Health Effects of Exposure to Cell Phone RF Radiation: Research Programs in the U.S.A.

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Question

Does exposure to radiofrequency radiation from cell phones or other wireless communications devices increase the risk of cancer or other adverse health outcome?

Epidemiology (Case-Control)

Inskip, Linet *et al*., New Engl. J. Med (2001)

- No association with brain tumor risk; study not designed to evaluate risks of long-term heavy use.

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Muscat *et al*., JAMA (2000), Neurology (2002)

- No association with risk of brain cancer or acoustic neuroma.

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Muscat *et al*., JAMA (2000), Neurology (2002)

- No association with risk of brain cancer or acoustic neuroma.

Linet *et al*., Inter. J. Cancer (2006)

- No overall association with risk of lymphoma.

Epidemiology (Other Designs)

Morgan *et al.*, Epidemiology (2000)

- No association with risk of brain cancer or acoustic neuroma (cohort study using job title as surrogate for total RF exposure [Motorola employees]).

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Morgan *et al.*, Epidemiology (2000)

- No association with risk of brain cancer or acoustic neuroma (cohort study using job title as surrogate for total RF exposure [Motorola employees]).

Kan *et al.*, J. Neurooncology (2008)

- No overall association with brain cancer risk; significantly increased risk (OR: 1.25) for $\geq$ 10 years of use (meta-analysis of case-control studies).

Epidemiology - Conclusions

General Consensus

- No compelling body of epidemiologic evidence exists to support the hypothesis that use of cellular telephones is associated with an increased risk of any type of neoplasm or other adverse health effect.

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However, important questions remain:

- Is risk increased with long-term use of cell phones?

Epidemiology - Conclusions

General Consensus

- No compelling body of epidemiologic evidence exists to support the hypothesis that use of cellular telephones is associated with an increased risk of any type of neoplasm or other adverse health effect.

However, important questions remain:

- Is risk increased with long-term use of cell phones?
- Is risk increased in sensitive sub-populations?

Challenges to RF Hazard Identification

Limitations to Epidemiology (General)

- exposure assessment (recall bias)

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Limitations to Epidemiology (General)

- exposure assessment (recall bias)
- limited sensitivity to detect quantitatively small effects superimposed on a finite background
- temporal variability of exposures: when is the "critical period" for exposure?

Challenges to RF Hazard Identification

Limitations to Epidemiology (RF-specific)

- exposure assessment: what is the relevant RF exposure metric?

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Limitations to Epidemiology (RF-specific)

- exposure assessment: what is the relevant RF exposure metric?
- limited duration of exposure in study populations
- unknown relative sensitivity of children or other potentially susceptible subpopulations

Challenges to RF Hazard Identification

Issues Associated with Sole Reliance on Epidemiology Data to Identify Health Hazards:

- Latency of hazard development

Challenges to RF Hazard Identification

Issues Associated with Sole Reliance on Epidemiology Data to Identify Health Hazards:

- Latency of hazard development
- Time required to identify hazards through epidemiology (*post-hoc* evaluation)

Application of Experimental Data to Human Hazard Identification

In situations where epidemiology data conflict, are inadequate, or are inconclusive, well-designed and controlled studies in experimental models may provide data that are critical to the rational identification of human health hazards.

Application of Experimental Data to Human Hazard Identification

Assessment of the possible hazards associated with human exposure to cell phone radio-frequency fields provides an ideal example of such a situation.

Application of Experimental Data to Human Hazard Identification

Challenges to Experimental Approaches

- high dose to low dose extrapolation

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- interspecies extrapolation
- relevance of exposure metric
- study power (usually limited by study size and logistics)

Experimental Studies

Adey *et al*., Radiation Research (1999); Cancer Research (2000)

- No effect of exposure to TDMA (836 MHz) on cancer incidence in F344 rats (2 year exposure, including gestational and neonatal periods).

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- No effect of TDMA exposure on cancer incidence in rats pre-exposed to CNS carcinogen (ENU).

Experimental Studies

Zook and Simmens, Radiation Research (2001, 2006)

- No effect of exposure to TDMA (860 MHz) on cancer incidence in the CNS, PNS, pituitary gland, thyroid gland, adrenal gland, or mammary gland.

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Experimental Studies

Roti-Roti *et al*., Radiation Research (2003)

- No effects of exposure to FDMA (835 MHz) or CDMA (847 MHz) on cancer incidence in F344 rats (2 year exposure).

