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Carcinogenicity Study of GSM and DCS Wireless Communication Signals in B6C3F1 Mice

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The purpose of this study using a total of 1170 B6C3F1 mice was to detect and evaluate possible carcinogenic effects in mice exposed to radio-frequency-radiation (RFR) from Global System for Mobile Communication (GSM) and Digital Personal Communications System (DCS) handsets as emitted by handsets operating in the center of the communication band, that is, at 902 MHz (GSM) and 1747 MHz (DCS). Restrained mice were exposed for 2 h per day, 5 days per week over a period of 2 years to three different whole-body averaged specific absorption rate (SAR) levels of 0.4, 1.3, 4.0 mW/g bw (SAR), or were sham exposed. Regarding the organ-related tumor incidence, pairwise Fisher's test did not show any significant increase in the incidence of any particular tumor type in the RF exposed groups as compared to the sham exposed group. Interestingly, while the incidences of hepatocellular carcinomas were similar in EMF and sham exposed groups, in both studies the incidences of liver adenomas in males decreased with increasing dose levels; the incidences in the high dose groups were statistically significantly different from those in the sham exposed groups. Comparison to published tumor rates in untreated mice revealed that the observed tumor rates were within the range of historical control data. In conclusion, the present study produced no evidence that the exposure of male and female B6C3F1 mice to wireless GSM and DCS radio frequency signals at a whole body absorption rate of up to 4.0 W/kg resulted in any adverse health effect or had any cumulative influence on the incidence or severity of neoplastic and non-neoplastic background lesions, and thus the study did not provide any evidence of RF possessing a carcinogenic potential. Bioelectromagnetics 28:173–187, 2007. © 2006 Wiley-Liss, Inc.

Key words: radiofrequency; mobile phones; cancer; animal study

INTRODUCTION

At the beginning of the 1970s, one of the first animal studies in the field of long term (pulsed) radiofrequency (RF) exposure [Prausnitz and Süsskind, 1962] raised much controversial attention by assuming an apparent correlation between the exposure and the development of ''leucosis'' in mice, while Roberts and Michaelson [1983], reanalyzing the (original) data more than 20 years later, could not prove such an association of RF exposure and cancer. More recently, huge public attention was raised by Lai and Singh [1995, 1996], who demonstrated DNA strand breaks and thus a possible link to tumorigenesis, related to RF exposure, although thereafter other in vitro studies could not confirm these findings [for a topical review see Verschaeve, 2005]. Today, much attention is still being paid to an Australian transgenic animal study [Repacholi et al., 1997], indicating a lymphoma increase in mice chronically exposed to cellular telephone radiation, although the results of a replication

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study [Utteridge et al., 2002, 2003], which attracted considerably less public interest, were negative.

Apart from other (methodical) shortcomings (e.g., one exposure level only, inaccurate dosimetry, insufficient group sizes, no standardized histopathological examination), the different signal characteristics applied so far (carrier frequency, pulsation, near and far fields, transfer rate, etc.) in the existing RF literature may illustrate the difficulty in comparing these studies and their exceedingly problematical assignment for risk assessment of the currently used cellular phone technology [for a topical review see e.g., Elder, 2003; Dasenbrock, 2005; Moulder et al., 2005]. In response to this insufficient state of data as it existed in the late 1990s, the research program with the acronym PERFORM-A, including two National Toxicology Program (NTP)-type (National Toxicology Program of the US National Institute of Environmental Health Sciences) carcinogenicity studies conducted in both sexes of two different rodent species [Chhabra et al., 1990], mice (PERFORM-A1) and rats (PERFORM-A2), and two studies using animals predisposed to tumor development mammary tumor (PERFORM-A3) and lymphoma (PERFORM-A4), was initiated to address research on potential long-term health implications from the use of mobile phones. The physical agents were fields simulating handset exposure from the dominant mobile communications systems in Europe, that is, Global System for Mobile Communications (GSM) and Digital Personal Communications System (DCS), applied at three exposure levels and sham, to also obtain information about the dose response. Strictly speaking, these animal experiments (PERFORM-A1/A2) were performed as ''classical'' combined chronic toxicity and carcinogenicity studies, equivalent to investigations routinely performed to evaluate the health risks of chemicals, pharmaceuticals, or environmental agents.

The long-term study presented below was conducted to detect and evaluate possible carcinogenic effects in B6C3F1 mice exposed to GSM and DCS signals for 2 h per day, 5 days per week over a period of 2 years.

MATERIALS AND METHODS

The study was approved according to the German Animal Welfare Act by the local authority at the Bezirksregierung, Hannover, Germany. In addition, the study was performed in compliance with the principles of Good Laboratory Practice (German Chemicals Law, § 19a, Appendix 1, June 28, 2002), with the exception of the technical aspects of electromagnetic field (EMF) exposure, and taking into consideration guideline No. 453 for the testing of chemicals of the Organisation for Economic Co-operation and Development (OECD).

The study, including histopathology, was performed blind to all scientists involved except for the IT'IS staff controlling/monitoring the daily RF exposure. In reverse, the IT'IS staff did not know the group identifier. The key codes and identifier were not disclosed until after completion of the histopathological evaluation and handover of the still blinded raw data to the representatives of the sponsors.

Animals and Environment

Male and female mice (B6C3F1/Crl BR), 4–5 weeks of age at delivery, were purchased from Charles River Deutschland (Sulzfeld, Germany). Prior to start of the exposure period, the mice were acclimatized for about 4 weeks in the animal facility. Starting in the first week after receipt of the animals, a training program was performed to accustom the animals to the exposure tubes for increasing periods of time, that is, from 3–5 min on the first day of training up to 2.5 h after 3–4 weeks. During this time, the animals were observed daily. Body weight and food consumption were measured in the last week of this period.

The animals accepted for this study demonstrated good general health based on the collected data. Male (585) and female (585) B6C3F1 mice were randomized by weight via a computer-generated randomization program into 9 male or female treatment groups (2 × 4 RF dose groups and one untreated cage control group,

TABLE 1. Study Groups

Decoded exposure level[a]	N	Sex	Frequency	Restraint duration (daily, 5 days/week)
—-	50 + 15	M	Cage control	—
—-	50 + 15	F	Cage control	—
Sham	50 + 15	M	902 MHz	2 h
Sham	50 + 15	F	902 MHz	2 h
Low	50 + 15	M	902 MHz	2 h
Low	50 + 15	F	902 MHz	2 h
Medium	50 + 15	M	902 MHz	2 h
Medium	50 + 15	F	902 MHz	2 h
High	50 + 15	M	902 MH+	2 h
High	50 + 15	F	902 MHz	2 h
Sham	50 + 15	M	1747 MHz	2 h
Sham	50 + 15	F	1747 MHz	2 h
Low	50 + 15	M	1747 MHz	2 h
Low	50 + 15	F	1747 MHz	2 h
Medium	50 + 15	M	1747 MHz	2 h
Medium	50 + 15	F	1747 MHz	2 h
High	50 + 15	M	1747 MHz	2 h
High	50 + 15	F	1747 MHz	2 h
Total	1170	M + F		

[a]Decoded exposure level after completion of the histopathological evaluation.

see Table 1), each consisting of 65 mice of the same gender, of which 50 mice were employed in the carcinogenicity study. The additional 15 animals were used for interim investigations, analyzing organ weights, hematology, gross pathology, and histopathology after a 12-month exposure period. The number of mice per sex and treatment group used was derived from the guidelines (NTP, OECD, EPA) successfully utilized for decades in testing chemicals and pharmaceuticals. Additionally, 30 males and 30 females (not included in Table 1) were assigned as sentinel animals for microbiological health status examination.

