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Results of the NTP Studies of Cell Phone Radio Frequency Radiation in Hsd: Sprague Dawley Rats

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

NTP Technical Report Peer-Review Meeting
March 26-28, 2018

Outline

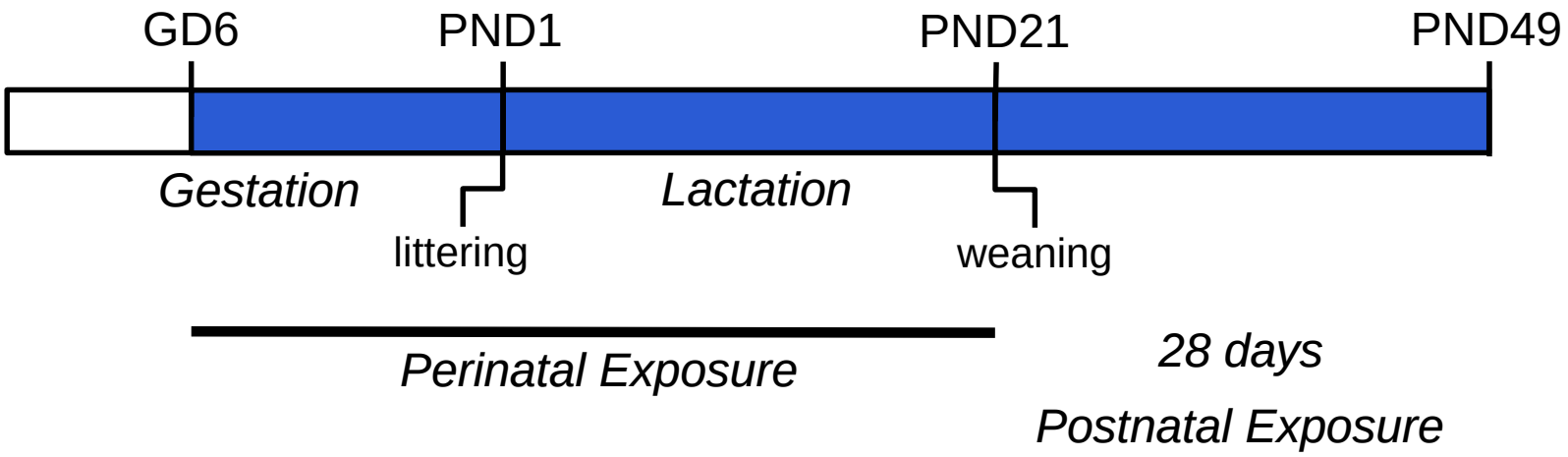
- Partial findings
- Study designs
- 28-Day results
  - GSM
  - CDMA
- 2-Year studies
  - GSM
    - 14-week interim evaluation
    - 2-year results
  - CDMA
    - 14-week interim evaluation
    - 2-year results
- Conclusions

Release of partial findings report

- Received final report from study lab (December 2015)
- Concern was raised regarding the findings in the brain and the heart
- Complete review of brain and heart lesions (Dr. Cesta)
- Partial findings report prepared
  - Report was peer reviewed
  - Released on bioRχiv (May 2016)
- Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats (Whole Body Exposure)
  - https://www.biorxiv.org/content/early/2018/02/01/055699

Cell phone RFR research program

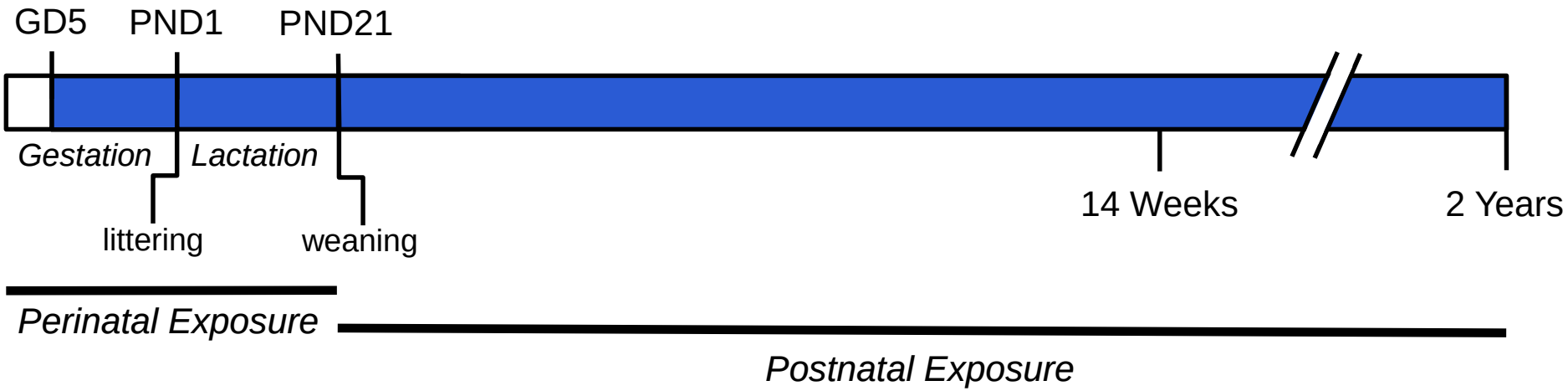
- **28-Day prechronic** toxicology studies in Harlan Sprague Dawley rats
  - Exposure to 0, 3, 6, and 9 W/kg GSM- or CDMA-modulated radiofrequency radiation (RFR)
  - Exposures initiated *in utero* on gestation day (GD) 6 and terminated 28 days after weaning on postnatal day (PND) 21



* All daily RFR exposures were for 9 hrs 10 min *(18 hrs 20 min per day in 10 min on/10 min off cycles)*

Cell phone RFR research program

- **2-Year** toxicology and carcinogenicity studies in Harlan Sprague Dawley rats
  - Exposure to 0, 1.5, 3, and 6 W/kg GSM- or CDMA-modulated RFR
  - Exposures initiated *in utero* on GD5
    - 14-week interim evaluation (histopathology, genetic toxicology, hematology, and clinical chemistry)
    - 2-year evaluation



* All daily RFR exposures were for 9 hrs 10 min *(18 hrs 20 min per day in 10 min on/10 min off cycles)*

