

Results of the NTP Studies of Cell Phone Radiofrequency Radiation in B6C3F1/N Mice

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Cell phone RFR research program

- 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 (series of 10 studies)
 - **28-day prechronic** toxicology studies
 - SARs in rats: 3, 6, and 9 W/kg (*in utero* exposures)
 - SARs in mice: 5, 10, and 15 W/kg
 - **2-year** toxicology and carcinogenicity studies
 - 14-week interim evaluation (histopathology, genetic toxicity, hematology)
 - SARs in rats: 1.5, 3, and 6 W/kg (*in utero* exposures)
 - SARs in mice: 2.5, 5, and 10 W/kg



- 28-Day studies
- 2-Year study designs
- Genetic toxicology test results
 - Micronucleus and comet assay
- Pathology results
- Level of Evidence conclusions



- 28-Day studies

- 10 male and female B6C3F1/N mice per power level (specific absorption rate, SAR), per modulation (GSM and CDMA)
- 5-weeks old at study initiation
- SAR exposures of 0, 5, 10, and 15 W/kg
 - 15 W/kg based on thermal pilot results demonstrating no significant radiofrequency radiation (RFR) exposure-related change in body temperature with exposures up to 12 W/kg
 - Upper limit based on the limitations of the capacity of the exposure system to deliver high levels of RFR
- Daily RFR exposures were for 9 hrs 10 min (*18 hrs 20 min per day in 10 min on/10 min off cycles*)
- Evaluation of body temperature with implanted microchips at 7 timepoints



Summary of findings – 28-Day study

- No exposure-related effects were observed on clinical signs of toxicity, organ weights, or histopathology
- In males there were increased incidences of higher body temperatures at several timepoints at ≥ 5 W/kg GSM and at ≥ 10 W/kg CDMA



- 2-Year studies
 - 105 Male and female B6C3F1/N mice per power level (SAR), per modulation (GSM and CDMA) for 7 days a week up to 106 weeks
 - 5-Weeks old at study initiation
 - SAR exposures of 0, 2.5, 5, and 10 W/kg
 - 10 W/kg based on limitations of the capacity of the exposure system to deliver high levels of RFR to a large number of animals
 - Daily RFR exposures were for 9 hrs 10 min (*18 hrs 20 min per day in 10 min on/10 min off cycles*)
 - 14-Week interim evaluation
 - 10 Male and female mice were evaluated for hematology, organ weights, histopathology, and sperm motility and count and vaginal cytology
 - 5 Male and female mice were evaluated for genetic toxicity (comet and micronucleus assays)



14-Week interim evaluation: Micronucleus test

- No increases in the frequencies of micronucleated immature or mature erythrocytes in male or female mice exposed to either modulation after 14 weeks of exposure

Species	Modulation	W/kg	Sex	Result
Mouse	CDMA	0, 2.5, 5, 10	Male	Negative
			Female	Negative
Mouse	GSM	0, 2.5, 5, 10	Male	Negative
			Female	Negative



14-Week interim evaluation: Comet assay results

- Tissues evaluated: Frontal cortex, hippocampus, cerebellum, liver, and blood

 Positive  Negative

		MALE MICE				
CDMA	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood	
GSM	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood	

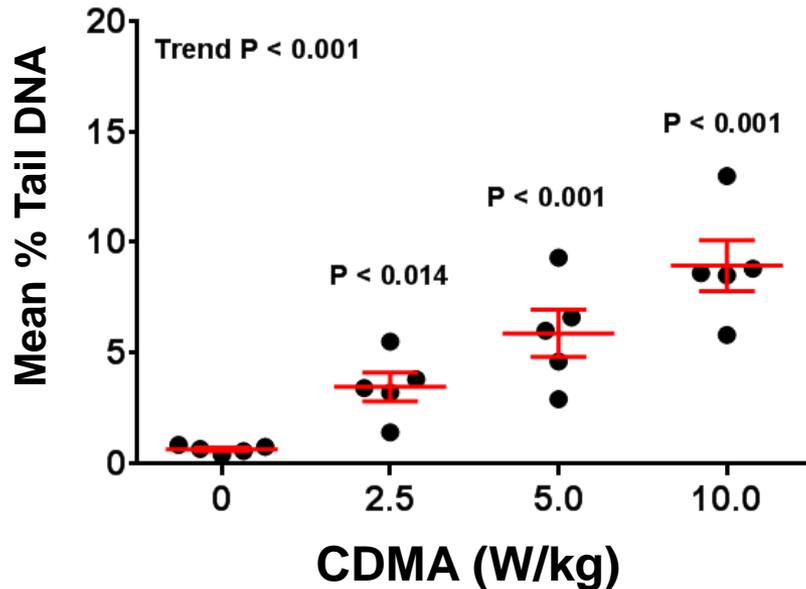
		FEMALE MICE				
CDMA	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood	
GSM	Frontal Cortex	Hippocampus	Cerebellum	Liver	Blood	