With the exception of the daily tube restraint (RF exposure: 2 h/day, 5 day/week), the animals were housed under barrier conditions in Makrolon® (polycarbonate) type II ($22 \times 16 \times 14$ cm) cages in two standard animal rooms, one for the GSM experiment and one for the DCS experiment. During the course of the study, except during the daily exposure (2 h/day, 5 days/week) in fixation tubes, males were caged individually, whereas females were housed two per cage. Absorbent softwood was used as bedding material in the cages (altromin 3/4, Altromin International, Lage, Germany). The cages were changed twice weekly. Food was offered fresh weekly. The diet used (altromin 1324N specially prepared) was supplied by Altromin International. Drinking water was from the Hannover city water supplier, offered fresh weekly in Makrolon® bottles ad libitum, except during exposure.

Temperature and relative humidity were recorded continuously. The values in the animal room were set at 22 ± 2 °C for temperature and 30–70% for relative humidity. The animal room lighting was on a 12 h light/dark cycle controlled by an automatic timing device. The air flow rate was adjusted to 12–15 air exchanges per hour.

The microbiological health status of the animals was monitored during the entire study according to FELASA recommendations [FELASA, 2002]. All animals were checked at least once a day for clinical symptoms, morbidity, or mortality. Food consumption and individual body weights were recorded weekly during the first 13 weeks of the study and after that once per month till study termination. All weight data were collected by on-line data acquisition (DATATOX, Instem Computer Systems, Stone, Great Britain, version rC.10).

To ensure that each animal would receive the same exposure/restraint time, loading and unloading in the exposure wheel was done in the same order of animals (time to load one complete wheel: 30 min; complete unloading time: 20 min), resulting in an additional restraint time up to 32 min for each mouse (first in–first out). Four animal caretakers (one for each wheel) were responsible for this procedure. Exposure of all (four) wheels (dose groups) per room/frequency was started simultaneously. In addition, the order of the two daily exposure shifts was reversed every week.

GSM and DCS Exposure Systems

Requirements on the two exposure systems posed by the experimental design included constant age-independent and uniform whole-body exposure of mice to EMFs simulating the fields induced in human tissues during usage of GSM and DCS handsets at three different exposure levels or sham. Further requirements were blinded exposure, minimal space, and compatibility with the experimental requirements of NTP. The dosimetry had to provide information about whole body, organ and peak spatial averaged specific absorption rates (SAR) as well as about uncertainty and instant and lifetime variations.

The exposure systems for mice consisted of a signal generation unit, control and monitoring unit, and four ''Ferris wheel'' exposure units for each frequency (see Fig. 1). Each exposure unit, enabling exposure of up to 65 animals, was excited to a different SAR level, resulting in four dose levels (high, medium, low, and sham). The ''Ferris wheel'' concept developed by Balzano et al. [2000] was adopted and optimized for this study. Each wheel consisted of two parallel, circular, stainless steel metal plates 117 mm apart, with a conical (GSM) or bi-conical (DCS) antenna in their center, and stainless steel poles constituting a short-cut of the cylindrical cavity at a radius of 755 mm. The positions of the animals, restrained in tubes similar to those used and approved for inhalation studies (see Fig. 2), were optimized for maximum uniformity (GSM at a radius

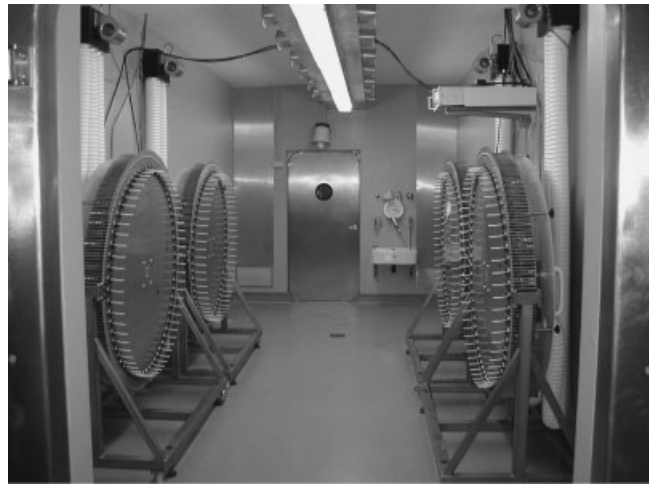

Fig. 1. Exposure setups. One of two animal rooms with an exposure system for mice (i.e., GSM [902 MHz] or DCS [1747 MHz]) consisting of four wheels, three for the different whole body SAR levels and a sham exposure wheel, and related ventilation system.

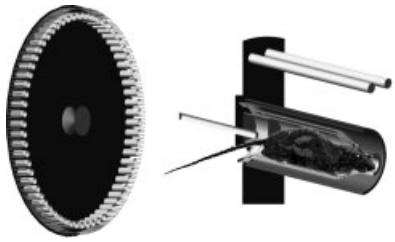

Fig. 2. Exposure wheel and restraint tube. Mouse exposure cavity showing the bi-conical antenna in the center, short-cut poles at the perimeter, the outer holding tubes and the inhalation-like tubes to restrain the mice (two sizes were used) including dielectric stopper that prevented the animals from turning [Ebert et al., 2006].

(center of wheel to center of tubes) of 700 mm; DCS at 670 mm). In order to maintain a symmetrical load, missing animals were replaced by conical plastic tubes filled with 36 ml of liquid simulating the dielectrical parameters of muscle tissue at the corresponding frequencies. The ventilation system guaranteed an airflow of 1 L/min at the snout of the animal.

The wheels were excited by one 200 W amplifier (LS Electronic, Spanga, Sweden). Each of the four active bursts (slot 0, 2, 4, 6) per frame of the output signal was sequentially multiplexed to the different wheels, that is, each wheel was excited by one slot. The frame signal, modulated by a standard random code, was produced by the vector signal generator SMIQ02B (Rhode & Schwarz, Munich, Germany). The subsequent digital control unit (SPEAG, Zurich, Switzerland) generated the appropriate frame structure and enabled switching between the discontinuous transmission mode (DTX) and non-DTX frames without interruption. The same unit also controlled the PIN-diode 4-channel switch at the output of the amplifier. The amplifiers were water-cooled to enable placement close to the wheels and therefore the use of short cables. The time multiplexing and the low losses in the cables reduced the peak power requirement and thus also the costs of amplifiers (Figs. 2–4).