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28-Day Study Results

GSM Modulation

28-Day GSM study results: Perinatal effects

- Negative trend for body weights in **dams** at GD21
- Decreased (9%) body weight gains over gestation period (GD6-21) in **dams** at 9 W/kg compared to controls
- No exposure-related effects on **maternal** survival, littering rates, total and live litter size throughout lactation
- Higher number of dead **pups** per litter and decreased survival ratio in 9 W/kg **pups** early in lactation period (PND1-4) compared to controls
- Decreased body weights and body weight gains in 9 W/kg **dams** throughout lactation compared to controls
  - Negative SAR-dependent trend generally observed throughout lactation
  - Significant decrease in all exposure groups at weaning (PND21) compared to controls
- Decreased (8-17%) adjusted **pup** weights throughout lactation period for males and females (combined) at 9 W/kg compared to controls
  - Decreased in males at 6 W/kg (6-8.5%)

28-Day GSM study results: Postnatal effects

- No exposure-related effects on survival or clinical signs
- Lower mean body weights at 6 and 9 W/kg in males, and at 9 W/kg in females throughout 28-day post-weaning exposure
  - In females, decreases mitigated over time; no difference at necropsy
- SAR-dependent decrease in body weights (7-18%) of males at necropsy
- Higher incidences of minimal chronic progressive nephropathy in all groups of exposed females compared to controls

28-Day GSM study results: Body temperature

- Increased body temperatures in dams at 6 and 9 W/kg during gestation and lactation compared to controls
  - Sporadic increases at 6 W/kg were < 1ºC compared to controls
  - Increases ≥ 1ºC higher than in controls were observed at 9 W/kg during lactation

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28-Day Study Results

CDMA Modulation

28-Day CDMA study results: Perinatal effects

- Negative trend for body weights in **dams** at GD21
- Decreased (11%) body weight gains over gestation period (GD6-21) in **dams** at 9 W/kg compared to controls
- No exposure-related effects on **maternal** survival, littering rates, total and live litter size throughout lactation
- Higher number of dead **pups** in the 9 W/kg group after culling (PND5-21), but no effect on survival ratio throughout lactation
- Decreased body weights and body weight gains in 9 W/kg **dams** during lactation compared to controls
  - Negative SAR-dependent trend generally observed throughout lactation
- Decreased (14-23%) adjusted **pup** weights throughout lactation period for males and females (combined) at 9 W/kg compared to controls
  - Decreased in males at 6 W/kg (4-16%)

28-Day CDMA study results: Postnatal effects

- No exposure-related effects on survival or clinical signs of toxicity
- Lower mean body weights were observed at 9 W/kg in males and females compared to controls
  - In males, lower mean body weights were observed throughout the postnatal exposure period and at necropsy
  - In females, decreases mitigated over time; no differences at necropsy
- Higher incidences of minimal chronic progressive nephropathy in all groups of exposed females compared to controls
  - Positive trend; increase significant at 6 W/kg

28-Day CDMA study results: Body temperature

- Increased body temperatures in dams at 9 W/kg during gestation and lactation compared to controls
  - Increases ≥ 1ºC higher than controls during lactation
- Sporadic increased body temperatures observed in dams at 6 W/kg during lactation were < 1ºC higher compared to controls

Exposure selection for 2-year studies

- Effects observed at 9 W/kg (28-day studies)
  - Reduced maternal and pup weights
  - Increased number of dead pups and decreased pup survival ratio (GSM only)
  - Increased body temperature in pregnant rats during gestation, and in dams during lactation (> 1ºC)
- Effects observed at 8 W/kg (Thermal pilot studies)
  - Increased body temperature (> 1ºC) in young male (GSM only) and “aged” male and female rats
- Effects observed at 6 W/kg (28-day and thermal pilot studies)
  - Decreased pup weights during lactation period and lower mean body weights throughout 28-day postnatal exposure in males
  - Increases in body temperature (< 1ºC) in pregnant dams and “aged” male and female rats
- **Exposures of 1.5, 3, and 6 W/kg were selected for 2-year studies**

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2-Year Study Results

GSM Modulation

2-Year GSM study results: Perinatal effects

- Negative trend for body weights in **dams** at GD18 and 21
- Decreased (7%) body weight gains over gestation period (GD6-21) in **dams** at 6 W/kg compared to controls
- No exposure-related effects on maternal survival, littering rates, total and live litter size throughout lactation, pup mortality or survival ratio
- Decreased body weights and body weight gains at 3 and 6 W/kg in **dams** throughout lactation compared to controls
  - Negative SAR-dependent trend generally observed throughout lactation
- Decreased (6-9%) adjusted **pup** weights throughout lactation period for males and females (combined) at 6 W/kg compared to controls
  - Decreased at 3 W/kg (5-7%) up to PND14

14-Week evaluation results

Male rats

Heart	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	10	10	10	10
Right ventricle cardiomyopathy	1 [1.0]	1 [2.0]	5 [1.2]	5 [1.0]
Cardiomyopathy (whole heart)	3 [1.3]	5 [1.2]	8* [1.1]	7 [1.0]
Lymph node (Mandibular)				
Number examined	10	10	10	10
Lymphocyte hyperplasia	0	0	0	4* [1.0]

Data presented as number of rats with the lesion [average severity]
* Statistically significant, $P < 0.05$