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Anderson *et al.*, Radiation Research (2004)

- No effects of exposure to IRIDIUM signal (1616 MHz) on cancer incidence in F344 rats (2 year exposure).

Overview of Experimental Data

- No evidence of oncogenicity in either rats or mice receiving chronic exposure to RF fields.

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- Comparable incidences of brain/CNS neoplasms in rats exposed to ENU alone versus ENU + chronic exposure to RF fields.

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- No evidence of oncogenicity in either rats or mice receiving chronic exposure to RF fields.
- Comparable incidences of brain/CNS neoplasms in rats exposed to ENU alone versus ENU + chronic exposure to RF fields.
- These results are in general agreement with the results of oncogenicity evaluations of RF fields conducted elsewhere.

Issues in Experimental Studies

- Group Size and Statistical Power

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  - exposure duration (hrs per day, days per week)
  - animal restraint during exposure
  - are specific subpopulations differentially sensitive to RF effects?

Studies to Evaluate the Toxic and Carcinogenic Potential of Cell Phone Radio Frequency Radiation in Laboratory Animals for the National Toxicology Program (NTP)

Principal Collaborators

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  - Thomas L. Horn, Ph.D., D.A.B.T. – Study Director
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- NIEHS – NTP (Research Triangle Park)
  - Ronald Melnick, Ph.D. – Project Officer

IITRI Cell Phone RF Laboratory

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- Access/return ("clean/dirty") corridor design
- Laboratory contains:
  - Exposure Chamber Area
  - Quarantine/Breeding Rooms
  - Engineering Control Room
  - Necropsy Laboratory
  - Cage Wash Area
  - Data Office
  - Feed/Bedding and other Storage Areas
  - Locker Rooms

IITRI Cell Phone RF Laboratory

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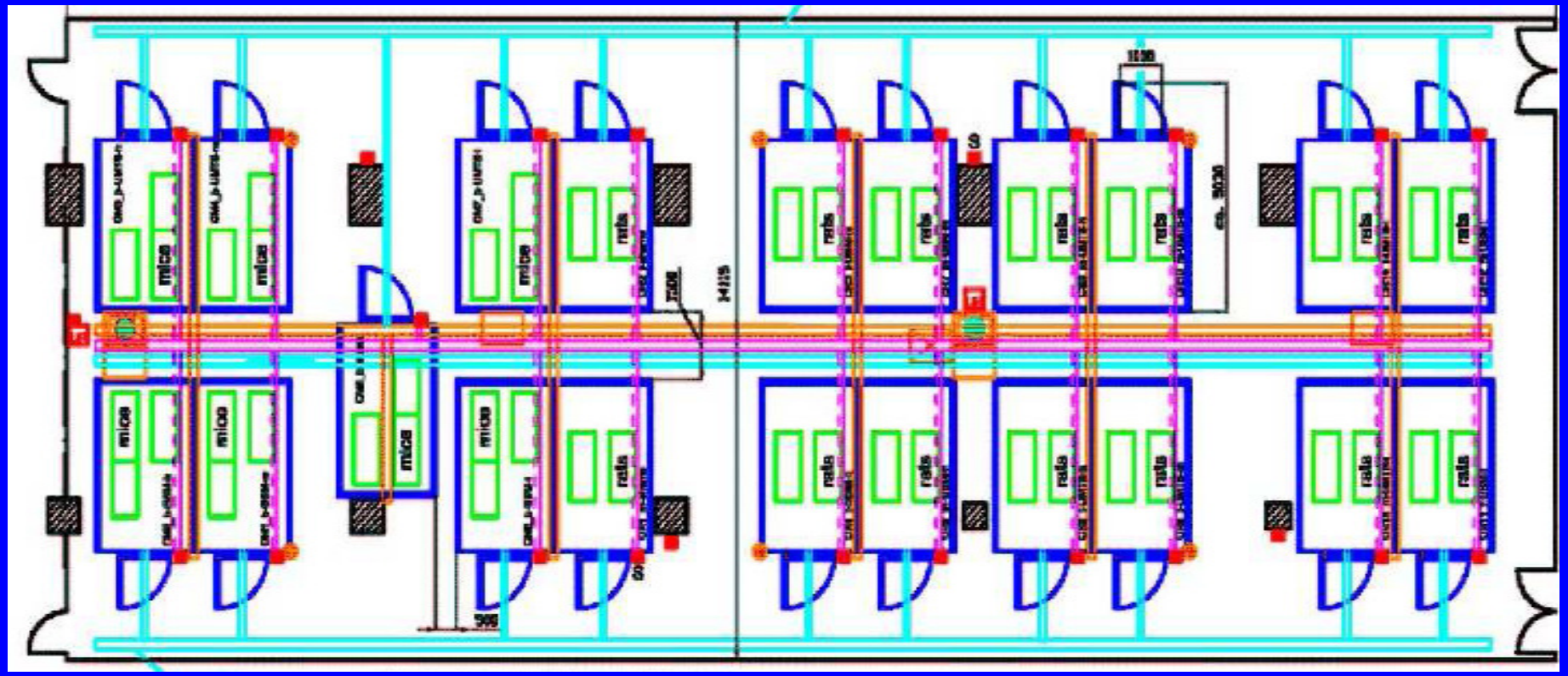
- RF exposure area contains 21 reverberation chambers (14 rat chambers [by sex], 7 mouse chambers)
- Each chamber holds 2 custom-designed racks (chamber capacity: 120 rats or 224 mice)
- Each chamber is continuously monitored for: RF signal characteristics (frequency, intensity), lighting, temperature, humidity, air flows