The ''Ferris wheel'' provides a very compact design with high efficiency but increased variations due to higher modes. The higher modes could be reduced through introduction of dielectric bricks between the animals at 902 MHz. Details of the setup and dosimetry are provided in Ebert et al. [2006].

Monitoring and Control of Exposure

During the entire experiment, exposure levels were controlled and monitored with two electric field sensors inside each wheel. Exposure levels were adjusted automatically (sampling rate 10 s) whenever there was any drift/change, ensuring stable exposure conditions inside the setup. Environmental parameters such as relative humidity, air temperature, and oxygen level were also recorded for each wheel at all times, even when no exposure took place. In addition to the ambient parameters, all hardware communication was saved in order to be able to reconstruct each experiment. To maximize data security, all data recorded were saved encoded at three different physical locations: the experiment computer, a file server at the Fraunhofer ITEM (Hannover, Germany), and a file server at IT'IS (Zurich, Switzerland) to which the data were transmitted automatically each night.

Exposure Signals and Levels

All signals applied were compliant with the definitions of the GSM or DCS standards. The carrier frequency was set to the mid band of the up-link band, that is, 902 MHz for GSM and 1747 MHz for DCS.

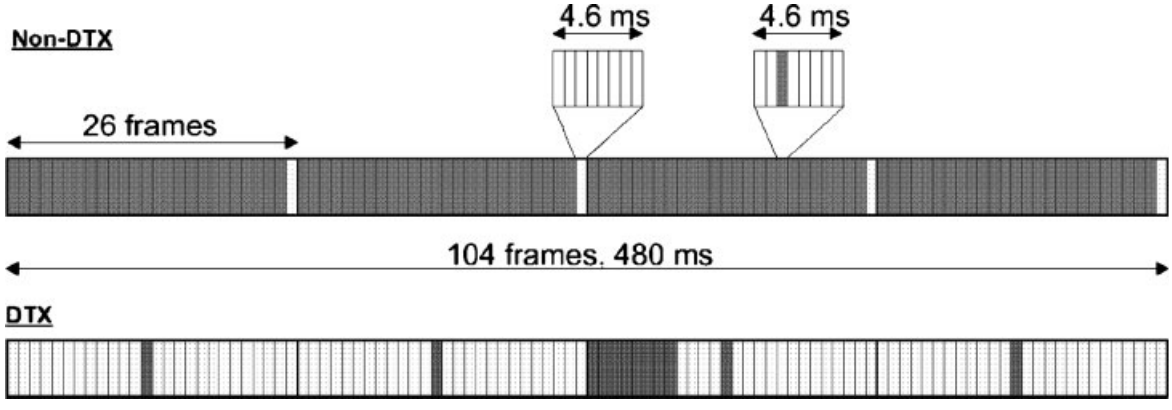

Fig. 3. Multiframe signal structure. Intermediate multiframe structure of the non-DTX and DTX modes, composed of 104 basic frames with a duration of 480 ms. One basic frame consists of eight time slots (0.57 ms with a duration of 4.6 ms. In non-DTX mode, up to 100 out of 104 frames are active, whereas in DTX mode transmission reduces to 12 active frames, that is, 11.5% of SAR value at non-DTX.

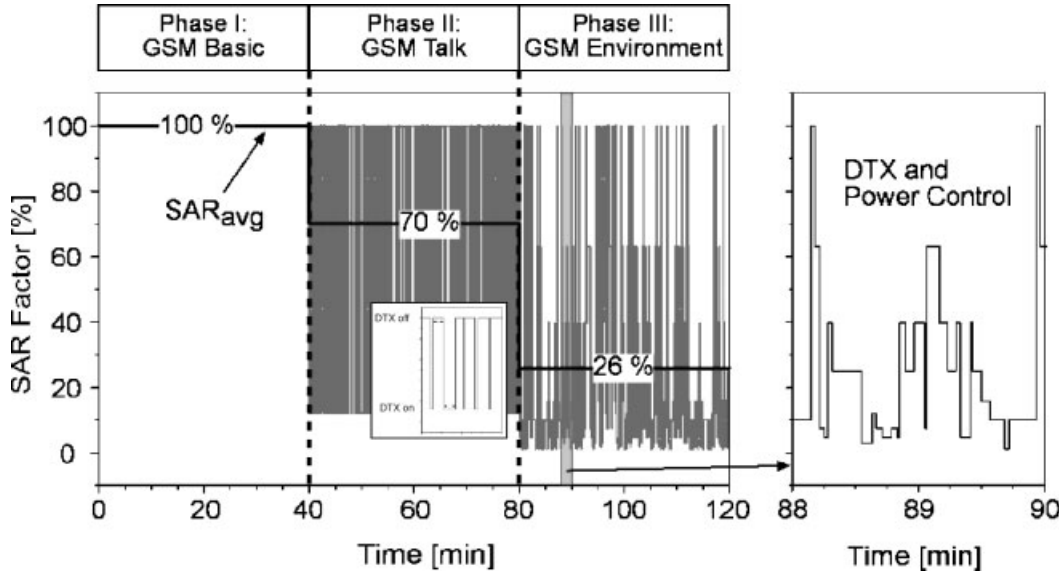

Fig. 4. Exposure phases. The applied exposure signal applied consists of three phases, each of 40 min duration. Phase I: GSM Basic signal modulation (no DTX, no power control). Phase II: GSM Talk consists of temporal changes between a non-DTX signal (average duration 10.8 s) and DTX signal (average duration 5.6 s). No power control features were active. Phase III: GSM Environment consists of a GSM Talk signal that is further amplitude-modulated by a power control function; the waveform of the power control function, as it would occur with movement in a GSM network environment, is statistically calculated, based on data presented by Wiart et al. [2001]. The peak SAR level for all three phases is constant; however, the resulting average SAR level varies: 100% (GSM Basic), 70% (GSM Talk), and 26% (GSM Environment).

In each exposure session (duration 2 h), all exposure elements as they occur during usage of a mobile phone in the environment were delivered in three phases of 40 min duration each (Fig. 4). Each slot was modulated with a random code by a standard setting of the signal generator (Fig. 3). In the first phase, non-DTX mode (''GSM Basic'') was applied with the exposure condition as it occurs during continuous talking, that is, one active slot per basic frame, while every 26th basic frame was idle. This exposure constitutes the highest time-averaged exposure condition. The second phase (''GSM Talk'') simulated a conversation, that is, a random change between the non-DTX (average time active: 2/3) and DTX (average time active: 1/3) modes. This signal provides the most coherent signal with strong amplitude-modulation component of 2, 8, and 217 Hz including their harmonics. The third phase (''GSM Environment'') simulated exposure during a conversation while moving in the environment. This included GSM features such as non-DTX, DTX, power control, and handovers etc. according to their statistical occurrence [Mertens et al., 2001]. The statistical parameters were derived from measurements performed by France Telecom [Wiart et al., 2001]. The condition provides a lower time-averaged exposure but the largest variety of possible low frequency amplitude-modulation components.