- No exposure-related effects observed in **female rats**

14-Week evaluation: Genetic toxicology results

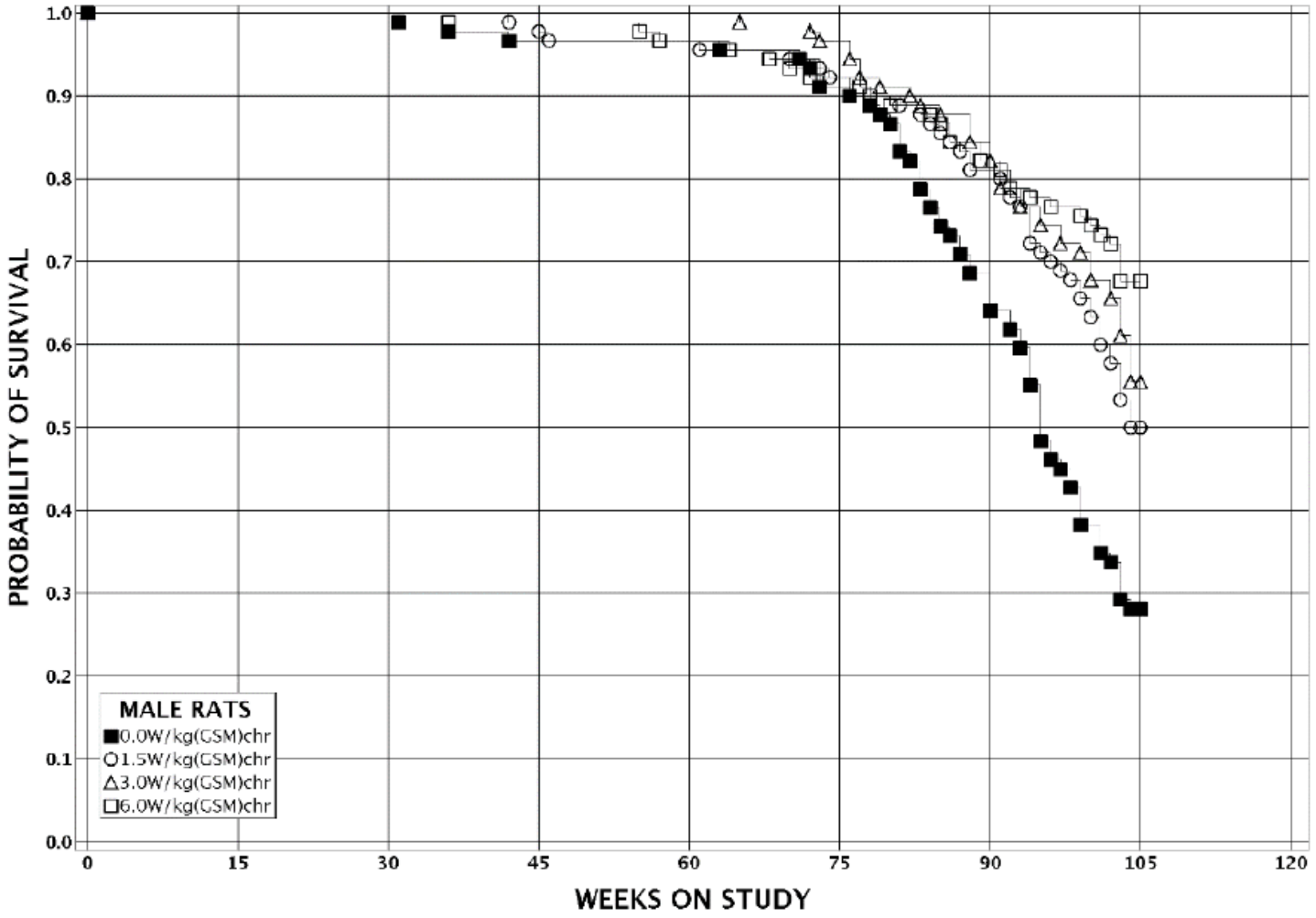
- No increases in the frequencies of micronucleated immature or mature erythrocytes in male or female rats exposed to GSM modulation

Species	Modulation	W/kg	Sex	Result
Rat	GSM	0, 1.5, 3, 6	Male	Negative
			Female	Negative

- Comet assay was **negative** for brain (frontal cortex, hippocampus, cerebellum), liver, and blood

2-Year survival: Males

- Greater survival in all groups of exposed males compared to controls; no differences in females

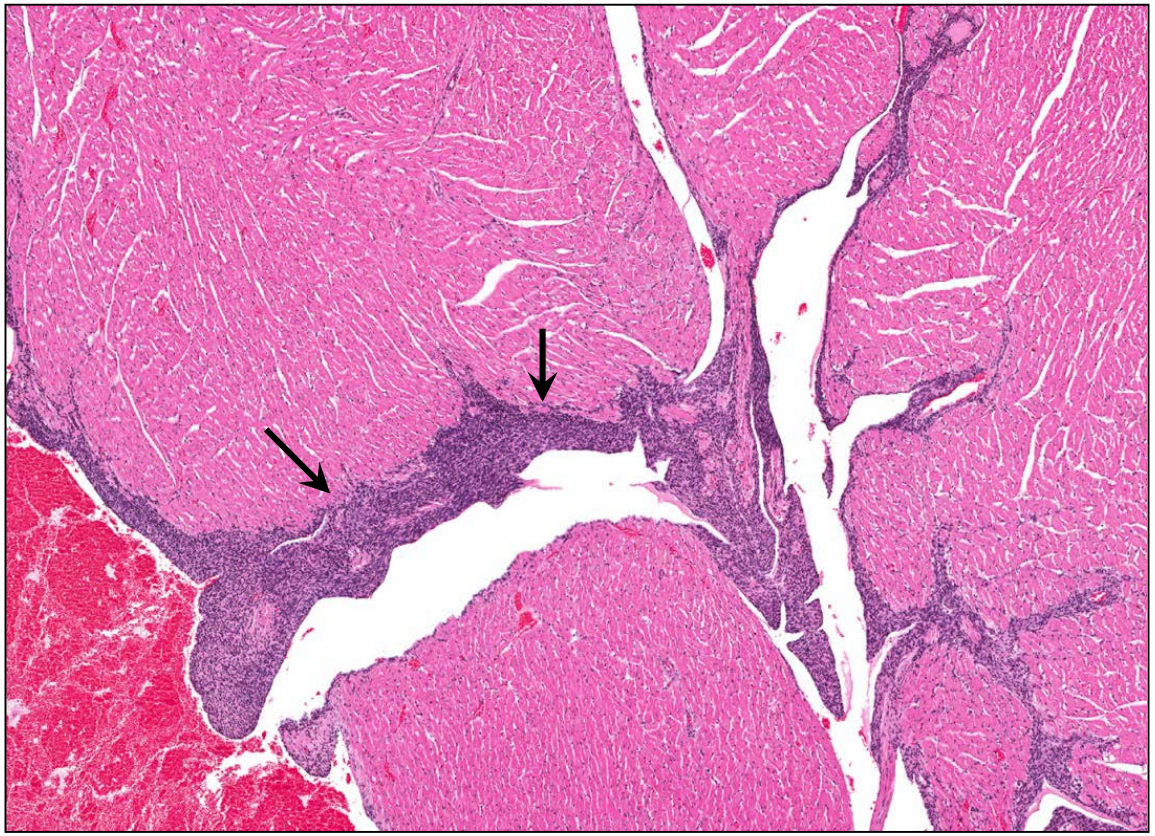


Survival: Males

- Greater survival in all groups of exposed males compared to controls; no differences in females
- **Lower survival in control group attributed to high severity of chronic progressive nephropathy**

