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Review

# Animal carcinogenicity studies on radiofrequency fields related to mobile phones and base stations

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**Abstract**

Since a report in 1997 on an increased lymphoma incidence in mice chronically exposed to a mobile phone radiofrequency signal, none of the subsequent long-term studies in rodents have confirmed these results. On the other hand, several of the follow-up co- and carcinogenicity studies are still underway or are presently being initiated. Most of the published long-term studies used 1 exposure level only and suffer from a poor dosimetry which does not consider the animal's growth. Additional points of criticism are a limited, in some cases, questionable histopathology and inadequate group sizes. Overall, if dealing with new chemicals or drugs, these studies would not be acceptable for registration with the responsible authorities. The major critical points are taken into consideration within the European co- and carcinogenicity projects (CEMFEC and PERFORM-A), which are in their final stages and in the US long-term studies in mice and rats which are about to be initiated. Nevertheless, the WHO evaluation for health risk assessment of long-term telephone use and base station exposure will start in late 2005.


*Keywords:* Radiofrequency; Mobile phones; Cancer; Animal studies

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*Abbreviations:* CDMA, code division multiple access; CEMFEC, Acronym of the European project "Combined effects of electromagnetic fields with environmental carcinogens"; CNS, central nervous system; DAMPS, digital advanced mobile phone systems; DCS, digital personal communications system; European, standard for digital mobile phone technology at 1800 MHz; DEN, diethylnitrosamine; DMBA, 7,12-dimethylbenz[a]anthracene; EMF, electromagnetic field; ENU, ethylnitrosourea; FDMA, frequency division multiple access; GLP, good laboratory practice according to national and OECD principles; GSM, global system for mobile communication; European, standard for cell phone systems; Gy, Gray; MHz, megahertz; MX, 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone; NADC, North American digital cellular; NIEHS/NTP, National Institute of Environmental Health Sciences/National toxicology program; NMT, Nordic mobile telephones; ODC, ornithine decarboxylase; PERFORM-A, Acronym of the European project "In vivo research on possible health effects related to mobile telephones and base stations (carcinogenicity studies in rodents)"; RF, radio frequency; SAR, specific absorption rate; TDMA, time division multiple access; TPA, 12-*O*-tetradecanoylphorbol-13-acetate; UMTS, universal mobile telecommunication system; UV, ultraviolet.

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## Introduction

After Repacholi et al. in 1997 observed a 2.4-fold lymphoma increase in transgenic *pim1* mice chronically exposed to a GSM signal, several long-term studies related to mobile telephony were initiated. These studies have addressed either a possible direct tumor incidence-increasing effect or/and a tumor-promoting/co-carcinogenic effect of radiofrequency (rf).

The following criteria were met by the reviewed studies discussed in this presentation:

- long-term exposure to an rf signal related to mobile telephony,
- co- or carcinogenesis including tumor promotion as study endpoint, and, if applicable,
- publication in a peer-reviewed journal.

Firstly, cancer studies will be discussed. The studies involve experiments without any pre-treatment of the animals; transgenic mice are included. All animals were long-term rf-exposed for 1.5 to 2 years and for minimum of 1 h per day, 4–7 days per week.

Secondly, in initiation promotion and co-carcinogenicity studies before exposure to the rf signal(s), the animals usually were administered a (strong) carcinogen, e.g., 7,12-dimethylbenz[a]anthracene (DMBA), diethylnitrosamine (DEN) or ethylnitrosourea (ENU), as a tumor-initiating chemical and were subsequently rf-exposed for several weeks or months.

Other investigators in their co-carcinogenicity studies (Juutilainen et al., 2000) preferred simultaneous exposure to a carcinogen, e.g., MX, ionizing or UV radiation, and to the (non-ionizing) rf.

## Cancer studies

In the most quoted study, Repacholi et al. (1997) found a significant (2.4-fold) increase in lymphomas in female *pim1* transgenic mice after 18 months (2 × 30 min/day) of exposure to a modulated 900 MHz GSM signal. In a far field, only one exposure level ("dose") with a large variation (0.008–4.2 W/kg SAR [whole body]) was used for the non-restrained mice. Due to further shortcomings of the study, two re-evaluation studies were started.