In each of the four or rather eight wheels, the tube-restrained animals received a different exposure: high, medium, low, and sham dose. Several pre-tests (902 MHz and 1747 MHz, continuous wave (cw) signals or a three-phase GSM/DCS signal exposure as used in this study) were conducted to confirm that the endpoints would not be affected at the highest dose levels [Kamlage, 2002]. In addition, the thermal threshold and breakdown levels were determined in a separate study [Ebert et al., 2005]. The latter revealed that the high dose level was close to, yet below, the thermal threshold.

The incident field was adjusted according to a numerically determined dose-weight function in order to maintain the same exposure independent of the animal's weight/age. Table 2 shows the dose levels applied for each of the three phases. The maximum slot-averaged whole-body average exposure was the same for all three phases and approximately corresponds to the maximum local exposure during a telephone conversation. Table 3 provides the exposure levels of each organ relative to the whole-body average SAR values including absolute SAR uncertainty ($k=2$) and instant and lifetime averaged variations ($k=1$) of the exposure. These values were assessed using the methodology of Kuster et al. [2006].

TABLE 2. Exposure Levels of GSM/DCS Averaged Over the Whole-body and 2 Years

	High dose	Medium dose	Low dose	Sham
	GSM/DCS exposures			
Maximum slot average exposure [mW/g]	33.2	11.1	3.7	Sham
Phase I: time- and whole body average exposure [mW/g]	4.0	1.3	0.4	Sham
Phase II: time- and whole body average exposure [mW/g]	2.8	0.93	0.35	Sham
Phase III: time- and whole body average exposure [mW/g]	1.0	0.35	0.11	Sham
Uncertainty ($k=2$) [dB][a]	±2.6/2.2	±2.6/2.2	±2.6/2.2	—
Instant variations ($k=1$) [dB]	±2.2/1.6	±2.2/1.6	±2.2/1.6	—
Life-time averaged variations ($k=1$) [dB]	±1.2/0.8	±1.2/0.8	±1.2/0.8	—

The corresponding values of the organs are given in Table 3.
[a]The uncertainties are provided as determined in Ebert et al. [2006].

The spatial peak SAR at 4 W/kg of 250 W/kg at GSM and 30 W/kg at DCS largely exceeds the maximum spatial peak SAR during mobile phones usage ranging from 0.1 to 2 W/kg depending on phone type. The averaged absorption in the brain of the mice of 2.5 W/kg at GSM and 5 W/kg at DCS were considerable larger than the average human brain exposure and even as the maximum spatial peak SAR in the human cortex

TABLE 3. Organ Averaged SAR

	SAR_{organ}/SAR_{WB} (group and lifetime average)		Uncertainty ($k=2$)		Variations (instant) ($k=1$)		Variations (lifetime averaged) ($k=1$)	
Tissue	GSM	DCS	GSM (dB)	DCS (dB)	GSM (dB)	DCS (dB)	GSM (dB)	DCS (dB)
Whole-body	1.0	1.0	±2.6	±2.2	±2.2	±1.6	±1.2	±0.8
Peak spatial (5 mg)	62	7.8	±6.0	±2.3	±4.4	±2.3	±2.6	±1.7
Peak spatial (0.5 mg)	85	10.2	±5.7	±3.2	±3.3	±2.8	±1.8	±2.1
Bladder	0.87	0.51	±4.0	±3.0	±3.6	±3.5	±1.6	±1.6
Blood	1.4	3.3	±2.7	±2.3	±2.9	±2.3	±2.1	±1.4
Bone marrow	0.35	0.25	±3.4	±3.2	±4.2	±3.2	±3.2	±2.4
Bones	0.18	0.18	±2.8	±2.3	±2.8	±2.3	±2.1	±1.7
Brain	0.62	1.26	±2.6	±2.3	±2.8	±3.1	±1.3	±2.0
Cartilages	0.68	1.4	±2.7	±2.5	±2.5	±3.0	±1.7	±2.0
Eyes	0.69	0.72	±2.6	±2.4	±2.4	±2.9	±1.3	±2.1
Fat	0.19	0.14	±3.0	±2.3	±2.7	±2.0	±1.5	±1.2
Gland, lacrimal	0.69	0.83	±2.6	±2.4	±2.3	±2.9	±1.3	±2.1
Glands	1.15	2.0	±2.9	±2.7	±3.8	±2.8	±1.8	±1.5
Heart	1.20	2.7	±3.0	±2.3	±3.8	±2.7	±2.2	±1.1
Kidneys	1.17	0.72	±2.7	±2.8	±3.3	±2.9	±1.6	±2.1
Large intestine	1.05	1.07	±2.8	±2.6	±3.3	±2.2	±1.7	±1.1
Liver	1.05	1.26	±2.7	±2.6	±2.6	±2.2	±1.7	±1.3
Lungs	1.5	2.8	±2.8	±2.5	±3.6	±2.5	±1.7	±1.3
Muscles	1.02	1.12	±2.6	±2.2	±2.6	±2.1	±1.7	±1.3
Nerves	0.51	0.87	±3.8	±3.1	±2.6	±2.7	±1.8	±2.0
Esophagus	1.12	2.5	±3.2	±3.1	±2.7	±2.4	±2.0	±1.9
Pharynx	0.81	1.20	±2.7	±2.9	±2.3	±2.8	±1.3	±2.1
Skin	0.85	0.54	±2.8	±2.3	±2.7	±2.0	±1.9	±1.2
Small intestine	1.9	1.5	±2.9	±2.5	±3.2	±2.1	±1.9	±1.1
Spinal cord	0.76	1.35	±2.6	±2.5	±2.7	±2.3	±1.7	±1.7
Spleen	1.15	0.37	±3.2	±3.0	±3.5	±2.3	±2.4	±1.1
Stomach	1.00	0.78	±2.9	±2.4	±3.3	±2.7	±2.3	±1.8
Tongue	1.05	1.15	±2.8	±3.3	±2.7	±2.6	±1.3	±2.1
Trachea	0.81	2.0	±2.6	±2.3	±2.7	±2.8	±1.3	±2.2

Spatial peak and organ averaged SAR relative to the whole-body average values (see Table 2) as well as the corresponding standard uncertainty and variations in dB ($dB = 10*\log_{10}\{ratio\}$) [Ebert et al., 2006].

[Kuster et al., 2004]. The whole-body exposure as well as the specific organ SAR were several magnitudes larger than those of humans during phone or base station exposure. The envelope of the signal well simulated exposure conditions occurring during daily usage of GSM handsets.

Pathology and Hematology

Each animal was subjected to complete necropsy. Any animals judged to be moribund were anesthetized with an overdose of CO_2 and necropsied. All animals found dead were necropsied immediately. The physical condition of the animal prior to euthanasia and all macroscopically visible tissue alterations detected during necropsy were described in detail in a necropsy protocol.