Summary of significant neoplastic findings

- Increased incidence of malignant schwannomas of the heart in male rats



GSM: Heart lesions

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Malignant schwannomas[a]	0*	2	1	5
Schwann cell hyperplasia	0	1 [1.0]	0	2 [2.0]
Right ventricular cardiomyopathy	54 [1.1]	62 [1.5]	72* [1.9]	74** [1.8]
Females				
Number examined	90	90	90	90
Malignant schwannomas	0	0	2	0
Schwann cell hyperplasia	0	0	0	0
Right ventricular cardiomyopathy	4 [1.0]	9 [1.1]	14* [1.1]	15* [1.2]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]
[a] Historical control incidence for 2-year studies (all routes): 2/240 (1.0% ± 1.2%, range 0%-2%)
* Statistically significant, $P < 0.05$
** Statistically significant, $P < 0.01$

GSM: Heart lesions

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Malignant schwannomas[a]	0*	2	1	5
Schwann cell hyperplasia	0	1 [1.0]	0	2 [2.0]
Right ventricular cardiomyopathy	54 [1.1]	62 [1.5]	72* [1.9]	74** [1.8]
Females				
Number examined	90	90	90	90
Malignant schwannomas	0	0	2	0
Schwann cell hyperplasia	0	0	0	0
Right ventricular cardiomyopathy	4 [1.0]	9 [1.1]	14* [1.1]	15* [1.2]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]
[a] Historical control incidence for 2-year studies (all routes): 2/240 (1.0% ± 1.2%, range 0%-2%)
* Statistically significant, $P < 0.05$
** Statistically significant, $P < 0.01$

Summary of equivocal neoplastic findings

GSM Males	
Organ	**Lesion**
Prostate	Adenoma or Carcinoma (combined)
Brain	Glioma Malignant
Brain	Meninges, Granular Cell Tumor (Benign and Malignant)
Pituitary Gland	Pars Distalis, Adenoma (Includes multiple)
Adrenal Medulla	Benign, Malignant or Complex Pheochromocytoma (combined)
Islets, Pancreas	Adenoma or Carcinoma (combined)
GSM Females	
None	

GSM: Neoplasms of the prostate gland

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Adenoma [a]	2	2	6	3
Carcinoma [b]	0	0	1	0
Adenoma or carcinoma [c]	2	2	7	3
Epithelium hyperplasia	5 [1.2]	13 [1.6]	11 [1.9]	11 [2.4]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]

[a] Historical control incidence for 2-year studies (all routes): 2/240 (0.6% ± 1.1%, range 0-2%)

[b] Historical control incidence for 2-year studies (all routes): 0/240 (0%)

[c] Historical control incidence for 2-year studies (all routes): 2/240 (0.6% ± 1.1%, range 0-2%)

GSM: Brain lesions

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Malignant glioma[a]	0	3	3	2
Glial cell hyperplasia	0	2 [2.0]	3 [3.0]	1 [4.0]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]

[a] Historical control incidence for 2-year studies (all routes): 2/190 (1.3% ± 2.3%, range 0-4%)

GSM: Brain lesions

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Granular cell tumor – benign[a]	1	3	3	3
Granular cell tumor – malignant	0	0	1	0
Granular cell tumor – benign or malignant[a]	1	3	4	3
Granular cell hyperplasia	1 [1.0]	0	1 [1.0]	0

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]
[a] Historical control incidence for 2-year studies (all routes): 3/190 (1.7% ± 2.1%, range 0-4%)

GSM: Neoplastic lesions of the pituitary gland

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Adenoma[a]	17	28	26	26

Data presented as number of rats with the lesion

[a] Historical control incidence for 2-year studies (all routes): 47/239 (19.8% ± 7.5%, range 10-28%)

GSM: Neoplasms of the adrenal medulla

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	88	90	89	87
Benign pheochromocytoma[a]	10	23*	25*	14
Malignant pheochromocytoma	1	1	4	0
Benign, malignant, or complex pheochromocytoma[b]	11	24*	28*	14
Females				
Number examined	86	90	90	86
Hyperplasia	13 [1.5]	19 [1.2]	14 [1.4]	25* [1.8]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]

[a] Historical control incidence for 2-year studies (all routes): 36/238 (15.8% ± 6.5%, range 10-24%)

[b] Historical control incidence for 2-year studies (all routes): 45/238 (20.1% ± 7.1%, range 13-28%)

* Statistically significant, $P < 0.05$

GSM: Neoplasms of the pancreatic islets

	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	89	86	85
Adenoma[a]	5	14	10	11
Carcinoma[b]	8	15	10	5
Adenoma or carcinoma[c]	13	27*	19	16

Data presented as number of rats with the lesion

[a] Historical control incidence for 2-year studies (all routes): 18/240 (7.9% ± 5.5%, range 4-16%)

[b] Historical control incidence for 2-year studies (all routes): 8/240 (2.2% ± 4.4%, range 0-9%)

[c] Historical control incidence for 2-year studies (all routes): 26/240 (10.1% ± 6.0%, range 4-16%)

* Statistically significant, $P < 0.05$

GSM: Other nonneoplastic lesions

Females	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	88	90	88
Thyroid, C-Cell hyperplasia	28 [2.3]	49** [1.6]	45** [1.8]	43** [1.7]
Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Kidney, Chronic progressive nephropathy	88 [3.7]	89 [3.2]	90 [2.9]	89 [2.6]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]
** Statistically significant, P < 0.01

- SAR-dependent decreases in the incidences and severities of a broad spectrum of lesions considered to be secondary effects of chronic progressive nephropathy
  - Bone, brain, epididymis, heart, intestine, kidney, liver, mesentery, pancreas, parathyroid gland, salivary gland, skeletal muscle, spleen, stomach, testis, and thymus*