Cell Phone Lab Exposure Area



Exposure Chamber Delivery

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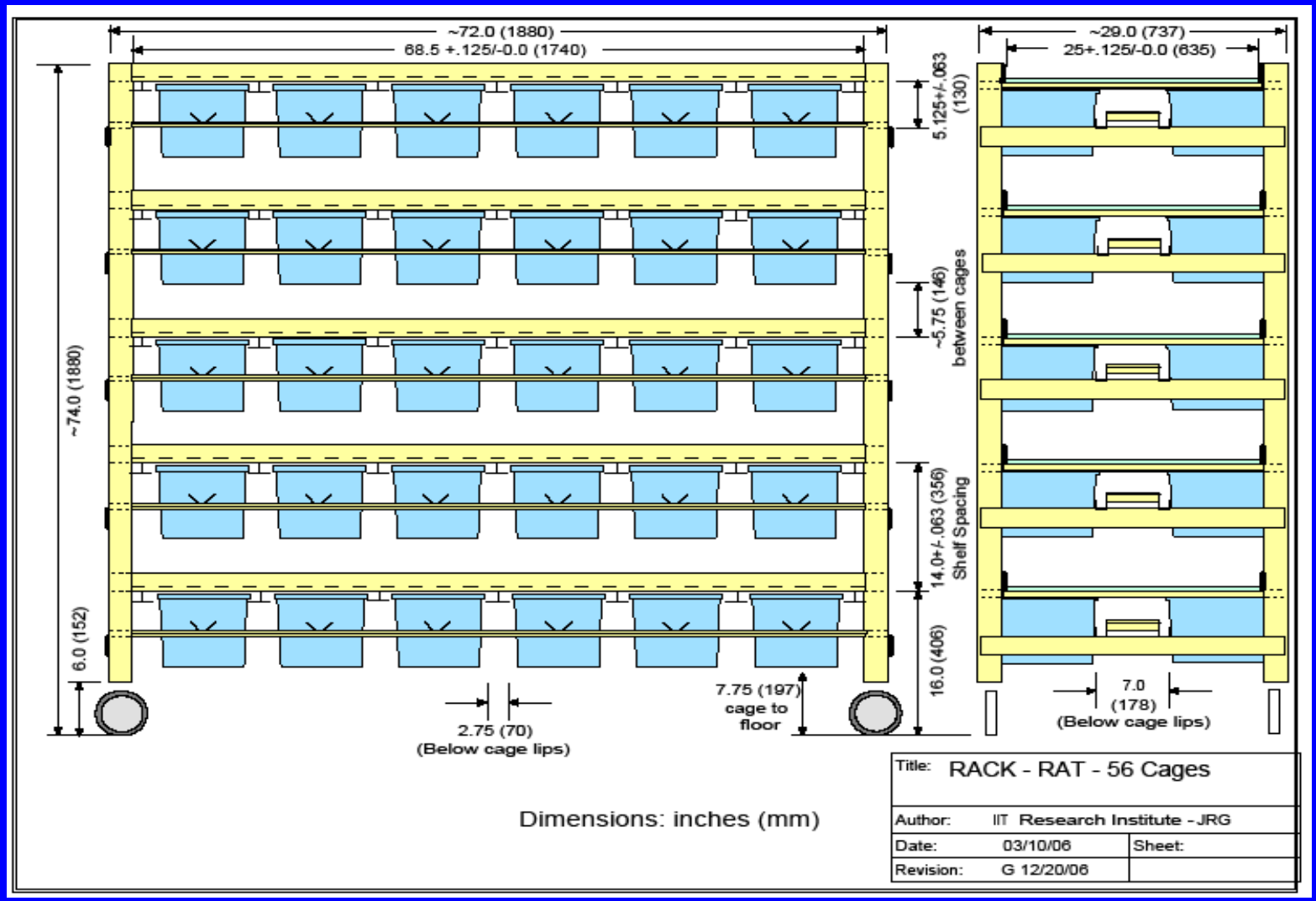
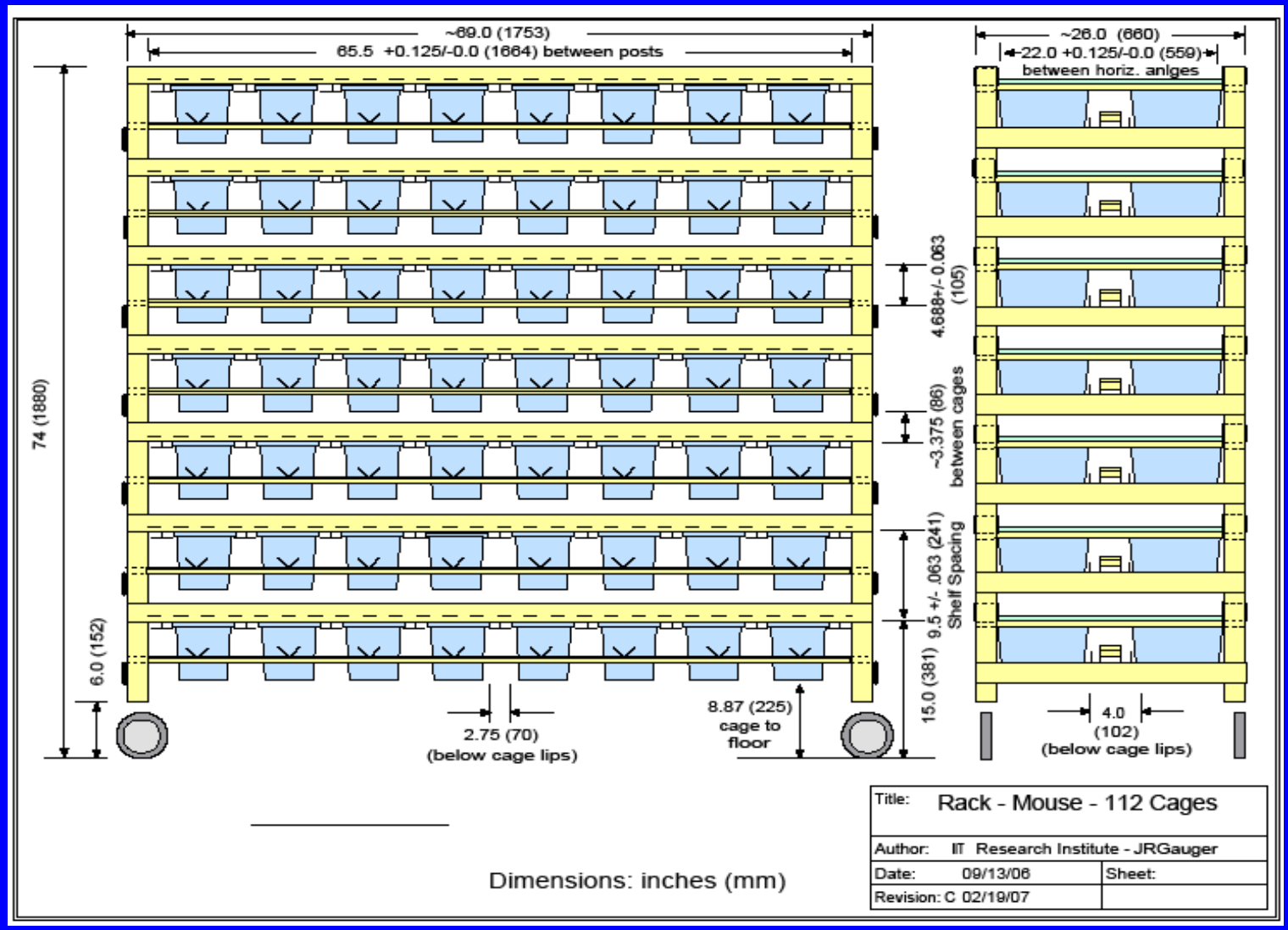
Cell Phone Lab Exposure Area

