>0.131 ± 0.044</td>
<td>0.175 ± 0.083</td>
</tr>
<tr>
<td>2.01</td>
<td>0.040 ± 0.026</td>
<td>0.0380 ± 0.0033</td>
<td>0.01839 ± 0.00044</td>
</tr>
<tr>
<td>4.67</td>
<td>0.0057 ± 0.0022</td>
<td>0.0174 ± 0.0014</td>
<td>0.022 ± 0.015</td>
</tr>
<tr>
<td>8.00</td>
<td>0.0035 ± 0.0021</td>
<td>0.0061 ± 0.0011</td>
<td>0.123 ± 0.046</td>
</tr>
<tr>
<td>13.00</td>
<td>0.0025 ± 0.0047</td>
<td>0.0251 ± 0.0021</td>
<td>0.0206 ± 0.0083</td>
</tr>
<tr>
<td>16.00</td>
<td>0.024 ± 0.021</td>
<td>0.0016 ± 0.0032</td>
<td>0.059 ± 0.030</td>
</tr>
<tr>
<td>24.00</td>
<td>-0.0029 ± 0.0017</td>
<td>0.0232 ± 0.0096</td>
<td>0.0162 ± 0.0033</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0193 ± 0.0093</td>
<td>0.0101 ± 0.0034</td>
<td>0.0116 ± 0.0073</td>
</tr>
<tr>
<td>64.00</td>
<td>0.0124 ± 0.0018</td>
<td>0.0171 ± 0.0047</td>
<td>0.0051 ± 0.0010</td>
</tr>
</tbody>
</table>

aData represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-12.

bSacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 14
Mean Percentage of Deposited Nickel Located in the Liver\(^a\)

<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>Exposure Concentration (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
</tr>
<tr>
<td>0.07</td>
<td>0.101 ± 0.038</td>
</tr>
<tr>
<td>0.19</td>
<td>2.040 ± 2.021</td>
</tr>
<tr>
<td>0.35</td>
<td>0.0278 ± 0.0074</td>
</tr>
<tr>
<td>1.01</td>
<td>0.030 ± 0.011</td>
</tr>
<tr>
<td>2.01</td>
<td>0.0184 ± 0.0014</td>
</tr>
<tr>
<td>4.67</td>
<td>0.0237 ± 0.0074</td>
</tr>
<tr>
<td>8.00</td>
<td>0.0093 ± 0.0019</td>
</tr>
<tr>
<td>13.00</td>
<td>0.00211 ± 0.00075</td>
</tr>
<tr>
<td>16.00</td>
<td>0.0048 ± 0.0011</td>
</tr>
<tr>
<td>24.00</td>
<td>0.0023 ± 0.0010</td>
</tr>
<tr>
<td>31.00</td>
<td>0.033 ± 0.017</td>
</tr>
<tr>
<td>64.00</td>
<td>0.047 ± 0.011</td>
</tr>
</tbody>
</table>

\(^a\)Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-13.

\(^b\)Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
<table>
<thead>
<tr>
<th>Days After End of Exposure&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Exposure Concentration (μg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>1.42 ± 0.96</td>
<td>0.037 ± 0.019</td>
<td>0.0437 ± 0.0026</td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>0.28 ± 0.12</td>
<td>0.018 ± 0.013</td>
<td>0.0374 ± 0.0067</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>0.41 ± 0.33</td>
<td>0.027 ± 0.010</td>
<td>0.049 ± 0.018</td>
<td></td>
</tr>
<tr>
<td>1.01</td>
<td>0.19 ± 0.12</td>
<td>0.0219 ± 0.0044</td>
<td>0.0253 ± 0.0046</td>
<td></td>
</tr>
<tr>
<td>2.01</td>
<td>0.124 ± 0.030</td>
<td>0.0316 ± 0.0035</td>
<td>0.0090 ± 0.0028</td>
<td></td>
</tr>
<tr>
<td>4.67</td>
<td>0.133 ± 0.059</td>
<td>0.0177 ± 0.0012</td>
<td>0.0242 ± 0.0043</td>
<td></td>
</tr>
<tr>
<td>8.00</td>
<td>0.0806 ± 0.0065</td>
<td>0.0265 ± 0.0036</td>
<td>0.055 ± 0.027</td>
<td></td>
</tr>
<tr>
<td>13.00</td>
<td>0.025 ± 0.014</td>
<td>0.055 ± 0.010</td>
<td>0.052 ± 0.029</td>
<td></td>
</tr>
<tr>
<td>16.00</td>
<td>0.0376 ± 0.0046</td>
<td>0.0127 ± 0.0040</td>
<td>0.044 ± 0.017</td>
<td></td>
</tr>
<tr>
<td>24.00</td>
<td>0.0064 ± 0.0018</td>
<td>0.0294 ± 0.0075</td>
<td>0.043 ± 0.015</td>
<td></td>
</tr>
<tr>
<td>31.00</td>
<td>0.0240 ± 0.0018</td>
<td>0.026 ± 0.012</td>
<td>0.107 ± 0.056</td>
<td></td>
</tr>
<tr>
<td>64.00</td>
<td>0.0116 ± 0.0014</td>
<td>0.0216 ± 0.0030</td>
<td>0.0438 ± 0.0076</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (originally, Table 3 here) (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-14.