*Full list of lesions: Table 29, page 113 of the Draft Technical Report

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2-Year Study Results

CDMA Modulation

2-Year CDMA study results: Perinatal effects

- No exposure-related effects on maternal body weights or survival, littering rates, total and live litter size on PND1
- Decrease in live pups per litter at 6 W/kg after PND4 compared to controls
  - Corresponds to decreased survival ratio at 6 W/kg (PND4-21)
- Decreased body weights and body weight gains at 3 and 6 W/kg in **dams** during lactation compared to controls
  - Negative SAR-dependent trend generally observed throughout lactation
- Decreased (9-14%) adjusted **pup** weights throughout lactation period for males and females (combined) at 6 W/kg compared to controls
  - Decreased at 3 W/kg (5%) only on PND4

14-Week evaluation results

Male rats

Heart	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	10	10	10	10
Right ventricle cardiomyopathy	1 [1.0]	5 [1.0]	4 [1.0]	4 [1.0]
Cardiomyopathy (whole heart)	3 [1.3]	5 [1.0]	6 [1.0]	6 [1.0]

Data presented as number of rats with the lesion [average severity]

No exposure-related effects observed in **female rats**

14-Week evaluation: Micronucleus results

- No increases in the frequencies of micronucleated immature or mature erythrocytes in male or female rats exposed to either modulation

Species	Modulation	W/kg	Sex	Result
Rat	CDMA	0, 1.5, 3, 6	Male	Negative
			Female	Negative
Rat	GSM	0, 1.5, 3, 6	Male	Negative
			Female	Negative

14-Week evaluation: Comet assay results

- Tissues evaluated: Brain (frontal cortex, hippocampus, cerebellum), liver, and blood

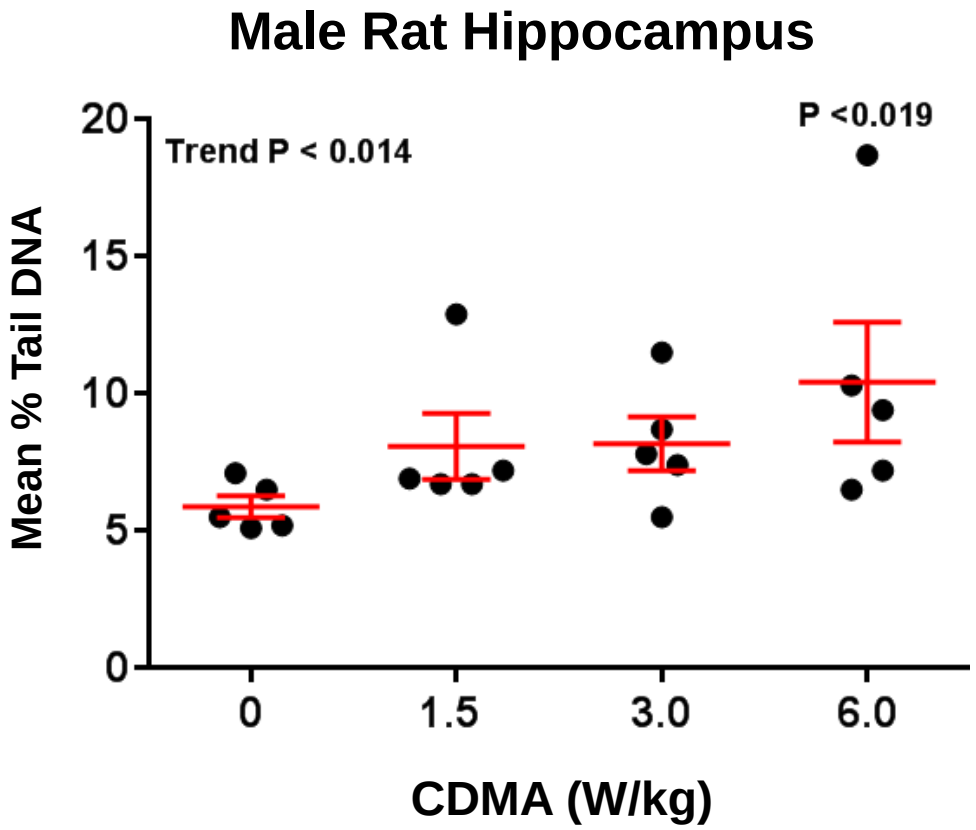
	MALE RATS				
CDMA	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood*
GSM	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood*

	FEMALE RATS				
CDMA	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood
GSM	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood

