Long-term effects of radiofrequency electromagnetic fields

Assessment of the study of D. Adang

Gezondheidsraad
Health Council of the Netherlands

To the Minister of Housing, Spatial Planning and the Environment

Subject : Presentation of advisory report *Long-term effects of radiofrequency electromagnetic fields; assessment of the study of D. Adang*
Your reference : RB/2009043028
Our reference : I-181-09/EvR/pm/673-G2
Enclosures : 1
Date : June 9, 2010

Dear Minister,

In June 2008 the thesis 'An Epidemiological Study on Low-level 21-month Microwave Exposure of Rats' by Dr D. Adang from Belgium raised publicity, because this research would show that long term exposure of rats to radiofrequency electromagnetic fields might lead to a decrease in survival. This raised questions in the House of Representatives whether it has been shown that rats would die earlier when exposed to GSM radiation. Motivated by these questions and the public interest in this subject, in a letter dated 2 July 2009 your predecessor requested the Health Council to provide a reaction to this study.

The Electromagnetic Fields Committee of the Council has performed a detailed study of the thesis and the scientific paper on this research that has been published in the meantime. Adang concludes that there are effects of long term exposure to radiofrequency electromagnetic fields on the blood picture and on survival. The Committee considers these conclusions to be scientifically untenable, as a result of a number of flaws in the execution of the study and in the statistical analysis of the data. In previous reports the Committee concluded on the basis of the state of science that no causal relationship has been demonstrated between health problems and exposure to the electromagnetic fields generated by mobile telephones and their base stations. The study by Adang is no reason to change this opinion.

With kind regards,
(signed)
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Assessment of the study of D. Adang

to:

the Minister of Housing, Spatial Planning and the Environment

the Minister of Economic Affairs

the Minister of Health, Welfare and Sport

the Minister of Social Affairs and Employment

No. 2010/09E, The Hague, June 9, 2010

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Contents

Summary

At the request of the Minister for Housing, Spatial Planning and the Environment, the Electromagnetic Fields Committee of the Health Council of the Netherlands in this advisory report presents an assessment of the results of a study described in the thesis of Dr D. Adang, entitled ‘An Epidemiological Study on Low-level 21-month Microwave Exposure of Rats’. In doing so, it has also considered the scientific publication that has been published on the research in the meantime. In this study, Adang investigated the effects of long-term exposure of rats, for 21 months, two hours a day, seven days a week, to three types of radio-frequency electromagnetic fields: a 970 MHz GSM-like signal, a 970 MHz signal without the pulses characteristic of GSM, and a 9.70 GHz signal; there was also a group that was sham-exposed, in other words: all circumstances were identical to those in the other groups, with the exception of the exposure. The exposure levels were approximately equal to that of the maximum permissible level for the general population for continuous exposure.

The Committee has come to the conclusion that the hypothesis of the research is interesting and relevant, but that the research suffers from methodological deficiencies and the analysis of the data contains several flaws.

Generator breakdown not reported

The fact that the 9.70 GHz generator failed after around six months and that consequently the group of animals concerned was not further exposed, are only described very summarily in the thesis. No mention whatsoever is made of this in the analysis of the data or the associated conclusions, nor in the scientific publication. Given the fact that the generator breakdown impacted the original aim of the experiment, the Committee considers this to be a serious omission.

No obvious effects on blood picture

The Committee cannot endorse Adang's conclusions that clear effects on the blood picture were found. Insofar as significant differences were found between the sham-exposed and the actually exposed groups for certain parameters and at certain times, these do not present any clear pattern. There is no time analysis of these data in the thesis. A graphical analysis carried out by the Committee did not reveal any unequivocal differences. In analysing the blood data, Adang did not use the most appropriate statistical analysis method.

The Committee conducted a literature study of similar experiments. The data in these studies do not support Adang's conclusions that there are effects on the blood picture.

Behavioural experiments too limited

Adang also carried out behavioural experiments, but only on the group that was exposed to the 970 MHz GSM-like signal. These experiments are insufficiently detailed to allow conclusions to be drawn about the effects of exposure on behaviour.