<sup>b</sup>Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 16

Mean Percentage of Deposited Nickel Located in the Adrenal Glands<sup>a</sup>

<table>
<thead>
<tr>
<th>Days After End of Exposure&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Exposure Concentration (µg/L)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
<td>1.96</td>
<td>11.7</td>
<td></td>
</tr>
<tr>
<td>0.07</td>
<td>0.0702 ± 0.0075</td>
<td>0.0068 ± 0.0034</td>
<td>0.061 ± 0.042</td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>0.0302 ± 0.0084</td>
<td>0.0152 ± 0.0077</td>
<td>0.030 ± 0.012</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>0.021 ± 0.012</td>
<td>0.022 ± 0.012</td>
<td>0.0134 ± 0.0024</td>
<td></td>
</tr>
<tr>
<td>1.01</td>
<td>0.0314 ± 0.0038</td>
<td>0.0078 ± 0.0086</td>
<td>0.056 ± 0.044</td>
<td></td>
</tr>
<tr>
<td>2.01</td>
<td>0.0158 ± 0.0055</td>
<td>0.0433 ± 0.0063</td>
<td>0.058 ± 0.050</td>
<td></td>
</tr>
<tr>
<td>4.67</td>
<td>0.0059 ± 0.0017</td>
<td>0.0196 ± 0.0079</td>
<td>0.0453 ± 0.0052</td>
<td></td>
</tr>
<tr>
<td>8.00</td>
<td>0.0099 ± 0.0032</td>
<td>0.0070 ± 0.0022</td>
<td>0.118 ± 0.061</td>
<td></td>
</tr>
<tr>
<td>13.00</td>
<td>0.0088 ± 0.0060</td>
<td>0.0415 ± 0.0052</td>
<td>0.081 ± 0.069</td>
<td></td>
</tr>
<tr>
<td>16.00</td>
<td>0.0098 ± 0.0047</td>
<td>0.0039 ± 0.0027</td>
<td>0.175 ± 0.083</td>
<td></td>
</tr>
<tr>
<td>24.00</td>
<td>-0.0065 ± 0.0036</td>
<td>0.026 ± 0.011</td>
<td>0.0133 ± 0.0014</td>
<td></td>
</tr>
<tr>
<td>31.00</td>
<td>0.0205 ± 0.0048</td>
<td>0.0071 ± 0.0023</td>
<td>0.032 ± 0.022</td>
<td></td>
</tr>
<tr>
<td>64.00</td>
<td>0.048 ± 0.016</td>
<td>0.0155 ± 0.0073</td>
<td>0.0157 ± 0.0020</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (originally, Table 3 here) (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-15.

<sup>b</sup>Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 17
Mean Percentage of Deposited Nickel Located in the Thyroid Glands