Positive Equivocal Negative

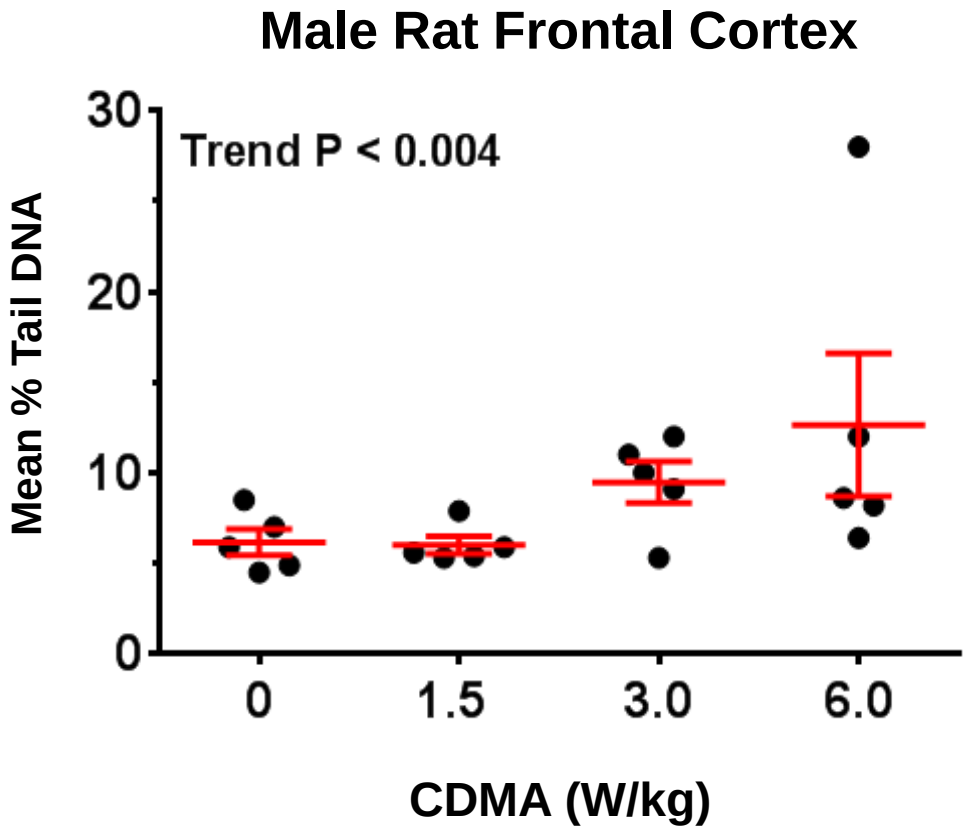
Comet assay results in male rats

Positive results



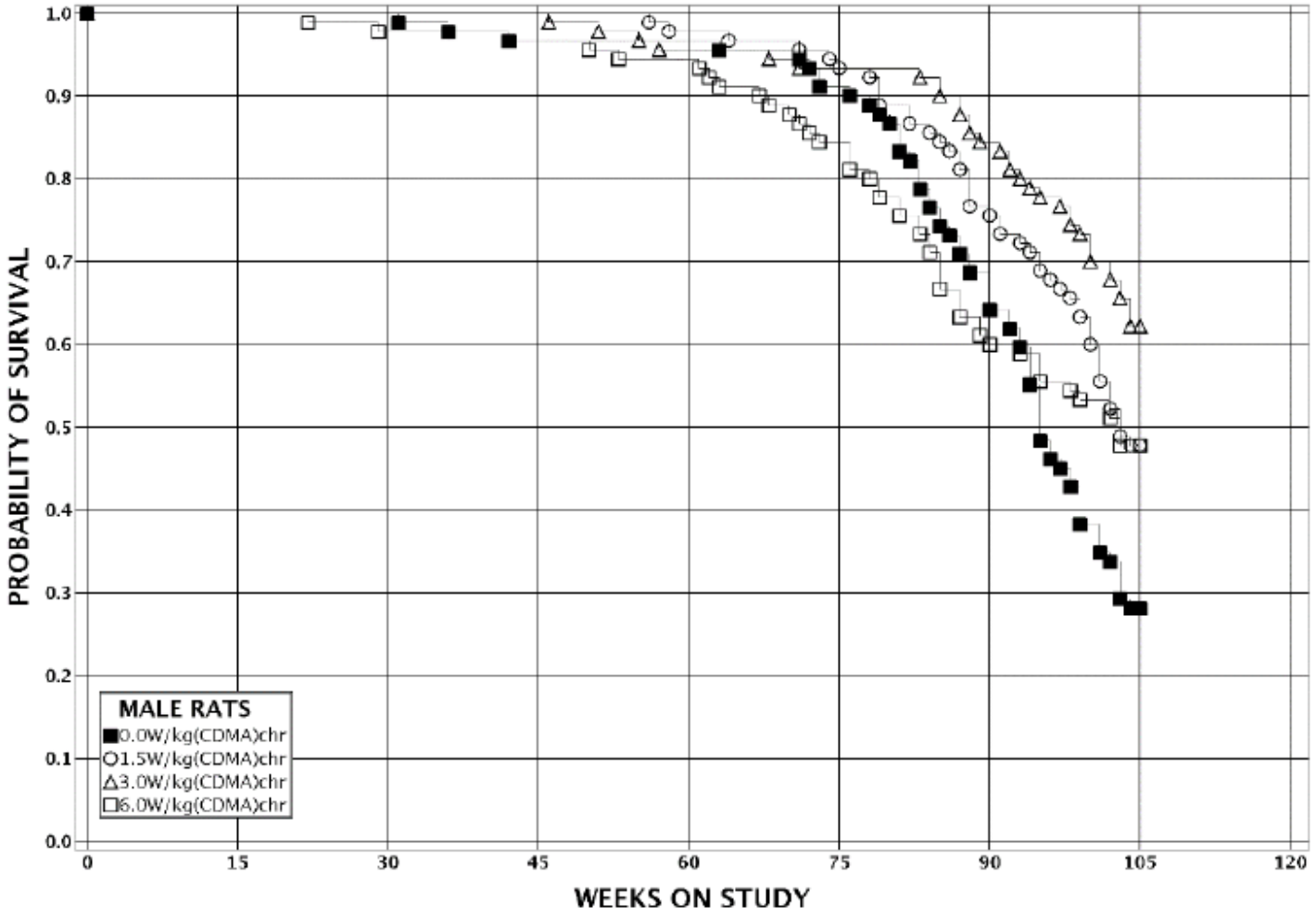
Comet assay results in male rats

Equivocal results



2-Year survival: Males

- Greater survival in all groups of exposed males compared to controls; significant at 1.5 and 3 W/kg