Analysis of survival data incomplete

Finally, Adang investigated survival in the different groups. The Committee takes the view that here, too, the analysis Adang carried out is incorrect and incomplete. Adang ought to have analysed the survival data over the entire period of 32 weeks for which the animals were studied, and not only over 28 weeks. Adang's conclusion that exposure to a 9.70 GHz electromagnetic field has an effect on survival is incorrect: an analysis carried out on the Committee's request, comparable to Adang's, but in which the survival data to 32 weeks are

included, does not demonstrate any statistically significant differences between any of the four groups.

Histopathological analysis was only conducted on a few animals and has merely illustrative value.

Finally, the data from an updated literature study offer no support to the hypothesis that long-term exposure to radiofrequency electromagnetic fields might have an effect on survival.

No health problems due to exposure

In earlier reports, the Committee concluded on the basis of the current state of scientific development that no causal link between health problems and exposure to the electromagnetic fields originating from mobile phones or base stations for mobile telephony has been demonstrated. The evaluation of Adang's research described in this report and the current data assembled from the literature by the Committee do not give it cause for modifying its conclusion.

Chapter 1

Introduction

On 2 July 2009, the Minister for Housing, Spatial Planning and the Environment sent the Health Council of the Netherlands a letter containing a request to issue an advisory report on the thesis of Dr D. Adang: 'An Epidemiological Study on Low-level 21-month Microwave Exposure of Rats'.[1] The motivation for this request arose from questions from the House of Representatives as to whether this research demonstrated that rats die earlier than normal when exposed to GSM radiation.

The Minister asked the Health Council to provide answers to the following questions:

- Could you provide a response with regard to the cited study?
- Do you expect that the results of this research will cause you to modify your earlier conclusions with regard to possible health effects of mobile telephony?

The complete text of the request for advice may be found in Annex A. The Vice President of the Health Council asked the Electromagnetic Fields Committee to respond to the questions. The composition of the Committee is given in Annex B. The Committee's findings are recorded in this advisory report.

Adang has also published part of his research findings in a scientific article that appeared after the request for advice was received.[2] The Committee has included this paper in its assessment.

In advance, the Committee wishes to emphasise what it has already stated on several occasions, most recently in the Electromagnetic Fields Annual Update 2008, that it bases its conclusions on all scientific information available on a particular subject, and that a single new, but similar study will seldom seriously change the weight-of-evidence analysis when a large quantity of data already exists – as is the case for electromagnetic fields. ‘Seldom’, but not ‘never’: for truly innovative research, such a change is of course possible.

In this report, the Committee firstly presents a short overview of the design and execution of Adang’s research. Thereafter, it gives a summary of the results and considers more deeply the two most important endpoints of the research: the analysis of 1) various parameters of the blood and 2) of the mortality pattern. It compares the two endpoints to the data obtained from the literature. Finally, the Committee formulates its conclusions and presents responses to the questions in the request for advice.

Chapter 2

Design and execution of the research

2.1 Design of the study

The thesis and the scientific publication describe a long-term study on rats: the aim was to expose the animals for several hours daily over the course of 21 months to field strengths such as may arise in the home and work environment as a result of the presence of telecommunication antennas. For this, the maximum level that is considered acceptable for continuous exposure of the general population was chosen. Other exposure levels were not investigated.

The male albino Wistar rats used were randomly allocated into four groups of 31 animals each. Each group underwent one of four different forms of treatment (see next section).

During the course of the experiment, blood was sampled and analysed every few months. Fifteen months after the start of the exposure, the animals' behaviour was investigated, while in a separate experiment, behavioural changes after two months were studied. Mortality was recorded during the entire duration of the experiment. After the exposure period of 21 months, the surviving animals were followed for another three months and then euthanised. The deceased or euthanised animals were preserved for histopathological investigation.

2.2 Exposure

Exposure to three different types of electromagnetic fields took place; in addition to this, there was a control group which underwent sham exposure:

- 970 MHz unmodulated (970 MHz-continuous)
- 970 MHz pulse-modulated (970 MHz-pulsed); this signal resembles the signal used in certain kinds of mobile telephony (GSM 900 MHz)
- 9.70 GHz unmodulated (9.70 GHz-continuous)
- sham (simulated exposure: identical treatment and circumstances to exposure, only the actual exposure was omitted).