At first, Utteridge et al. (2002, 2003) could not confirm Repacholi's results. Again, a modulated GSM signal (898.4 MHz, 217 Hz pulse, 0.6 ms pulse width) was used for exposure in a "ferris-wheel" system. Female heterozygous *pim1* transgenic (lymphoma-prone) and wild-type mice ($n$ = 120 per group) were rf-radiated in restrainer tubes for 1 h/day, 5 days/week during 24 months at 4 different SAR [whole body] levels of 0, 0.25, 1.0, 2.0 and 4.0 W/kg. In addition, a positive control treated with 50 mg/kg ENU and a non-restrained cage control group were included in the study. Overall, there was no lymphoma increase in the rf-radiated groups of the various SAR levels.

Secondly, at Serono-RBM, Ivrea, Italy, male and female *pim1* transgenic mice were exposed to a modulated GSM signal (902 MHz, 217 Hz pulse, 0.5 ms pulse width). The study is part of the European project PERFORM-A (Dasenbrock et al., 2003), was blinded and run under GLP conditions. In a ferris-wheel system (Goerlitz et al., in press), tube-restrained mice ($n$ = 50/group/sex) were rf-radiated for 1 h/day, 7 days/week, up to 18 months, at SAR levels [whole body] of 0, 0.5, 1.4, 4.0 W/kg. The draft report of this study is almost finalized (Oberto et al., in progress).

Supplementary to the above experiments, Sommer et al. (submitted for publication) studied in female mice of the (high-leukemia) inbred strain AKR the long-term influence of a 9-month continuous rf exposure at 0.4 W/kg SAR [whole-body] to a GSM signal (890 MHz modulated). In a radial waveguide system, 168 females were sham- and 168 rf-radiated in their cages (7 mice per cage). No increase in the incidence of leukemia and lymphomas was detected, but only 1 "dose" was applied. Recently, the same group started an identical experiment testing the long-term rf radiation (1966 MHz modulated) at 0.4 W/kg SAR [whole body] using a generic UMTS test signal for bio-experiments (Bitz et al., 2004; Ndoumbè Mbonjo Mbonjo et al., in press). The in-life phase is still in progress.

La Regina et al. (2003) tube-exposed F344 rats in carousel systems for 4 h/day, 5 days/week during 24 months. Two different rf radiations (835.62 MHz FDMA, 847.74 MHz CDMA) at one brain SAR level of 1.3 ± 0.5 W/kg each were applied to the animals. Each group (2 rf and 1 sham) consisted of 160 rats (80/80). No significant differences between treated and sham-exposed animals were found regarding any brain tumor and a number of non-CNS tumors.

In two NTP-like carcinogenicity studies at the Fraunhofer ITEM, Hannover, Germany, in a ferris-wheel system (Goerlitz et al., in press), tube-restrained B6C3F1 mice were exposed for 24 months, 5 days/week, 2 h/day to a GSM signal cocktail at 902 MHz or to a DCS signal cocktail at 1747 MHz. One sham control and three rf groups (target SAR [whole body]): 0, 0.4, 1.3, 4.0 W/kg) per signal were complemented by one cage control group ($n$ = 65/group/sex). This GLP study is also blinded and part of PERFORM-A, results will be available in spring 2005 (Dasenbrock et al., 2003, in progress).

A further two identical NTP-like blinded GLP studies using Wistar rats were initiated within PERFORM-A at RCC Ltd., Itingen, Switzerland. A new ferris-wheel system was used (Froelich et al., 2001; Nikoloski et al., 2002). Again, rats of one sham control and three rf groups (target SAR [whole body]): 0, 0.3, 1.4, 4.0 W/kg) per signal ($n$ = 65/group/sex) were exposed in restrainer tubes for 24 months, 5 days/week, 2 h/day to a GSM signal cocktail at 902 MHz or to a DCS signal cocktail at 1747 MHz; one cage control group was also included. Results will be