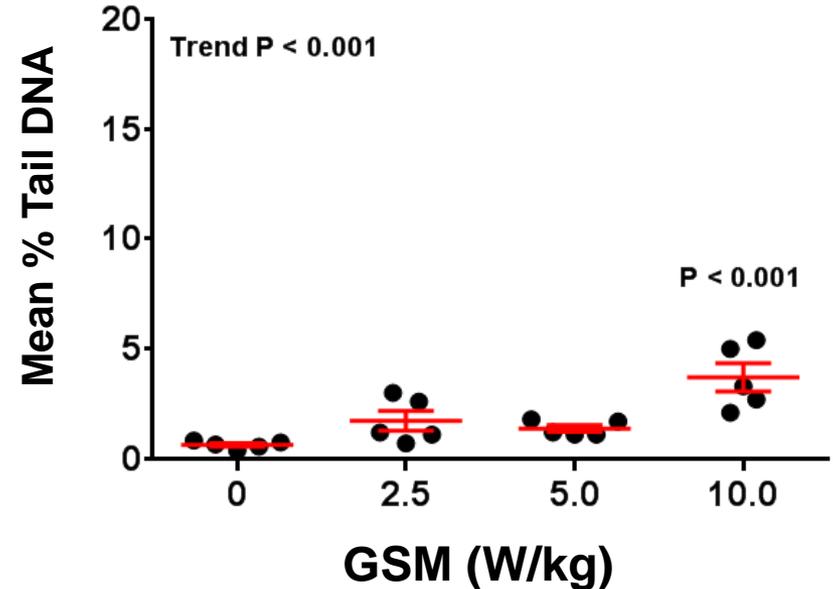
Comet assay results in male B6C3F1/N mice