A control group in which the handling of the animals associated with the exposure was not conducted (cage control) was absent from the study.

The animals were exposed for two hours a day for seven days a week during 21 months. However, the exposure to the 9.70 GHz continuous signal only took place for around six months. In the analysis of the data in the thesis, little reference is made to this, and in the publication it is not mentioned at all. On page 122 of the thesis, the author writes: ‘In the current of the sixth month of the exposure campaign, the amplifier connected to the 9.70-GHz microwave generator fell down’. The amplifier could not be repaired, so this group was not actually exposed after the generator breakdown.

For all three signals, the animals were in a situation which is comparable to exposure to signals from mobile phone system antennas, not to exposure during the use of a mobile phone. The animals were exposed in self-constructed exposure boxes, in which the antenna, lighting and ventilation were installed in the lid (see Figure 1).

Adang measured the exposure levels in the exposure boxes without rats being present. The field strengths at the bottom of the boxes were reasonably homogeneous in the central part; around the edges, the levels were lower than the assumed field strengths. No actual check of the position of the rats during the daily exposure sessions was conducted.

2.3 Behaviour

In two different experiments, research was done into the exploratory behaviour with new and known objects.

Figure 1 Top photo: overview of the exposure boxes. A 970 MHz antenna may be seen on the inside of the lid of the front box. Bottom photo: Exterior view of the 9.70 GHz box with two horn antennas in the closed lid. Source: thesis Adang.[1]

Firstly, separate from the main study, a behavioural experiment was conducted in which two groups of 32 animals were exposed for two hours a day, five days a week for two months to the same field strength as in the main experiment.

In addition to this, in two groups from the main experiment – sham and 970 MHz-pulsed – behaviour was investigated after 15 months exposure for two hours a day, seven days a week.

2.4 Blood analysis

In total, blood was sampled six times during the 21 months when exposure took place: at the start of the exposure, and after 3, 8, 11, 14 and 18 months.

Adang determined the numbers of red and white blood cells (erythrocytes and leucocytes respectively), and also the numbers of two specific types of leucocytes: monocytes and eosinophils. The haemoglobin content was also determined.

The concentration in the blood of two stress-related hormones was determined too: adrenocorticotropic hormone (ACTH) and corticosterone.

2.5 Mortality and histopathology

Mortality before the end of the experiment was recorded and the deceased animals were prepared for histopathological investigation.

Histopathological investigation of the liver, lungs, kidneys, heart, thymus, bladder, spleen, brain, testes and gastro-intestinal tract was carried out on a selected number of animals from each of the four groups.

2.6 Statistical analyses

Adang analysed the blood parameters in two ways: using an analysis of variance (ANOVA) procedure at each of the blood sampling time points, differences were sought among the four groups simultaneously; and using the Student's *t*-test, separate comparisons were made between the sham and each of the exposed groups.

The mortality data up to a lifetime of 28 months were investigated by Adang using a Kaplan-Meier analysis, in which a log-rank test was carried out on the data.

Chapter 3

Results of the study and the Committee's observations

3.1 Dosimetry

The dosimetry was carried out according to the criteria applicable at the time, subject to a number of assumptions, for example regarding the animals' position in the exposure boxes. The exact exposure of the rats cannot be determined, because their position was not monitored, as was done in other studies.[3]

The exposure is expressed as Specific Absorption Rate (SAR), a quantity that indicates how much energy is absobed by the body from the electromagnetic field. Based on current mathematical models, the position of the maximum SAR in a rat's body at 970 MHz is very different from that at 9.70 GHz. Also, due to the rat's anatomy, the SAR in the tail is usually higher than that in the rest of the body. (The only exception happens at what is known as the resonant frequency: the SAR is then equal throughout the body.*) Berdiñas Torres found that, at 970 MHz, the difference between the average SAR in the tail and that in the body can be as high as a factor of 4, while this can be a factor of 10 at 5 GHz.[4] The Committee assumes that this difference will also be considerable at 9.70 GHz. Moreover, it considers it not improbable that, as a result of increased heating in the tail, the animals will adopt a different posture at 9.70 GHz from that at 970 MHz, which could possibly lead to differences in the exposure pattern.