Custom Rat Rack Design



Custom Mouse Rack Design



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- RF Signal Generation:
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  - Mice exposed to 1900 MHz GSM and CDMA

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  - Rats exposed to 900 MHz GSM and CDMA
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- Experimental exposures 10 minutes on, 10 minutes off, 20 hours per day, 5 days per week

General Experimental Approach

- All studies are conducted in both
  - Sprague-Dawley Rats
  - B6C3F1 Mice

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- All studies are conducted in both
  - Sprague-Dawley Rats
  - B6C3F1 Mice
- All studies include parallel evaluations of GSM and CDMA signals
- All studies performed in full compliance with
  - U.S. Food and Drug Administration (FDA) Good Laboratory Practice (GLP) regulations
  - U.S. National Toxicology Program (NTP) specifications

RF Toxicology Study Designs

- Thermal Pilot Study
  - Goal: Identify maximum RF flux density that will not increase body temperature by > 1 ^{o}C

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  - Goal 2: Evaluate effects of RF on integrity of the blood-brain barrier, lens quality, DNA damage
- Chronic Toxicity/Oncogenicity Study
  - Goal: Identify possible oncogenic effects of RF

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- Exposure Groups: CDMA and GSM exposures at time-averaged SARS of 4, 6, 8, 10, and 12 W/kg (10 min on/10 min off).
  - 5/sex/group/species, 5 weeks of age
  - 5/sex/group/species, 20 weeks of age
  - 5 pregnant dams/group/species, gestation day 10

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  - 5/sex/group/species, 20 weeks of age
  - 5 pregnant dams/group/species, gestation day 10
- Exposure Duration: 20 hrs per day for 5 days

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- In-Life Experimental Endpoints:
  - Survival
  - Body Weight
  - Clinical Observations
  - Body Temperature (via implantable microchips)

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- Post-mortem Experimental Endpoints:
  - Lens Quality
  - Brain Morphology (via magnetic resonance microscopy)

Perinatal/Prechronic Toxicity Study

- Goal: Identify toxic effects of subchronic exposure to non-thermal RF fields

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- Goal: Identify toxic effects of subchronic exposure to non-thermal RF fields
- Exposure Groups: GSM and CDMA exposures at 3 power levels each (selected using data from the Thermal Pilot Study) + controls.
  - 10 pregnant dams/group/species, gestation day 6
  - Litters culled to 4/sex on post-natal day 4,
  - Litters culled to 2/sex on post-natal day 21
  - Post-lactational exposure (10/sex/species/group) from post-natal day 21 through post-natal day 49

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Perinatal/Prechronic Toxicity Study

- In-Life Experimental Endpoints:
  - Survival
  - Clinical Observations
  - Body Weight
  - Body Temperature
- Post-mortem Experimental Endpoints:
  - Organ Weights
  - Gross Pathology
  - Microscopic Pathology (all tissues, all animals)
  - Integrity of the Blood-Brain Barrier Integrity (vascular permeability using fluorescent dextrans)
  - Neonatal Brain Morphology

Chronic Toxicity/Oncogenicity Study

- Goal: Identify toxic and oncogenic effects of chronic exposure to non-thermal RF fields

Chronic Toxicity/Oncogenicity Study

- Goal: Identify toxic and oncogenic effects of chronic exposure to non-thermal RF fields
- Exposure Groups: GSM and CDMA exposures at 3 power levels each (selected using data from the Prechronic Toxicity Study) + controls.
  - 50 pregnant dams/group/species, gestation day 6
  - Litters culled to 4/sex on post-natal day 4,
  - Litters culled to 2/sex on post-natal day 21
  - Post-lactational exposure (105/sex/species/group) from post-natal day 21 until 110 weeks of age

Chronic Toxicity/Oncogenicity Study

- In-Life Experimental Endpoints:
  - Survival
  - Clinical Observations
  - Hematology
  - Sperm Morphology
  - Body Weight
  - Body Temperature
  - DNA Strand Breaks
  - Vaginal Cytology

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Projected Program Schedule

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  - Exposures begin August, 2008
  - Completion in October, 2008

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  - Exposures begin October/November, 2008
  - Completion in March, 2009

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  - Completion in October, 2008
- Perinatal/Prechronic Toxicity Study
  - Exposures begin October/November, 2008
  - Completion in March, 2009
- Chronic Toxicity/Oncogenicity Study
  - Exposures begin January/February, 2009
  - Completion in Fall, 2011