Positive results

A Male Mouse Frontal Cortex



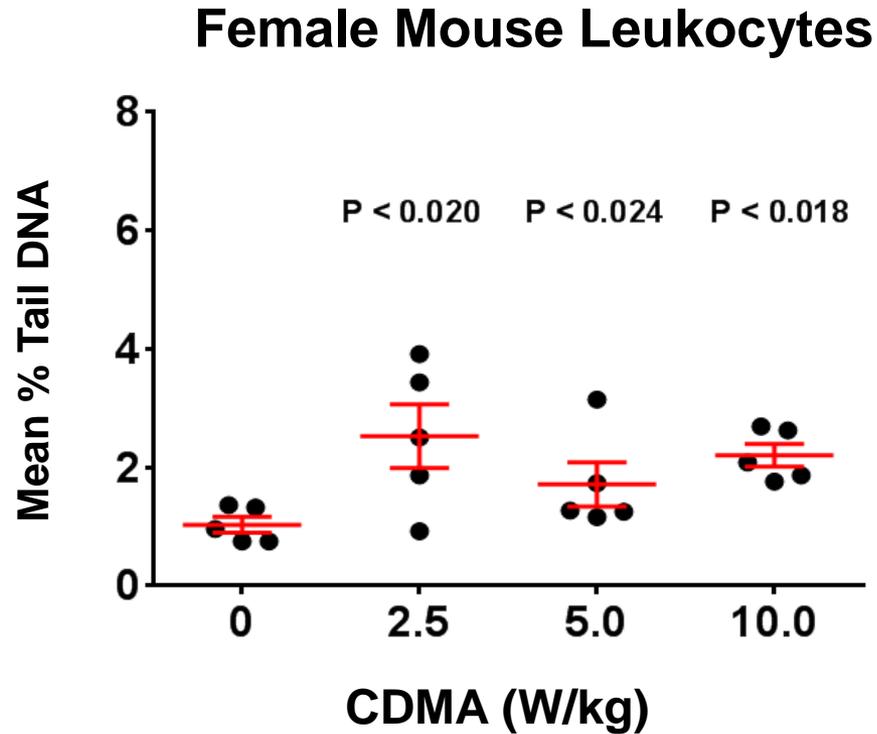
B Male Mouse Frontal Cortex





Comet assay results in female B6C3F1/N mice

Positive results

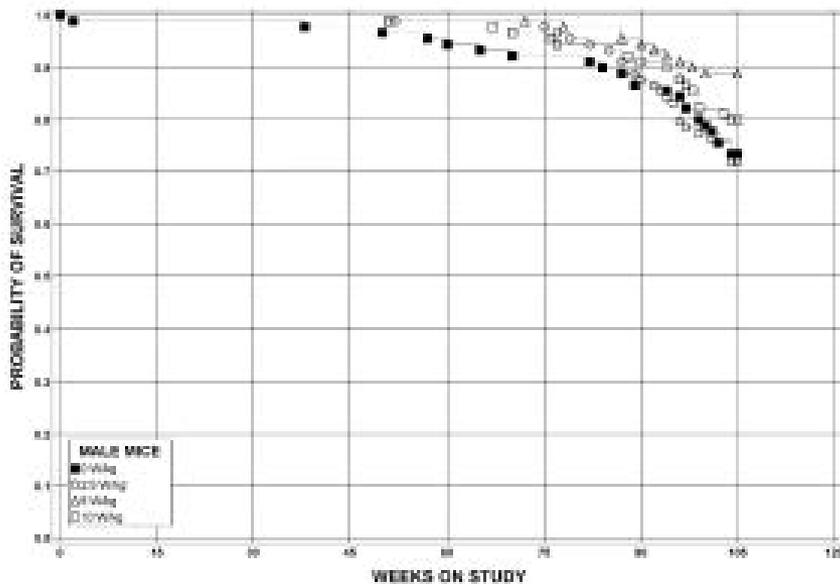




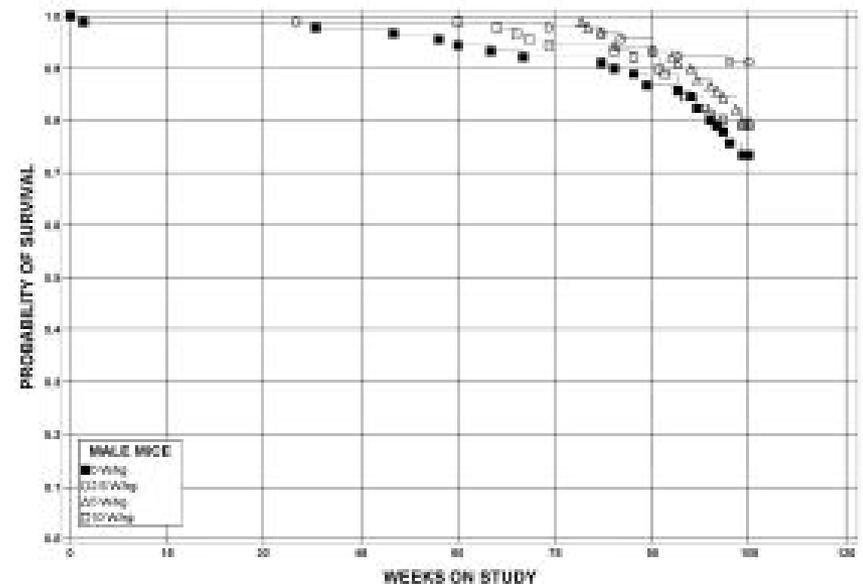
Summary of findings – 2-Year studies

- Increased survival in males at 5 W/kg GSM and at 2.5 W/kg CDMA

Survival Curve for GSM Males



Survival Curve for CDMA Males





Summary of findings – 2-Year studies

- All histopathological findings in mice were considered equivocal findings

GSM Males		CDMA Males	
Organ	Lesion	Organ	Lesion
Skin	Malignant Fibrous Histiocytoma	Liver	Hepatoblastoma
Lung	Alveolar/Bronchiolar Adenoma or Carcinoma (combined)	-----	-----
GSM Females		CDMA Females	
Organ	Lesion	Organ	Lesion
All organs	Malignant Lymphoma	All organs	Malignant Lymphoma



GSM: Neoplastic lesions in males

Skin	0 W/kg	2.5 W/kg	5 W/kg	10 W/kg
Number examined	90	89	90	90
Malignant fibrous histiocytopoma ^a	1	0	5	3
Fibrosarcoma, sarcoma, or malignant fibrous histiocytopoma ^b	1	1	5	4

Data presented as number of mice with the lesion

^a Historical control incidence for 2-year studies (all routes): 2/589 (0.3% ± 0.7%, range 0%-2%)

^b Historical control incidence for 2-year studies (all routes): 5/589 (0.8% ± 1.0%, range 0%-2%)