* The resonant frequency varies from roughly 700 to 900 MHz depending on the size of the rat. The resonant frequency is lower for a large rat than for a small one.

The above complications have the consequence that the effects on rats found in this study after exposure to 9.70 GHz cannot simply be extrapolated, as Adang supposes, to exposure of humans to 970 MHz.

3.2 Behaviour

In the first behavioural experiment (see section 2.3), Adang found no difference between the exploratory behaviour of animals exposed for two months to 970 MHz-pulsed and that of sham-exposed animals.

In rats that were exposed for 15 months in the main experiment, differences were indeed found between sham and 970 MHz-pulsed. According to Adang, the exposed group displayed a deviation from normal behaviour causing there to be no difference between the exploration time of a known and a new object; the sham group did show such difference. This conclusion is not in fact justifiable on the basis of independent *t*-tests, as described in the thesis. In such an analysis of multiple measurements in which two groups are compared, an ANOVA for repeated measurements must be conducted. The authors of the article on which Adang based his experiment did in fact carry out such an analysis on their data.[5]

Adang found no significant differences in six other indices of behaviour between sham and 970 MHz-pulsed. The groups exposed to 970 MHz-continuous and 9.70 GHz-continuous were not studied for behaviour.

The behavioural experiments were insufficiently elaborated to allow any conclusions to be drawn about the effects of exposure to electromagnetic fields on the behaviour of the experimental animals.

3.3 Blood analysis

The baseline values that were determined at the start of the exposure are not reported in either the thesis or the publication. This is a deficiency, because it is not possible to investigate whether the daily contact with the animals in lifting them into and out of the exposure boxes had an influence on the blood picture, for example due to one or more groups having contracted an infection. An infection can easily spread throughout the entire exposure group because the animals remain together for several hours per day in the same exposure box. The pathogenic status of the various groups was not determined either.

The Committee obtained baseline values for the various blood parameters for the strain used by Adang, from the supplier of the rats (Charles River Laboratories). These were based on data from control groups from around 30 different studies, in total around 180 rats.[6]

Adang carried out the blood analyses with the same type of equipment as the supplier used to determine the baseline values. Nevertheless, Adang sometimes finds considerably deviating values. For example, the values for monocytes (a certain type of white blood cell) that Adang reports in all groups throughout the duration of the experiment are higher than the values the supplier provides for the control groups (see Annex C). This may indicate a systematic error, or an infection (that in that case must have been present in all groups). An infection might affect the results for the other parameters, particularly the mortality. For the other parameters measured in the blood there is also sometimes a considerable difference between the supplier's data and those in the study. Adang does not discuss these differences.

The data from the blood tests are presented in the thesis and the publication as differences between two groups each time: the sham and each of the actually exposed groups, at each of the different assessement times. Adang reports that various parameters exhibit significant differences at various assessement times between the sham and one or more exposed groups (see Table C1 in Annex C). However, in the view of the Committee, no clear pattern is to be observed in this. The data on stress hormones in the blood indicate that the differences in blood cell parameters between the various groups that Adang observes at various assay times cannot be explained by differences in stress. Adang fails to discuss this.

From the graphs presented in the thesis and publication it is apparent that in many cases there is a difference between the median and mean values. These differences are too large to assume a normal distribution of the values. This means that carrying out a *t*-test is not immediately justifiable. A log transformation of the data could have avoided this problem, but Adang did not apply this. According to the Committee, Adang therefore erroneously concludes that exposure to the various signals can have effects on the blood picture.

A second problem with Adang’s analysis method is that information may be lost because the course of the values over time is not considered. An ANOVA for repeated measurements ought to have been done over the data for all time points (including the non-reported analysis prior to the exposures).

The Committee does not have access to the raw data and cannot therefore carry out such an analysis (or have one carried out). It has, however, conducted a simple graphical time analysis on the data in the thesis, using as baseline values the data obtained from the supplier. The Committee concludes from this analysis (see Annex C) that no clear and ambiguous changes in the blood picture are demonstrated. The variations found for some parameters at some assay times give no reason to assume that long-term exposure to any of the three types of electromagnetic fields has an effect.