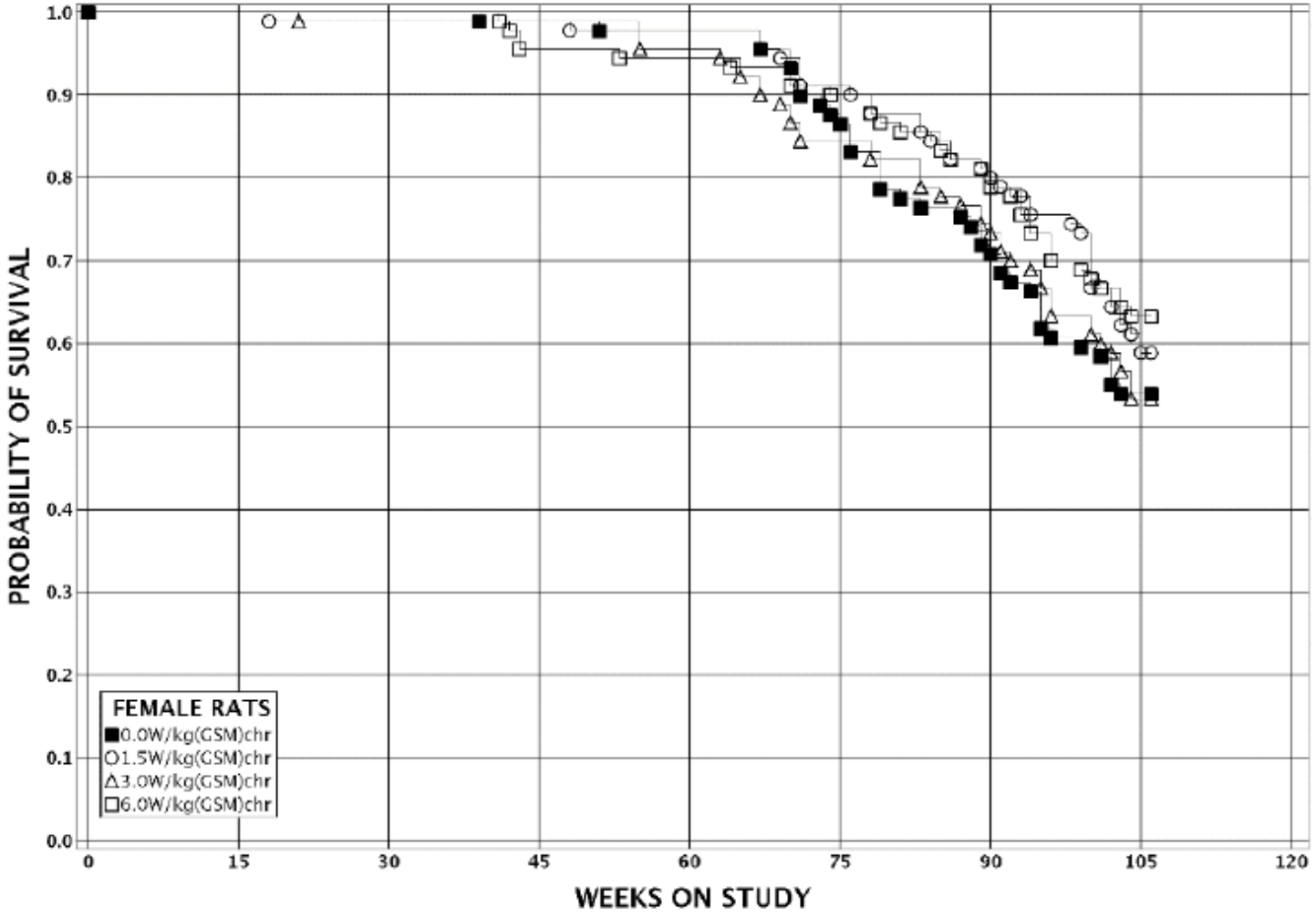


Survival: Males

- Greater survival in all groups of exposed males compared to controls; significant at 1.5 and 3 W/kg
- **Lower survival in control group attributed to high severity of chronic progressive nephropathy**

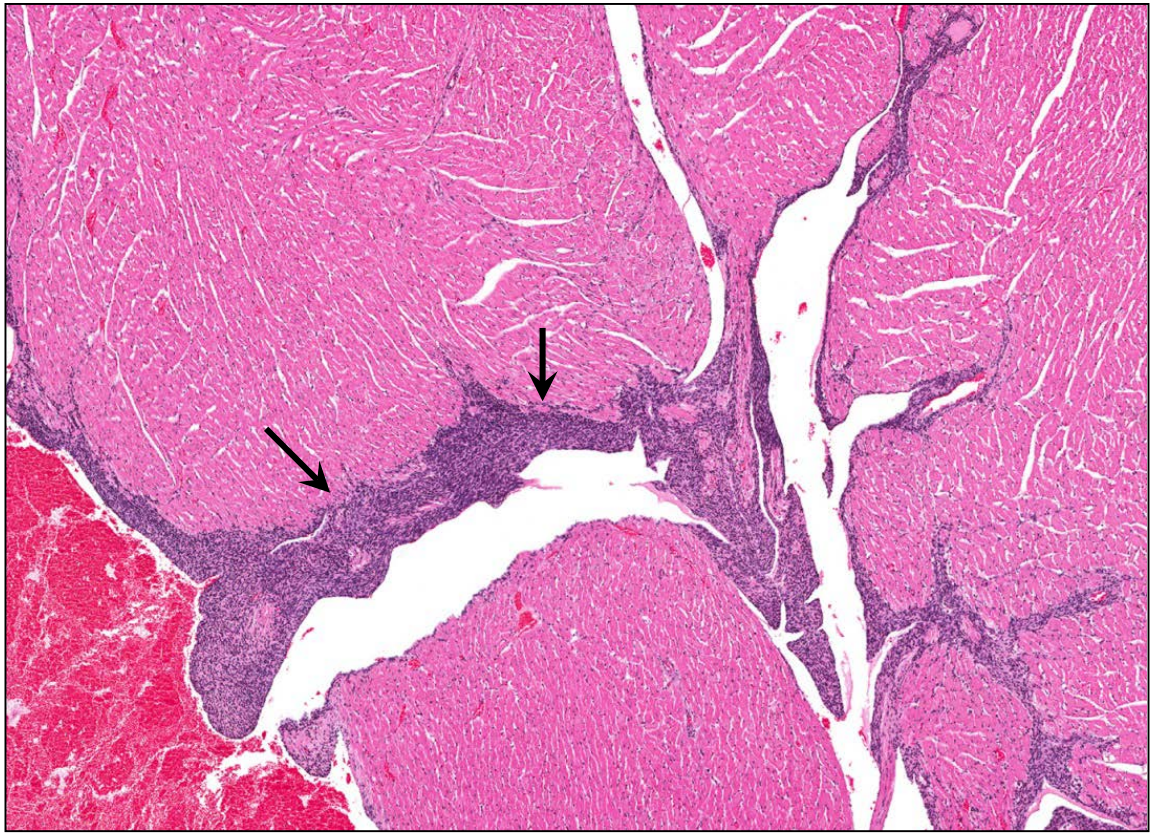
Survival: Females

- Greater survival in 6 W/kg females compared to controls



Summary of significant neoplastic findings

- Increased incidence of malignant schwannomas of the heart in male rats



CDMA: Heart lesions

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Malignant schwannomas[a]	0*	2	3	6*
Schwann cell hyperplasia	0	0	0	3
Right ventricular cardiomyopathy	54 [1.1]	45 [1.2]	62 [1.3]	74* [1.7]
Females				
Number examined	90	90	90	90
Malignant schwannomas	0	2	0	2
Schwann cell hyperplasia	0	1	1	1
Right ventricular cardiomyopathy	4 [1.0]	7 [1.0]	9 [1.0]	9 [1.0]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]