Organ weights (brain, heart, lungs, liver, spleen, adrenals, kidneys, gonads) were recorded and blood samples taken on all animals that were sacrificed at the ''chronic toxicity'' time point (12 months of exposure, 15 mice/group/sex). At least 0.5 ml blood per mouse for hematological analysis was obtained in tubes coated with K_2-EDTA (1.5–2 mg/ml) by puncture of the vena cava caudalis. Erythrocyte count, hemoglobin, hematocrit, mean erythrocyte volume, mean erythrocyte hemoglobin mass, mean erythrocyte hemoglobin concentration, platelet count, and total and differential leukocyte counts were analyzed.

Fixation of the lung lobes was carried out by careful intratracheal instillation while all other tissues were immersion-fixed in 10% buffered formalin, trimmed [Bahnemann et al., 1995] and embedded in paraffin. Skulls and bones with macroscopic findings were decalcified in equal portions of sodium citrate (20%) and formic acid (45%) prior to embedding. Embedded tissues were sectioned (3–4 μm thick sections) and stained with hematoxylin and eosin (H&E).

A complete histopathological examination was performed (blind to group/dose level assignment) on all exposed animals, that is, on 1040 mice of the long-term study. Since the untreated/unhandled controls showed a similar mortality as the restrained mice and macroscopic examination during necropsy showed no abnormalities, it was decided to disregard their histopathological examination and the tissues of these 130 cage control animals were just fixed, trimmed, embedded in paraffin, and stored in the archives of the Fraunhofer ITEM.

The slides were examined by light microscopy and observations recorded using an on-line computer program (P.L.A.C.E.S. 2000, Instem Computer Systems). After histopathological examination by the study pathologist, various lesions were selected by an external advisor for a (small-scale) Pathology Working Group (PWG) panel. The selected slides were examined by the PWG and consensus diagnoses were reached on all questionable cases. Neoplasms and pre-neoplastic lesions were diagnosed and classified according to the WHO/IARC nomenclature [WHO-IARC, 2001].

After completion of the histopathological evaluation (all blinded raw data were stored on CD-ROM at the sponsors' site), the assignments between exposure units and dose groups were disclosed by IT'IS.

Statistical Evaluation

Statistical tests on the comparison of treatment groups were performed at the level of $\alpha = 0.05$. Body weight, food consumption, organ weights, and hematology data were analyzed using analysis of variance as a global test. Pairwise comparison of the means of the treatment groups with the means of the sham exposure group were performed using Dunnett's modification of the t-test, two-sided at a level of $\alpha = 0.05$. The experiment-wise error rate was thus controlled in this multiple testing procedure. When appropriate, other statistical tests were used.

Survival data of the animals were analyzed using the Kaplan–Meier test. Peto's analysis was used as a trend test to compare tumor incidences in the groups. For the Peto test, scores were determined according to Peto et al. [1980], where tumors which kill their hosts either directly or indirectly are said to be observed in a fatal context, while other tumors observed at necropsy in animals which died of some unrelated cause are said to be observed in an incidental context. The strata variable is constructed from whether the animal is terminally sacrificed, died by natural death, or is preterminally sacrificed in a moribund condition. All tumors found in terminally sacrificed animals were classified as incidental for analytical purposes. Peto's analysis was conducted with the SAS software (SAS [r] Proprietary Software Release 6.12 TS020).

Significance of differences of the frequencies of histopathological findings was evaluated as pairwise comparison between sham exposure and treatment groups using Fisher's exact test. These tests were performed at the local significance level of $\alpha = 0.05$.

Calculations were done on Alpha Server (SAS) and VAX 6500 (DATATOX) computers (Digital Equipment Corporation) with the Open VMS VAX operating system, version 6.2, and the software packages DATATOX (Instem Computer Systems, version rC.10) and SAS (SAS Institute, CARY, NC, version 6.12).

RESULTS

Exposure Duration

Over a period of 2 years, complete RF exposures (2 h/day) were performed on 98% (GSM) and 99%

(DCS) of the planned 500 target days. During the 2 h of daily exposure, the air supplied to the animals had a temperature of 24 ± 2 °C, oxygen of $20.5 \pm 1\%$ and the humidity between 30 and 70% for both groups.

Health Status

Bacteriological investigations revealed positive results (*Staphylococcus aureus*, *Pasteurella pneumotropica*) without clinical relevance on the mucosal surfaces of single animals. Parasitological and virological examinations during the course of the study revealed no abnormalities, indicating an undisturbed animal study.

Clinical Observations

Main clinical findings were hair loss (alopecia) of the hind limbs, corresponding histologically to atrophy of hair follicles and hyperkeratosis, and joint stiffening of the knee joints (all of slight severity) corresponding to osteoarthropathy. These lesions were observed with increasing incidence during the course of the study in all exposure groups including sham, whereas cage control animals were not affected.

Food Consumption, Body Weight, and Mortality

Compared to the sham exposure group, altered food intake was detected in various RF exposure groups. Differences (increased and decreased consumption), however, were limited to few and singular weeks, revealing no consistency in time or in the different/increased RF dose levels.

Repeated measurements analysis of variance as a global test showed differences in body weight gain for the complete course of the study. Nevertheless, compared to the sham exposure group, differences (decreased and increased body weights) were detected only with some singular measurements, revealing no consistency in respect of time or RF dose level.

At the terminal sacrifice time point at the end of the 2-year exposure period, mortality in the various groups of tube-restrained mice was between 10 and 20% for males and between 20 and 30% for females. Comparing the mortality of the sham and three RF exposure groups statistically, Kaplan–Meier test revealed no remarkable differences in the long-term GSM and DCS exposed groups, either in male or in female mice.

Interim Sacrifices

Thickened skin areas (pressure sores) mainly of the hind limbs were a common finding observed at necropsy after 12 months. Female mice (13–60% of all (sham) exposure groups) were more affected than males (0–7%). Circumscribed hair loss (alopecia) was found in male (0–13%) and female (0–47%) mice of nearly all treatment groups. As mentioned in the clinical observations, cage control animals were not affected, so that both skin lesions have to be considered to be related to the daily restraint in exposure tubes.

Hematological analysis after 12 months of RF exposure showed values in all groups within the normal limits of control animals.

Relative organ weights of the brain, heart, lungs, liver, spleen, adrenals, kidneys, and gonads did not indicate RF exposure-related effects. Significant differences were found only in the lung weights of the males in the DCS study (decreased mean lung weight of the medium-dose group compared to the sham exposure group).

In addition to the above-mentioned skin and hair alterations, which were obviously restraint-related, histopathological results revealed a large variety of sporadic findings, all of which were within the normal range of background alterations commonly seen in mice of this age and strain. All tumor types observed occurred incidentally in single animals of different groups. There were no significant differences (pairwise Fisher's test) in the tumor incidences between any of the exposure groups (GSM, DCS), either in males or in females.