Adang makes a comparison in the publication between his data and data about effects on blood parameters from two other studies. These studies are in fact insufficiently similar in design to Adang's study to make such a comparison possible. In the study of Busljeta *et al.*[7] rats were only exposed for fifteen days; in the study by Heikkinen *et al*.[8] mice were exposed to a combination of X-rays and electromagnetic fields.

The Committee carried out a literature search into studies that are similar in design to Adang's investigation: studies in which rodents were exposed to radiofrequency electromagnetic fields for a longer period (more than six months). Studies in which exposure took place simultaneously with other factors, or in which tumours were induced using chemical agents, were not included. The results of this literature study are shown in the table in Annex D. It shows that in only one study on rats temporary slight decreases were found in the numbers of eosinophils and neutrophils (certain types of white blood cells).[9] In the six other studies where the blood picture was investigated in rats, wild-type mice and tumour-prone mice, no effect on the blood picture was found, not even for exposures where a higher exposure level was used than by Adang.

The Committee concludes that the literature data provides no support for Adang's findings.

3.4 Mortality

It may be gathered from the thesis that exposure started at an age of 4 months (the animals were purchased at an age of 3 months and acclimatised in the laboratory for one month). The exposure lasted for 21 months and was therefore terminated at an age of 25 months. Adang then determined the mortality 3 months later, so at an age of 28 months. From the graph in Chapter 2.4 of the thesis, which refers to the Kaplan-Meier analysis of the survival data, it is apparent that the mortality was actually recorded up to an age of 32 months. Adang did not include the mortality during these last 4 months in his analysis.

According to the thesis, animals that were euthanised for ethical reasons were not included in the analysis, but according to the publication, this actually did happen. Euthanised animals must not in fact be included in the further analysis. Both in the thesis and in the publication, the number of animals in each group at all reported time points is 31, in other words, the number with which the experiment started. Adang therefore based his analysis on animals that either died spontaneously or were euthanised. Neither in the thesis nor in the publication is it indicated how many animals were euthanised and in which groups.

Table 1 Mortality percentages.

	Mortality (%)		
Age (months)	24	25	28
Supplier controls	14.5-34.5[a]		
Sham	19.9	22.5	29.0
970 MHz continuous	32.3	38.7	48.4
970 MHz pulsed	32.3	38.7	51.8
9.70 GHz continuous	25.8	35.5	61.3

[a] 10 groups of 55 animals each; the average percentage mortality is 21.2.

The mortality at age 24 months was determined by Adang because this may be compared with the mortality in control groups as provided by the supplier (see Table 1). It is apparent from this that the mortality in the three exposed groups is indeed higher than in the sham group, but that the percentages come entirely within the variation in the controls.

At the end of the exposure period, at an age of 25 months, the mortality had increased in all groups; the same applies to the reported mortality 3 months later, while from the survival curves in the Kaplan-Meier analysis performed by Adang it is apparent that the mortality increases still further up to 32 weeks (see Figure 2).

In the Kaplan-Meier analysis, Adang compared pairs of mortality curves: the sham and each of the actual exposures. He concludes that analysis of the survival curves to 3 months after the end of the exposure (in other words, to an age of 28 months) yields a significant difference between the sham and the animals exposed to 9.70 GHz-continuous. For both 970 MHz modalities – continuous and pulsed – there is no difference from the sham group according to Adang.

However, the analysis should have been conducted over the entire followup period up to an age of 32 months, with simultaneous comparison of the four graphs using a log-rank test. The Committee has had this analysis done. The results show no significant difference in survival among the four different groups: the statistical analysis (log-rank test) yields a *p*-value of 0.13*. The analysis Adang conducted is therefore incorrect.

The comparison Adang makes with data on mortality from similar studies is incomplete. As indicated in section 3.3, the Committee carried out a literature study in which a search was done for mortality data in studies in which rodents

* A p-value of less than 0.05 indicates that there is a statistically significant difference.