[a] Historical control incidence for 2-year studies (all routes): 2/240 (1.0% ± 1.2%, range 0%-2%)

* Statistically significant, $P < 0.05$

Summary of equivocal neoplastic findings

CDMA Males	
Organ	**Lesion**
Brain	Glioma Malignant
Pituitary Gland	Pars Distalis, Adenoma (Includes multiple)
Liver	Hepatocellular Adenoma or Carcinoma (combined)
CDMA Females	
Organ	**Lesion**
Brain	Glioma Malignant
Adrenal Medulla	Benign, Malignant or Complex Pheochromocytoma (combined)

CDMA: Brain lesions

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	90
Malignant glioma[a]	0	0	0	3
Glial cell hyperplasia	0	2 [1.5]	0	2 [2.5]
Females				
Number examined	90	90	90	90
Malignant glioma[b]	0	3	0	0
Glial cell hyperplasia	0	0	1 [2.0]	1 [2.0]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]

[a] Historical control incidence for 2-year studies (all routes): 2/190 (1.3% ± 2.3%, range 0-4%)

[b] Historical control incidence for 2-year studies (all routes): 1/190 (0.7% ± 1.2%, range 0-2%)

CDMA: Neoplastic lesions of the pituitary gland

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	89	90	90	90
Adenoma[a]	17	25	34*	13

Data presented as number of rats with the lesion

[a] Historical control incidence for 2-year studies (all routes): 47/239 (19.8% ± 7.5%, range 10-28%)

* Statistically significant, $P < 0.05$

CDMA: Neoplasms of the adrenal medulla

Females	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	86	89	87	88
Benign pheochromocytoma[a]	1	7	3	4
Malignant pheochromocytoma[b]	0	2	1	0
Benign, malignant, or complex pheochromocytoma[c]	1	9*	5	4

Data presented as number of rats with the lesion

[a] Historical control incidence for 2-year studies (all routes): 4/235 (1.8% ± 2.9%, range 0-6%)

[b] Historical control incidence for 2-year studies (all routes): 2/235 (1.0% ± 2.0%, range 0-4%)

[c] Historical control incidence for 2-year studies (all routes): 6/235 (2.8% ± 4.8%, range 0-10%)

* Statistically significant, $P < 0.05$

CDMA: Neoplasms of the liver

Males	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	89	88
Hepatocellular adenoma[a]	0	2	4	0
Hepatocellular carcinoma[b]	0	0	1	1
Hepatocellular adenoma or carcinoma[c]	0	2	4	1

Data presented as number of rats with the lesion

[a] Historical control incidence for 2-year studies (all routes): 1/240 (0.5% ± 1.0%, range 0-2%)

[b] Historical control incidence for 2-year studies (all routes): 0/240 (0%)

[c] Historical control incidence for 2-year studies (all routes): 1/240 (0.5% ± 1.0%, range 0-2%)

CDMA: Other nonneoplastic lesions in males

Prostate Gland	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	85
Epithelial hyperplasia	5	11	9	15*
Kidney	0 W/kg	1.5 W/kg	3 W/kg	6 W/kg
Number examined	90	90	90	87
Chronic progressive nephropathy	88 [3.7]	90 [3.3]	90 [3.0]	86 [2.3]

Data presented as number of rats with the lesion; non-neoplastic lesions: incidence [average severity]
* Statistically significant, $P < 0.05$

- SAR-dependent decreases in the incidences and severities of a broad spectrum of lesions considered to be secondary effects of chronic progressive nephropathy
  - Bone, brain, epididymis, heart, intestine, kidney, liver, mesentery, pancreas, parathyroid gland, salivary gland, skeletal muscle, spleen, stomach, testis, and thymus*

*Full list of lesions: Table 55, page 148 of the Draft Technical Report

NTP Conclusions – Males: GSM Modulation

Male Hsd: Sprague Dawley rats exposed to GSM-modulated cell phone RFR at 900 MHz

- ***Some evidence of carcinogenic activity***
  - Incidences of malignant schwannoma in the heart
- May have been related to cell phone RFR exposure (equivocal evidence)
  - Incidences of adenoma or carcinoma (combined) in the prostate gland
  - Incidences of malignant glioma and benign or malignant granular cell tumors in the brain
  - Incidences of adenoma of the pars distalis in the pituitary gland
  - Incidences of pheochromocytoma (benign, malignant, or complex combined) in the adrenal medulla
  - Incidences of pancreatic islet cell adenoma or carcinoma (combined)

Nonneoplastic lesions occurred in the heart, brain, and prostate gland

NTP Conclusions – Females: GSM Modulation

Female Hsd: Sprague Dawley rats exposed to GSM-modulated cell phone RFR at 900 MHz

- ***No evidence of carcinogenic activity***

Nonneoplastic lesions occurred in the heart, thyroid, and adrenal gland

NTP Conclusions – Males: CDMA Modulation

Male Hsd: Sprague Dawley rats exposed to CDMA-modulated cell phone RFR at 900 MHz

- ***Some evidence of carcinogenic activity***
  - Incidences of malignant schwannoma in the heart
- May have been related to cell phone RFR exposure (equivocal evidence)
  - Incidences of malignant glioma in the brain
  - Incidences of adenoma of the pars distalis in the pituitary gland
  - Incidences of adenoma or carcinoma (combined) of the liver

Nonneoplastic lesions occurred in the heart, brain, and prostate gland

NTP Conclusions – Females: CDMA Modulation

Female Hsd: Sprague Dawley rats exposed to GSM-modulated cell phone RFR at 900 MHz

- ***Equivocal evidence of carcinogenic activity***
  - Incidences of malignant glioma in the brain
  - Incidences of pheochromocytoma (benign, malignant, or complex combined) in the adrenal medulla

Nonneoplastic lesions occurred in the brain