<table>
<thead>
<tr>
<th>Days After End of Exposure b</th>
<th>Exposure Concentration (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
</tr>
<tr>
<td>0.07</td>
<td>0.33 ± 0.19</td>
</tr>
<tr>
<td></td>
<td>0.003 ± 0.011</td>
</tr>
<tr>
<td></td>
<td>0.51 ± 0.34</td>
</tr>
<tr>
<td>0.19</td>
<td>0.116 ± 0.069</td>
</tr>
<tr>
<td></td>
<td>0.020 ± 0.020</td>
</tr>
<tr>
<td></td>
<td>0.046 ± 0.016</td>
</tr>
<tr>
<td>0.35</td>
<td>0.063 ± 0.024</td>
</tr>
<tr>
<td></td>
<td>0.088 ± 0.044</td>
</tr>
<tr>
<td></td>
<td>0.16 ± 0.14</td>
</tr>
<tr>
<td>1.01</td>
<td>0.135 ± 0.053</td>
</tr>
<tr>
<td></td>
<td>0.045 ± 0.040</td>
</tr>
<tr>
<td></td>
<td>0.049 ± 0.027</td>
</tr>
<tr>
<td>2.01</td>
<td>0.036 ± 0.034</td>
</tr>
<tr>
<td></td>
<td>0.0263 ± 0.0079</td>
</tr>
<tr>
<td></td>
<td>0.0027 ± 0.0095</td>
</tr>
<tr>
<td>4.67</td>
<td>0.0101 ± 0.0023</td>
</tr>
<tr>
<td></td>
<td>0.0435 ± 0.0038</td>
</tr>
<tr>
<td></td>
<td>0.098 ± 0.052</td>
</tr>
<tr>
<td>8.00</td>
<td>0.0112 ± 0.0067</td>
</tr>
<tr>
<td></td>
<td>0.0329 ± 0.0031</td>
</tr>
<tr>
<td></td>
<td>0.94 ± 0.67</td>
</tr>
<tr>
<td>13.00</td>
<td>-0.008 ± 0.012</td>
</tr>
<tr>
<td></td>
<td>0.137 ± 0.028</td>
</tr>
<tr>
<td></td>
<td>0.96 ± 0.20</td>
</tr>
<tr>
<td>16.00</td>
<td>0.024 ± 0.017</td>
</tr>
<tr>
<td></td>
<td>-0.010 ± 0.014</td>
</tr>
<tr>
<td></td>
<td>0.120 ± 0.040</td>
</tr>
<tr>
<td>24.00</td>
<td>-0.0263 ± 0.0020</td>
</tr>
<tr>
<td></td>
<td>0.0764 ± 0.0042</td>
</tr>
<tr>
<td></td>
<td>0.076 ± 0.050</td>
</tr>
<tr>
<td>31.00</td>
<td>0.0724 ± 0.0099</td>
</tr>
<tr>
<td></td>
<td>0.095 ± 0.022</td>
</tr>
<tr>
<td></td>
<td>0.066 ± 0.042</td>
</tr>
<tr>
<td>64.00</td>
<td>0.045 ± 0.018</td>
</tr>
<tr>
<td></td>
<td>0.118 ± 0.068</td>
</tr>
<tr>
<td></td>
<td>0.0311 ± 0.0031</td>
</tr>
</tbody>
</table>

aData represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-16.

bSacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 18
Mean Percentage of Deposited Nickel Located in the Testes\textsuperscript{a}

<table>
<thead>
<tr>
<th>Days After End of Exposure</th>
<th>Exposure Concentration (\textmu g/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>0.01982 ± 0.00056</td>
<td>-0.0022 ± 0.0015</td>
<td>0.0159 ± 0.0021</td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>0.035 ± 0.016</td>
<td>0.0076 ± 0.0044</td>
<td>0.019 ± 0.010</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>0.0190 ± 0.0069</td>
<td>0.0101 ± 0.0050</td>
<td>0.0134 ± 0.0045</td>
<td></td>
</tr>
<tr>
<td>1.01</td>
<td>0.0127 ± 0.0035</td>
<td>0.0018 ± 0.0028</td>
<td>0.036 ± 0.027</td>
<td></td>
</tr>
<tr>
<td>2.01</td>
<td>0.022 ± 0.018</td>
<td>0.0200 ± 0.0017</td>
<td>0.0006 ± 0.0010</td>
<td></td>
</tr>
<tr>
<td>4.67</td>
<td>0.00077 ± 0.00044</td>
<td>0.00783 ± 0.00072</td>
<td>0.026 ± 0.012</td>
<td></td>
</tr>
<tr>
<td>8.00</td>
<td>-0.00079 ± 0.00021</td>
<td>0.0061 ± 0.0013</td>
<td>0.0183 ± 0.0079</td>
<td></td>
</tr>
<tr>
<td>13.00</td>
<td>-0.0016 ± 0.0021</td>
<td>0.0238 ± 0.0040</td>
<td>0.145 ± 0.060</td>
<td></td>
</tr>
<tr>
<td>16.00</td>
<td>0.00205 ± 0.00032</td>
<td>-0.0012 ± 0.0029</td>
<td>0.079 ± 0.029</td>
<td></td>
</tr>
<tr>
<td>24.00</td>
<td>-0.0046 ± 0.0017</td>
<td>0.0264 ± 0.0080</td>
<td>0.0105 ± 0.0046</td>
<td></td>
</tr>
<tr>
<td>31.00</td>
<td>0.0167 ± 0.0012</td>
<td>0.01003 ± 0.00063</td>
<td>0.0055 ± 0.0047</td>
<td></td>
</tr>
<tr>
<td>64.00</td>
<td>0.0155 ± 0.0018</td>
<td>0.0168 ± 0.0018</td>
<td>0.0046 ± 0.0014</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-17.