Histopathology

With respect to the number of tumor-bearing animals (TBAs), no substantial differences were observed after 2 years between the sham exposure group and the GSM low, medium, and high dose RF exposure groups (Table 4), either in males or in females. The number of TBAs was about 10% higher in females than in males, irrespective of the dose group.

In males, the number of TBAs was 34/50 (68%) in the GSM sham exposure group, 31/50 (62%) in the GSM low, 33/50 (66%) in the medium, and 32/50 (64%) in the high dose groups. With 39/50 (78%), the number of tumor-bearing females was identical in the sham exposure, the low and high dose groups of GSM exposure, while 37/50 (74%) females of the medium dose group (GSM) had tumors.

In the DCS exposed males, there was a marked dose-dependent decrease in the number of TBAs compared to the sham exposure group (Table 4). The incidence of tumor-bearing males was 37/50 (74%) in the sham exposure group, 30/50 (60%; $P = .202$) in the low, 25/50 (50%; $P = .023$) in the medium, and 24/50 (48%; $P = .013$) in the high dose groups of lifetime DCS exposure. With 37/50 (74%), the number of tumor-bearing females was also highest in the sham exposure group (DCS), while 31/50 (62%; $P = .284$), 35/50

TABLE 4. Tumor Summary—(A) 902 MHz Exposure; (B) 1747 MHz Exposure

A. 902 MHz

	Males				Females			
	902 MHz sham control	902 MHz low dose	902 MHz medium dose	902 MHz high dose	902 MHz sham control	902 MHz low dose	902 MHz medium dose	902 MHz high dose
Number of animals	50	50	50	50	50	50	50	50
Number of animals with tumors	34	31	33	32	39	39	37	39
Number of animals with single tumors	19	18	14	17	21	21	18	19
Number of animals with multiple tumors	15	13	19	15	18	18	19	20
Number of animals with benign tumors	26	21	25	22	26	26	24	26
Number of animals with malignant tumors	15	18	21	18	29	24	29	27
Number of animals with metastasizing tumors	1	3	4	6	2	0	3	1
Total number of tumors	53	47	61	50	62	64	64	64
Total number of benign tumors	35	27	36	27	31	35	30	31
Total number of malignant tumors	18	20	25	23	31	29	34	33
Total number of metastasizing tumors	1	3	5	6	2	0	3	1
% animals with tumors	68	62	66	64	78	78	74	78
% animals with single tumors	38	36	28	34	42	42	36	38
% animals with multiple tumors	30	26	38	30	36	36	38	40
% Animals with benign Tumors	52	42	50	44	52	52	48	52
% animals with malignant tumors	30	36	42	36	58	48	58	54
% animals with metastasizing tumors	2	6	8	12	4	0	6	2

B. 1747 MHz

	Males				Females			
	1747 MHz sham control	1747 MHz low dose	1747 MHz medium dose	1747 MHz high dose	1747 MHz sham control	1747 MHz low dose	1747 MHz medium dose	1747 MHz high dose
Number of animals	50	50	50	50	50	50	50	50
Number of animals with tumors	37	30	25*	24*	37	31	35	33
Number of animals with single tumors	25	16	15	17	23	15	23	16
Number of animals with multiple tumors	12	14	10	7	14	16	12	17
Number of animals with benign tumors	27	21	17	12*	18	18	21	20
Number of animals with malignant tumors	16	19	14	16	29	24	25	24
Number of animals with metastasizing tumors	3	1	2	2	3	1	2	2
Total number of tumors	49	49	36	31	58	53	51	53
Total number of benign tumors	32	28	22	15	27	29	24	28
Total number of malignant tumors	17	21	14	16	31	24	27	25
Total number of metastasizing tumors	3	2	2	2	3	1	2	2
% animals with tumors	74	60	50	48	74	62	70	66
% animals with single tumors	50	32	30	34	46	30	46	32
% animals with multiple tumors	24	28	20	14	28	32	24	34
% animals with benign tumors	54	42	34	24	36	36	42	40
% animals with malignant tumors	32	38	28	32	58	48	50	48
% animals with metastasizing tumors	6	2	4	4	6	2	4	4

Significance of difference in a pairwise Fisher's test between control and treatment groups.
*$P < .05$.

(70%; $P = .824$), and 33/50 (66%; $P = .513$) females of the DCS low-, medium-, and high-dose groups, respectively, had developed tumors.

In the male mouse groups, the total number of tumors (TNT) was 53 (sham exposure), 47 (low dose), 61 (medium dose), and 50 (high dose) with GSM exposure and 49 (sham exposure), 49 (low dose), 36 (medium dose), and 31 (high dose) with DCS exposure. The total number of neoplasms in females was 62 (sham exposure) and 64 (low, medium, and high dose groups each) with GSM exposure and 58 (sham exposure), 53 (low dose), 51 (medium dose), and 53 (high dose) with DCS exposure.

Furthermore, statistical analysis between the sham exposed controls and their related three dose-level groups did not reveal RF-related increases with respect to the ratio of benign to malignant tumors (tumor dignity), tumor multiplicity, or the number of metastasizing tumors.

With respect to the organ-related tumor incidence, the pairwise Fisher test did not show any significant increase in the incidence of any particular tumor type in the RF exposed groups as compared to the sham exposed group, either with GSM or with DCS exposure. What statistical examination did reveal was a dose-dependent decrease of the incidence of hepatocellular adenomas in males, while the incidences of hepatocellular carcinomas were similar in EMF and sham exposed groups. The decrease of hepatocellular adenomas was significantly different from that in the sham exposed animals in the male high dose groups with GSM ($P = .048$) and DCS ($P = .015$) exposures.

In males, five (GSM exposure) and four (DCS exposure) organs showed incidences of single or multiple tumor types above the 10% level. In decreasing order of tumor incidences, these were liver, lungs, Harderian glands, hematopoietic/lymphoreticular system, and adrenals (GSM exposure only). In females, incidences of single or multiple tumor types above 10% were observed in the following six (GSM exposure) or four (DCS exposure) organs: lymphoreticular/hematopoietic system, pituitary gland, lungs (GSM exposure only), Harderian glands, uterus, and liver (GSM exposure only). The specific group incidences of these ''10% tumor organs'' are given in detail in Table 5. Subclassification of the lymphomas/tumors of the hematopoietic/lymphoreticular system revealed mainly lymphomas of the pleomorphic (follicular) type with no differences between sham-exposed and RF exposure groups.

The complete (extensive) histopathological examination of all organs/tissues, as defined by Bahnemann et al. [1995], revealed no occurrence of rare tumor types (i.e., neoplasms of the brain) in any of the RF-exposed groups (data not shown).

Peto's analysis between the sham exposure and the low, medium, and high dose groups was negative with the exception of a significant difference ($P = .0251$) in the simple test procedure for endometrial stromal polyp between the sham exposure (incidence: 5/50) and both the medium and high dose groups (incidence: 0/50 each). With the multiple test procedure, however, no difference was found.