GSM: Neoplastic lesions in males

Skin	0 W/kg	2.5 W/kg	5 W/kg	10 W/kg
Number examined	90	89	90	90
Malignant fibrous histiocytoma ^a	1	0	5	3
Fibrosarcoma, sarcoma, or malignant fibrous histiocytoma ^b	1	1	5	4
Lung				
Number examined	90	89	90	90
Alveolar/bronchiolar adenoma ^c	13	13	18	16
Alveolar/bronchiolar carcinoma ^d	13	12	16	18
Alveolar/bronchiolar adenoma or carcinoma ^e	23*	24	32	34

Data presented as number of mice with the lesion

^a Historical control incidence for 2-year studies (all routes): 2/589 (0.3% ± 0.7%, range 0%-2%)

^b Historical control incidence for 2-year studies (all routes): 5/589 (0.8% ± 1.0%, range 0%-2%)

^c Historical control incidence for 2-year studies (all routes): 84/589 (14.3% ± 5.4%, range 8%-24%)

^d Historical control incidence for 2-year studies (all routes): 66/589 (11.0% ± 4.4%, range 4%-20%)

^e Historical control incidence for 2-year studies (all routes): 142/589 (24.0% ± 5.3%, range 16%-34%)

* Statistically significant, P < 0.05



GSM: Malignant lymphoma in females

All organs	0 W/kg	2.5 W/kg	5 W/kg	10 W/kg
Number examined	90	90	90	90
Malignant lymphoma ^a	2	13*	9*	6

Data presented as number of mice with the lesion

^a Historical control incidence for 2-year studies (all routes): 89/590 (16.0% \pm 8.3%, range 2%-36%)

* Statistically significant, $P < 0.05$



CDMA: Neoplastic lesions in males

Liver	0 W/kg	2.5 W/kg	5 W/kg	10 W/kg
Number examined	90	89	90	90
Hepatocellular adenoma ^a	52	66*	55	62
Hepatocellular carcinoma ^b	28	18	25	31
Hepatoblastoma ^c	6	6	16*	7
Hepatocellular adenoma, hepatocellular carcinoma, or hepatoblastoma ^d	68	70	69	75

Data presented as number of mice with the lesion

^a Historical control incidence for 2-year studies (all routes): 308/589 (51.9% ± 10.3%, range 34%-70%)

^b Historical control incidence for 2-year studies (all routes): 164/589 (27.6% ± 8.3%, range 16%-42%)

^c Historical control incidence for 2-year studies (all routes): 19/589 (3.0% ± 2.2%, range 0%-7%)

^d Historical control incidence for 2-year studies (all routes): 408/589 (68.8% ± 8.6%, range 53%-80%)

* Statistically significant, P < 0.05



CDMA: Malignant lymphoma in females

All organs	0 W/kg	2.5 W/kg	5 W/kg	10 W/kg
Number examined	90	89	90	90
Malignant lymphoma ^a	2	9*	6	7

Data presented as number of mice with the lesion

^a Historical control incidence for 2-year studies (all routes): 89/590 (16.0% \pm 8.3%, range 2%-36%)

* Statistically significant, $P < 0.05$



Conclusions – GSM Modulation

Male B6C3F1/N mice exposed to GSM-modulated cell phone RFR at 1,900 MHz

- ***Equivocal evidence of carcinogenic activity***
 - Combined incidence of fibrosarcoma, sarcoma, or malignant fibrous histiocytoma in the skin
 - Incidences of alveolar/bronchiolar adenoma or carcinoma (combined) in the lung

Female B6C3F1/N mice exposed to GSM-modulated cell phone RFR at 1,900 MHz

- ***Equivocal evidence of carcinogenic activity***
 - Incidences of malignant lymphoma (all organs)

Exposure to GSM-modulated cell phone RFR at 1,900 MHz did not increase the incidence of any nonneoplastic lesions in male or female B6C3F1/N mice



Conclusions – CDMA Modulation

Male B6C3F1/N mice exposed to CDMA-modulated cell phone RFR at 1,900 MHz

- ***Equivocal evidence of carcinogenic activity***
 - Incidences of hepatoblastoma of the liver

Female B6C3F1/N mice exposed to CDMA-modulated cell phone RFR at 1,900 MHz

- ***Equivocal evidence of carcinogenic activity***
 - Incidences of malignant lymphoma (all organs)

Exposure to CDMA-modulated cell phone RFR at 1,900 MHz did not increase the incidence of any nonneoplastic lesions in male or female B6C3F1/N mice