\textsuperscript{b}Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 19

Mean Percentage of Deposited Nickel Located in the Kidneys<sup>a</sup>

<table>
<thead>
<tr>
<th>Days After End of Exposure&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Exposure Concentration (μg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td></td>
<td>0.299 ± 0.021</td>
<td>0.037 ± 0.013</td>
<td>0.102 ± 0.029</td>
</tr>
<tr>
<td>0.19</td>
<td></td>
<td>0.158 ± 0.038</td>
<td>0.121 ± 0.030</td>
<td>0.174 ± 0.058</td>
</tr>
<tr>
<td>0.35</td>
<td></td>
<td>0.281 ± 0.034</td>
<td>0.107 ± 0.018</td>
<td>0.118 ± 0.033</td>
</tr>
<tr>
<td>1.01</td>
<td></td>
<td>0.122 ± 0.037</td>
<td>0.059 ± 0.014</td>
<td>0.081 ± 0.016</td>
</tr>
<tr>
<td>2.01</td>
<td></td>
<td>0.151 ± 0.098</td>
<td>0.060 ± 0.010</td>
<td>0.097 ± 0.019</td>
</tr>
<tr>
<td>4.67</td>
<td></td>
<td>0.0435 ± 0.0061</td>
<td>0.0404 ± 0.0070</td>
<td>0.0579 ± 0.0052</td>
</tr>
<tr>
<td>8.00</td>
<td></td>
<td>0.0372 ± 0.0044</td>
<td>0.0209 ± 0.0010</td>
<td>0.117 ± 0.038</td>
</tr>
<tr>
<td>13.00</td>
<td></td>
<td>0.027 ± 0.014</td>
<td>0.072 ± 0.021</td>
<td>0.046 ± 0.019</td>
</tr>
<tr>
<td>16.00</td>
<td></td>
<td>0.035 ± 0.026</td>
<td>0.0322 ± 0.0048</td>
<td>0.0287 ± 0.0059</td>
</tr>
<tr>
<td>24.00</td>
<td></td>
<td>0.0068 ± 0.0032</td>
<td>0.055 ± 0.012</td>
<td>0.028 ± 0.012</td>
</tr>
<tr>
<td>31.00</td>
<td></td>
<td>0.0325 ± 0.0016</td>
<td>0.0167 ± 0.0017</td>
<td>0.054 ± 0.019</td>
</tr>
<tr>
<td>64.00</td>
<td></td>
<td>0.047 ± 0.013</td>
<td>0.0255 ± 0.0029</td>
<td>0.01026 ± 0.00066</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-18.

<sup>b</sup>Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 20

Mean Percentage of Deposited Nickel Located in the Urinary Bladder\(^a\) (without contents)