In regard to the various non-neoplastic findings observed after 2 years of RF exposure, there were no statistically significant (pairwise Fisher's test) increases in the GSM and DCS exposure groups as compared to their respective sham exposure groups.

DISCUSSION

The increased popularity of mobile phones has caused growing concern regarding possible health effects from this form of ubiquitous electromagnetic exposure of the human population. Besides comparative observation of variously exposed groups of people (epidemiological studies), such an issue can be addressed also by (predefined) animal studies under controlled experimental conditions. As the available literature of experimental studies using frequencies and modulation characteristics specific to the popular wireless telephone systems is limited [Dasenbrock, 2005], the European Commission, the Swiss and Austrian governments, and the mobile phone industry have been supporting research addressing potential long-term health implications from the use of mobile phone systems. To overcome unclear RF exposure conditions or dosimetry shortcomings sometimes noticeable in older publications, a new setup, optimized for uniform whole-body exposure, was developed and employed by IT'IS [Görlitz et al., 2005], who were also responsible for the continuous monitoring of the exposure and environmental data, including transmission and documentation of the recorded exposure information (sets).

The 2-year bioassay in mice presented here was performed as a ''classical'' combined chronic toxicity and carcinogenicity study using three dose levels and was designed like studies routinely performed for hazard identification of chemicals, pharmaceuticals, or environmental agents. Exclusion of thermal stress for the animals was assured by several prestudies of EMFs (902 and 1747 MHz) with increasing specific adsorption rates [Kamlage, 2002; Ebert et al., 2005]. Continuous rectal body temperature measurements revealed a (slight and compensated) temperature increase of the restrained B6C3F1 mice starting at a

TABLE 5. Summary of Tumor Incidence (Selection of Common Tumor Sites); (A) 902 MHz Exposure; (B) 1747 MHz Exposure

A. 902 MHz

	Incidence of tumors (percent)							
	Males				Females			
	902 MHz sham control	902 MHz low dose	902 MHz medium dose	902 MHz high dose	902 MHz sham control	902 MHz low dose	902 MHz medium dose	902 MHz high dose
Pituitary	(50)	(50)	(50)	(50)	(50)	(50)	(49)	(50)
Carcinoma, pars distalis [M]	0	0	0	0	0	0	2	0
Adenoma(ta), pars distalis [B]	2	0	0	0	14	20	18	20
Adenoma, pars intermedia [B]	0	0	0	0	2	0	0	0
Harderian glands	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Adenocarcinoma [M]	0	0	0	0	0	2	0	0
Adenoma [B]	4	12	16	18	14	8	2	6
Lungs	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Carcinoma, bronchiolo-alveolar [M]	12	8	16	6	8	2	2	4
Adenoma(ta), bronchiolo-alveolar	20	18	20	18	14	10	10	8
Liver	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Carcinoma(ta), hepatocellular [M]	14	12	16	18	2	0	0	2
Adenoma(ta), hepatocellular [B]	30	20	20	12*	2	2	2	6
Tumor, Ito cell [B]	2	0	0	0	0	0	2	0
Hemangiosarcoma(ta) [M]	0	4	0	0	4	0	0	2
Adrenals	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Adenoma, subcapsular cell [B]	8	2	12	2	0	0	0	0
Adenoma, cortical [B]	2	2	0	0	0	0	0	0
Pheochromocytoma [M]	0	0	0	0	0	0	0	2
Pheochromocytoma [B]	0	0	0	0	4	4	2	2
Uterus					(50)	(50)	(50)	(50)
Adenocarcinoma [M]					0	2	2	2
Adenoma [B]					0	0	0	2
Polyp(s), endometrial stromal [B]					2	12	8	2
Polyp(s), glandular [B],					0	4	0	4
Sarcoma, endometrial stromal [M]					2	0	0	2
Leiomyosarcoma [M]					0	2	6	0
Leiomyoma [B]					0	2	0	0
Hemangiosarcoma [M]					2	0	4	0
Hematop./lymphoret. tissue	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Lymphoma [M]	10	8	10	8	36	36	40	40
Sarcoma, histiocytic [M]	0	2	0	0	2	4	4	6

(*Continued*)

TABLE 5. (*Continued*)

B. 1747 MHz

	Incidence of tumors (percent)							
	Males				Females			
	1747 MHz sham control	1747 MHz low dose	1747 MHz medium dose	1747 MHz high dose	1747 MHz sham control	1747 MHz low dose	1747 MHz medium dose	1747 MHz high dose
Pituitary	(50)	(50)	(49)	(50)	(50)	(50)	(50)	(50)
Adenoma(ta), pars distalis [B]	0	0	2	0	12	20	20	12
Adenoma, pars intermedia [B]	0	0	2	0	0	2	0	0
Harderian glands	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Adenocarcinoma [M]	2	0	0	0	2	2	0	0
Adenoma [B]	18	6	6	6	10	4	8	10
Lungs	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Carcinoma(ta), bronchiolo-alveolar [M]	12	10	8	8	2	0	0	0
Adenoma(ta), bronchiolo-alveolar [B]	14	12	12	14	4	6	2	8
Liver	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Carcinoma, hepatocellular [M]	14	12	4	14	2	2	2	4
Adenoma(ta), hepatocellular [B]	22	16	14	4*	4	4	4	6
Tumor, Ito cell [B]	0	4	2	0	0	0	0	0
Hemangiosarcoma(ta) [M]	0	4	4	2	2	0	0	0
Hemangioma [B]	0	0	0	0	0	2	2	0
Adrenals	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Adenoma, subcapsular cell [B]	2	6	4	2	0	2	0	0
Adenoma, cortical [B]	0	2	0	0	0	0	0	0
Pheochromocytoma [M]	0	0	2	0	0	0	0	0
Pheochromocytoma [B]	4	0	2	0	0	0	2	0
Uterus					(50)	(50)	(50)	(50)
Adenocarcinoma [M]					2	0	0	0
Adenoma [B]					0	2	0	2
Polyp, endometrial stromal [B]					10	4	0	0
Polyp(s), glandular [B],					0	0	4	6
Sarcoma, endometrial stromal [M]					0	0	2	0
Leiomyosarcoma [M]					2	0	0	0
Leiomyoma [B]					0	4	2	2
Hematop./lymphoret. tissue	(50)	(50)	(50)	(50)	(50)	(50)	(50)	(50)
Lymphoma [M]	2	12	8	8	44	32	36	34
Sarcoma, histiocytic [M]	2	4	0	0	0	6	0	4
Tumor, mast cell [M]	0	0	0	0	0	0	0	2

Significance of difference in a pairwise Fisher's test between control and treatment groups. Figures in brackets represent the number of animals from which this tissue was examined microscopically.

B, benign tumor; M, malignant tumor.

