Thermal Pilot Studies of Cell Phone Radiofrequency Radiation

Michael Wyde, PhD
Toxicology Branch
National Institute of Environmental Health Sciences

NTP Technical Report Peer-Review Meeting
March 26-28, 2018
Three-phase toxicology and carcinogenicity studies in Harlan Sprague Dawley rats and B6C3F₁ mice

- **5-day thermal pilot** studies at specific absorption rates (SARs) of 4-12 W/kg in young and aged rats and mice and pregnant rats (10 studies)

- 28-day prechronic toxicology studies

- 2-year toxicology and carcinogenicity studies

• Goals of the thermal pilot studies
• Thermal pilot study design
• Rat studies: Results
• Mouse studies: Results
• Summary & Discussion
5-Day thermal pilot studies: Goals

• Evaluate a wide range of specific absorption rates (SARs) to determine the threshold for potential thermal effects of cell phone radiofrequency radiation (RFR)
  – Determine power levels for exposure at which rodents can maintain thermoregulation
  – Identify power levels that do not induce an excessive increase in body temperature (> 1°C)

• Determine impact of animal size and pregnancy status on body temperature
  – Evaluated effects in young and aged rats and mice, and pregnant rats

• Determine potential effects of RFR exposure on pregnancy in rats
Conducted series of 10 studies
- Young, aged, and pregnant rats exposed to (GSM* or CDMA) RFR
- Young and aged mice exposed to (GSM or CDMA) RFR
- 5 animals per sex for each exposure group

Daily exposure to 0, 4, 6, 8, 10, 12 W/kg for 9 hrs 10 min for 5 days
- 18 hrs 20 min per day in 10 min on/10 min off cycles
- Rats exposed to signals at 900 MHz; mice exposed at 1900 MHz
- Pregnant rats exposed during gestation days (GD) 10-15
- Due to the number of chambers, exposures were conducted in multiple cohorts

* GSM = Global System for Mobile Communication; CDMA = Code Division Multiple Access
5-Day thermal pilot studies

- Collected body temperatures via implanted microchips at multiple time points over 5 days
  - Collected 3 times per day on Days 1, 3, and 5 immediately after cessation of exposure during the 10-minute off period
  - Collected after daily shutdown for husbandry prior to initiation on Days 2 and 4
- Dams from the control group and 10 and 12 W/kg evaluated by Cesarean section for potential effects of exposure on pregnancy

### Body weights at study initiation

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>GSM</th>
<th>CDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Young rats</strong></td>
<td>Male</td>
<td>157</td>
<td>158</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>122</td>
<td>120</td>
</tr>
<tr>
<td><strong>Aged rats</strong></td>
<td>Male</td>
<td>504</td>
<td>470</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>298</td>
<td>261</td>
</tr>
<tr>
<td><strong>Pregnant rats</strong></td>
<td>Female</td>
<td>248</td>
<td>253</td>
</tr>
<tr>
<td><strong>Young mice</strong></td>
<td>Male</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td><strong>Aged mice</strong></td>
<td>Male</td>
<td>52</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>57</td>
<td>54</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>GSM</th>
<th>CDMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Young rats</strong></td>
<td>Male</td>
<td>157</td>
<td>158</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>122</td>
<td>120</td>
</tr>
<tr>
<td><strong>Aged rats</strong></td>
<td>Male</td>
<td>504</td>
<td>470</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>298</td>
<td>261</td>
</tr>
<tr>
<td><strong>Pregnant rats</strong></td>
<td>Female</td>
<td>248</td>
<td>253</td>
</tr>
<tr>
<td><strong>Young mice</strong></td>
<td>Male</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td><strong>Aged mice</strong></td>
<td>Male</td>
<td>52</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>57</td>
<td>54</td>
</tr>
</tbody>
</table>
Rat Study Results

1. Young males and females GSM
2. Young males and females CDMA
3. Aged males and females GSM
4. Aged males and females CDMA
5. Pregnant dams GSM
6. Pregnant dams CDMA
Body temperature in young male rats

- SAR-dependent increase in body temperature following RFR exposure
- No significant differences in young females

Data presented as the mean of the 9 time points on Days 1, 3, and 5
Body temperature in aged male rats

• GSM modulation
  – All aged **male** rats exposed to 10 or 12 W/kg RFR died during the first day of exposures.
  – In **female** rats, exposures to 12 W/kg GSM were discontinued on the first day due to excessive increases in body temperature (> 3ºC)

• CDMA modulation
  – All aged **male** rats exposed to 12 W/kg died during the first day of exposures
  – In aged **male** rats exposed to 10 W/kg were discontinued on the first day due to increases in body temperature (> 3ºC)

Body temperature in aged male rats

• SAR-dependent increase in body temperature following RFR exposure at ≥ 6 W/kg GSM or CDMA

• Increases greater than 1°C at ≥ 8 W/kg GSM or CDMA


● Cohort 1 (0, 4, 6, and 8 W/kg)
○ Cohort 2 (0, 10, and 12 W/kg)
* Significantly different than controls (P < 0.05)
Effects in aged and pregnant female rats

• Results similar for aged female and pregnant female rats

• SAR-dependent increase in body temperature following RFR exposure at ≥ 6 W/kg GSM or CDMA
  – Increases greater than 1°C at ≥ 8 W/kg GSM or CDMA

• Increase in the number of resorptions at 12 W/kg compared to controls (GSM only)

• No treatment-related effects on the number of live/dead pups, number of corpora lutea, number of implantation sites, or mean fetal weight

Summary: Results for 5-day pilot study in rats

- **10 and 12 W/kg**
  - Excessive increases in body temperature in pregnant and aged male and female rats with increased mortality in aged males
  - Increase in early resorptions at 12 W/kg GSM in pregnant rats

- **8 W/kg**
  - Several instances of increased body temperature considered excessive (> 1ºC) in pregnant and aged male and female rats

- **6 W/kg**
  - Some increases (< 1ºC) in body temperature in young and aged males and aged females

- **Overall, effects more robust** in aged (larger) than young (smaller) rats, and in males compared to females
Mouse Study Results

1. Young males and females GSM
2. Young males and females CDMA
3. Aged males and females GSM
4. Aged males and females CDMA
Body temperature in aged mice

- **GSM**

  - Females

  - Body Temperature (°C)

<table>
<thead>
<tr>
<th>W/kg</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **CDMA**

  - Females

  - Body Temperature (°C)

<table>
<thead>
<tr>
<th>W/kg</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Significantly different than controls (P < 0.05)

- Similar results observed for aged males, young male and female mice

• Sporadic increases in body temperature
• Increases not considered exposure related
• No differences between males and females, GSM or CDMA
• These data suggest that higher SARs could be tolerated
**Summary: Rats and mice**

**Rat Studies**
- Lethal effects and excessive increases in body temperatures were observed in rats at 10 and 12 W/kg.
- Increase in early resorptions and decreased body weight gain in pregnant dams at 12 W/kg GSM.
- Based on these data, SARs of ≥ 10 W/kg were not recommended for further study in rats.
- 3, 6, and 9 W/kg selected for 28-day studies.

**Mouse Studies**
- No thermal effects observed at SARs up to 12 W/kg regardless of age, sex, or modulation.
- 5, 10, and 15 W/kg selected for 28-day studies.