<table>
<thead>
<tr>
<th>Days After End of Exposure(^b)</th>
<th>Exposure Concentration (μg/L)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.735</td>
<td>1.96</td>
<td>11.7</td>
<td></td>
</tr>
<tr>
<td>0.07</td>
<td>0.22 ± 0.12</td>
<td>0.0065 ± 0.0030</td>
<td>0.112 ± 0.042</td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>0.0824 ± 0.0082</td>
<td>0.0307 ± 0.0044</td>
<td>0.078 ± 0.024</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>0.062 ± 0.017</td>
<td>0.087 ± 0.047</td>
<td>0.063 ± 0.031</td>
<td></td>
</tr>
<tr>
<td>1.01</td>
<td>0.0333 ± 0.0059</td>
<td>0.0081 ± 0.0071</td>
<td>0.096 ± 0.067</td>
<td></td>
</tr>
<tr>
<td>2.01</td>
<td>0.0067 ± 0.0036</td>
<td>0.0201 ± 0.0083</td>
<td>0.0057 ± 0.0034</td>
<td></td>
</tr>
<tr>
<td>4.67</td>
<td>0.0047 ± 0.0045</td>
<td>0.0133 ± 0.0059</td>
<td>0.047 ± 0.024</td>
<td></td>
</tr>
<tr>
<td>8.00</td>
<td>0.0003 ± 0.0016</td>
<td>0.0070 ± 0.0018</td>
<td>0.22 ± 0.14</td>
<td></td>
</tr>
<tr>
<td>13.00</td>
<td>0.0030 ± 0.0077</td>
<td>0.0347 ± 0.0037</td>
<td>0.308 ± 0.014</td>
<td></td>
</tr>
<tr>
<td>16.00</td>
<td>0.0104 ± 0.0068</td>
<td>0.0015 ± 0.0048</td>
<td>0.111 ± 0.076</td>
<td></td>
</tr>
<tr>
<td>24.00</td>
<td>-0.0083 ± 0.0049</td>
<td>0.0224 ± 0.0034</td>
<td>0.062 ± 0.025</td>
<td></td>
</tr>
<tr>
<td>31.00</td>
<td>0.0214 ± 0.0085</td>
<td>0.0087 ± 0.0021</td>
<td>0.017 ± 0.018</td>
<td></td>
</tr>
<tr>
<td>64.00</td>
<td>0.0184 ± 0.0079</td>
<td>0.0216 ± 0.0054</td>
<td>0.0137 ± 0.0042</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here](Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-19.

\(^b\)Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 21
Mean Percentage of Deposited Nickel Located in the Urine Contained in the Urinary Bladder\textsuperscript{a}

<table>
<thead>
<tr>
<th>Days After End of Exposure \textsuperscript{b}</th>
<th>Exposure Concentration (\textmu g/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>2.830 ± 0.030</td>
<td>0.90 ± 0.42</td>
<td>1.7513 ± 0.5829</td>
<td></td>
</tr>
<tr>
<td>0.19</td>
<td>2.006 ± 0.041</td>
<td>0.93 ± 0.11</td>
<td>1.5681 ± 0.3576</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>2.245 ± 0.069</td>
<td>1.01 ± 0.25</td>
<td>0.9713 ± 0.1958</td>
<td></td>
</tr>
<tr>
<td>1.01</td>
<td>0.216 ± 0.025</td>
<td>0.24 ± 0.13</td>
<td>0.5920 ± 0.1561</td>
<td></td>
</tr>
<tr>
<td>2.01</td>
<td>0.0889 ± 0.0097</td>
<td>0.028 ± 0.013</td>
<td>0.3010 ± 0.1469</td>
<td></td>
</tr>
<tr>
<td>4.67</td>
<td>0.030 ± 0.014</td>
<td>0.0105 ± 0.0056</td>
<td>0.128 ± 0.060</td>
<td></td>
</tr>
<tr>
<td>8.00</td>
<td>0.0058 ± 0.0024</td>
<td>0.0082 ± 0.0034</td>
<td>0.044 ± 0.015</td>
<td></td>
</tr>
<tr>
<td>13.00</td>
<td>0.0035 ± 0.0013</td>
<td>0.00023 ± 0.00061</td>
<td>0.0167 ± 0.0061</td>
<td></td>
</tr>
<tr>
<td>16.00</td>
<td>0.00131 ± 0.00049</td>
<td>-0.015 ± 0.013</td>
<td>0.0118 ± 0.0098</td>
<td></td>
</tr>
<tr>
<td>24.00</td>
<td>-0.0014 ± 0.0045</td>
<td>0.0069 ± 0.0024</td>
<td>0.40 ± 0.39</td>
<td></td>
</tr>
<tr>
<td>31.00</td>
<td>0.0139 ± 0.0049</td>
<td>0.0055 ± 0.0036</td>
<td>-0.0103 ± 0.011</td>
<td></td>
</tr>
<tr>
<td>64.00</td>
<td>-0.0034 ± 0.0032</td>
<td>0.0100 ± 0.0063</td>
<td>-0.0072 ± 0.0065</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data represent mean percent/gram tissue ± SEM. Total nmoles Ni given in Table 6 [originally, Table 3 here] (Subgroup B) were used as the mean estimate of nmoles deposited for these rats. Data for individual animals are in Appendix E, Table E-20.