*$P < .05$.

whole-body averaged SAR of 5 W/kg. As the animals compensated for the RF-related temperature load during the 2-h exposure sessions, indicating that they were within the thermal regulatory region of the mice [for details see Ebert et al., 2005], selection of an athermal high-dose exposure level (4 W/Kg bw) was assured under similar experimental conditions.

Routine health status supervision of the sentinels during the entire course of the study, body mass development, mortality data, and daily clinical observation of the sham treated and RF-exposed male and female mice indicated an undisturbed animal study.

The histopathological findings revealed no increases in the number of TBAs in any of the GSM and DCS exposure groups as compared to the sham exposure group. On the contrary, a marked dose-dependent decrease of TBAs in the DCS exposure groups as compared to the sham exposure group was found.

In all GSM groups and in the DCS medium and high dose groups, the number of TBAs and the TNT was about 15% higher in females than in males.

A remarkable finding was the higher number of TBAs (about 9%) and higher TNT (about 15%) in females (all GSM groups) as compared to the DCS exposure groups. In males, markedly lower numbers of TBAs and TNT were found only in the DCS medium and high dose groups as compared to all other groups.

The reason for these differences between the GSM and the DCS (sham) exposure groups is unclear. Both exposures were conducted almost simultaneously under similar (laboratory, environmental, ''technical'') conditions. Nevertheless, a small difference between both studies did exist: Due to technical reasons, DCS exposure was started 1 week later, so that these mice received an additional training week to acclimatize to the tube restraint, which may have influenced/reduced the stress in the exposure tubes. In principle, the influence of chronic stress, for example, tube restraint, through suppressed immunity increasing susceptibility to disease or cancer is widely accepted in the scientific community, and several models to explain the pathways/mechanisms have been presented so far [Dhabhar and McEwen, 1997; Yang and Glaser, 2002; Karpinets and Foy, 2004]. An influence of the GSM or DCS exposure can be excluded, as the related sham exposure groups showed nearly similar numbers of TBAs and TNT compared to their corresponding dose groups.

Regarding the organ-related tumor incidence, pairwise Fisher's test did not show a significant increase in any specific tumor type in the GSM and DCS exposure groups as compared to the related sham-exposed groups, contradicting an adverse (neoplastic) health effect by the long term RF exposure.

Interestingly, while the incidences of hepatocellular carcinomas were similar in EMF and sham exposed groups, in both studies the incidences of liver adenomas in males decreased with increasing dose levels, the incidences in the high dose groups being statistically significantly different from those in the sham exposed groups. Although this finding does not seem to be incidental, any firm conclusion regarding its biological significance in terms of a protective effect of GSM and DCS on the development of liver cancer in males would be premature, particularly since the incidences of liver cell carcinomas were similar in GSM/DCS and sham exposed groups.

As mentioned before, a comparison of our results to the broad spectrum of other RF studies using different signal characteristics, frequencies and polarizations in non-mouse species, analyzing exclusively one organ/tissue/system in tumor-prone mice [Repacholi et al., 1997; Utteridge et al., 2002; Sommer et al., 2004], or using RF exposure to promote an X-ray-initiated effect [Heikkinen et al., 2001] or enhance UV-induced skin tumorigenesis [Heikkinen et al., 2003], has been avoided on purpose.

Hitherto, a ''similar'' finding of tumor reduction by RF exposure has been mentioned in one mouse and one rat study: Adey et al. [1999] supposed a CNS tumor-inhibiting effect on spontaneous and ethylnitrosourea-induced tumors of the CNS by long term 836.55 MHz field exposure with North American Digital Cellular (NADC) modulation in Fischer 344 rats that provides similar signal characteristics to GSM, but with a dominant amplitude-modulation frequency of 50 HZ compared to the 217 Hz of this study. The same experiment with the non-amplitude-modulated but frequency-modulated 836.55 MHz signal did not result in a CNS tumor-protective effect [Adey et al., 2000]. Unfortunately, only tumors of the CNS were investigated.

In a long-term study with lymphoma-prone mice [Utteridge et al., 2002], replicating the study of Repacholi et al. [1997], who found a significant increased lymphoma incidence by GSM-exposure in transgenic mice, a significant decreased lymphoma incidence was mentioned in the ''replication'' study. One hundred twenty female Eμ-Pim1 heterozygous mice and 120 wild-type females were exposed in Ferris wheels (tube restraint) up to 104 weeks (1 h/day, 5 days/week) to GSM-modulated 898.4 MHz radiation. Using four exposure level and sham (SAR: 0.25, 1.0, 2.0, 4.0 W/kg), a decreased incidence of lymphoblastic lymphoma was found in three (0.25, 1.0, 2.0 W/kg) of the (transgenic) exposure groups (not dose-dependent), while the high dose Eμ-Pim1 mice group showed a similar incidence as compared to the sham exposed

animals. In addition, lymphoblastic lymphomas were detected only in single wild-type mice without relation to the GSM-exposure. The comparison of the incidences of non-lymphoblastic lymphomas, neurological and other tumors revealed no influence by RF exposure neither in the transgenic or in the wild-type mice. On the other hand, analyzing a (''summarized'') tumor incidence of the hematopoietic/lymphoreticular system (not shown in the article of Utteridge et al.), as usual by WHO/IARC nomenclature, this (apparent) reducing effect by RF exposure would not be apparent/visible.

To our knowledge, long-term mouse studies exclusively analyzing the cancer risk from exposure to GSM/DCS radiofrequency fields have not been published so far and the above- mentioned studies differ in various aspects and are not comparable with our B6C3F1 mouse study.

Comparison with historical control data from about 1350 male and 1100 female B6C3F1 mice from NTP carcinogenicity studies [Haseman et al., 1999] has shown that the tumor rates observed in the present studies are within the range of the NTP tumor data, although for some organs (liver, Harderian glands, hematopoietic system) marked differences between both data sets exist.

The main tumor types observed in the present studies were also well in line with the corresponding tumor incidences in 213 male and 213 female untreated cage control B6C3F1 mice from a transgeneration carcinogenicity study recently conducted at the Fraunhofer ITEM [Dasenbrock et al., 2005]. In this study, the incidence of hepatocellular tumors was 30% in males and 10% in females as compared to group-based ranges of 16–40% in males and 2–10% in females, of the present studies. Lung tumors were observed in 27 and 14% of males and females, respectively, as compared to ranges of 20–30% in males and 2–22% in females per group of the present studies. Malignant lymphomas occurred in 13% of the male and 40% of the female control mice of the transgeneration carcinogenicity study as compared to ranges of 2–12% and 32–44% per group in males and females, respectively, of the present studies. In conclusion, the present study produced no evidence that the exposure of B6C3F1 mice to RF of 902 MHz and 1747 MHz at an absorption rate of up to 4.0 W/kg for 2 h per day, 5 days per week, over a period of up to 24 months had any adverse health effect or any influence on the increase in the incidence or severity of the background non-neoplastic and neoplastic lesions observed. The study thus did not provide any evidence of RF possessing a carcinogenic potential.

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