\textsuperscript{b}Sacrifice times are the mean sacrifice times for all 9 animals per time point (3 per exposure, per time point).
Table 22

Half-Times for Elimination of Nickel from the Respiratory Tract After Inhalation Exposure to Aerosols of Nickel Sulfate Hexahydrate

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Exposure Concentration (μg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turbinates</td>
<td></td>
<td>1.6 (19)</td>
<td>3.0 (50)</td>
<td>0.55 (42)</td>
</tr>
<tr>
<td>Skull (brain removed)</td>
<td></td>
<td>1.1 (22)</td>
<td>1.3 (30)</td>
<td>0.55 (25)</td>
</tr>
<tr>
<td>Trachea</td>
<td></td>
<td>0.53 (8.7)</td>
<td>1.4 (19)</td>
<td>0.16 (25)</td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td>0.73 (14)</td>
<td>1.5 (27)</td>
<td>1.7 (24)</td>
</tr>
<tr>
<td>Lung-Associated Lymph Nodes</td>
<td>b</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

aData represent half-times in days with percent standard error in parentheses.

bCould not be determined, because of the low levels of activity in this tissue.
Table 23
Half-Times for Elimination of Nickel from the Gastrointestinal Tract and Liver After Inhalation Exposure to Aerosols of Nickel Sulfate Hexahydrate

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Exposure Concentration (µg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td></td>
<td>0.12 (17)</td>
<td>0.15 (8.1)</td>
<td>0.091 (10)</td>
</tr>
<tr>
<td>Stomach(^b)</td>
<td></td>
<td>0.11 (22)</td>
<td>--(^c)</td>
<td>--(^c)</td>
</tr>
<tr>
<td>Small Intestine(^b)</td>
<td></td>
<td>0.11 (22)</td>
<td>2.0 (70)</td>
<td>--(^c)</td>
</tr>
<tr>
<td>Large Intestine(^b)</td>
<td></td>
<td>0.82 (120)</td>
<td>2.9 (89)</td>
<td>1.7 (100)</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td>0.46 (150)</td>
<td>--(^c)</td>
<td>--(^c)</td>
</tr>
</tbody>
</table>

\(^a\)Data represent half-times in days with percent standard error in parentheses.

\(^b\)Not including contents.

\(^c\)Could not be determined, because of the low levels of activity in this tissue.
Table 24
Half-Times for Elimination of Nickel from the Internal Organs and Blood After Inhalation Exposure to Aerosols of Nickel Sulfate Hexahydrate

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Exposure Concentration (µg/L)</th>
<th>0.735</th>
<th>1.96</th>
<th>11.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td></td>
<td>0.074 (26)</td>
<td><strong>b</strong></td>
<td><strong>b</strong></td>
</tr>
<tr>
<td>Thyroids</td>
<td></td>
<td>0.094 (39)</td>
<td><strong>b</strong></td>
<td><strong>b</strong></td>
</tr>
<tr>
<td>Adrenals</td>
<td></td>
<td>1.1 (96)</td>
<td><strong>b</strong></td>
<td><strong>b</strong></td>
</tr>
<tr>
<td>Testes</td>
<td></td>
<td>2.0 (73)</td>
<td><strong>b</strong></td>
<td><strong>b</strong></td>
</tr>
<tr>
<td>Kidneys</td>
<td></td>
<td>2.0 (38)</td>
<td>23 (64)</td>
<td>13 (38)</td>
</tr>
<tr>
<td>Bladder</td>
<td></td>
<td>0.12 (19)</td>
<td>28 (160)</td>
<td>60 (170)</td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td>0.39 (7.7)</td>
<td>0.46 (31)</td>
<td>0.59 (23)</td>
</tr>
</tbody>
</table>

aData represent half-times in days with percent standard error in parentheses.

bCould not be determined, because of the low levels of activity in this tissue.

cNot including contents.

dPresent in the bladder at sacrifice.