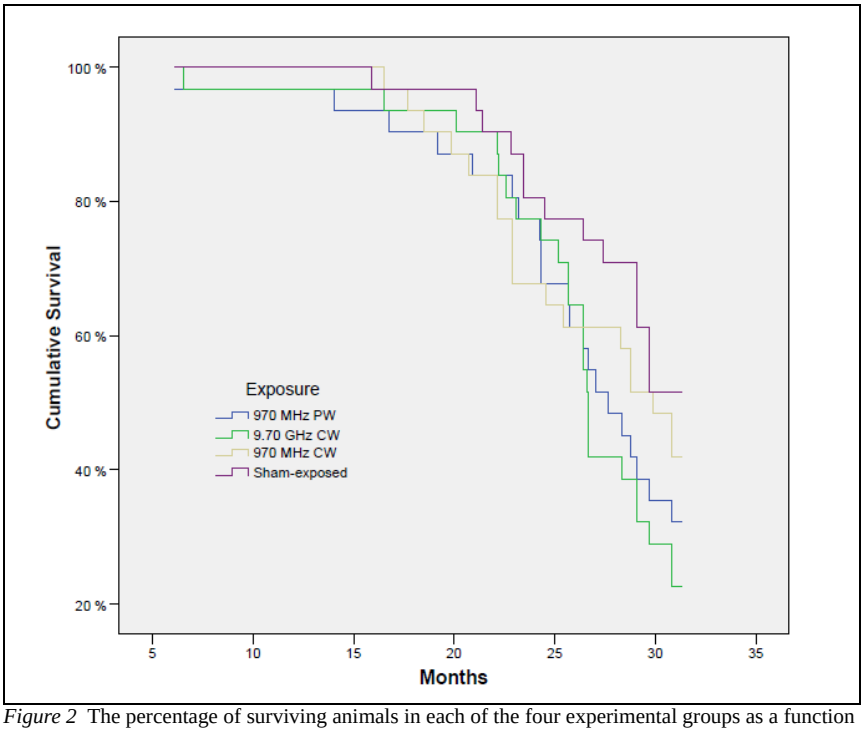

Figure 2 The percentage of surviving animals in each of the four experimental groups as a function of age. Source: thesis Adang.[1]

were exposed to radiofrequency electromagnetic fields for a long period (more than 6 months, see Appendix D).

From this summary it is apparent that, apart from the Adang study, no effect on mortality pattern was found in any study on rats, not even in studies in which a higher exposure level and a longer daily exposure were applied. The studies on wildtype or tumour-prone mice yielded four studies in which the mortality was raised or accelerated in animals exposed for long periods.[10-13] The exposure level in these studies was however a factor of 10 to 100 higher than in Adang's experiments. It is probable that in these experiments, thermal effects played a role. These findings are interesting as such and merit further research. However, the currently available data is not unambiguous and no conclusion can be drawn as to whether certain types of long-term exposure, or exposure repeated over a longer period, may in general cause an acceleration of tumour growth.

3.5 Histopathology

Adang performed a histopathological analysis of only 19 of the 124 rats. Based on this limited histopathology – and thus incomplete data – no conclusions may be drawn with regard to the cause of any changes in mortality in certain groups.

Chapter 4

Conclusions

The Committee takes the view that the hypothesis of the study is interesting and relevant, but concludes that the research itself and the analysis of the data suffer from several flaws. It is thus not possible to draw scientifically valid conclusions about the effects of long-term exposure to radiofrequency electromagnetic fields on health on the basis of this study. Extrapolation of the findings to humans is not possible.

The Committee will first consider the flaws it indentified in the research, and then respond to the two questions in the request for advice.

4.1 Flaws in the research

Generator breakdown

The fact that the 9.70 GHz generator failed after around six months, and the consequence that the group of animals concerned was not further exposed, are only described very summarily in the thesis. No mention whatsoever is made of this in the analysis of the data or the associated conclusions, nor in the scientific publication. Given the fact that the generator breakdown impacted the original aim of the experiment, the Committee considers this to be a serious omission.

Analysis effects on the blood picture

The Committee cannot endorse Adang's conclusions that clear effects on the blood picture were observed.

Insofar as significant differences were found between the sham (control group that underwent simulated exposure) and actually exposed groups for certain blood parameters and at certain times, these do not present any clear pattern. There is no time analysis of these data nor any initial values in the thesis. Neither does the graphical time analysis carried out by the Committee reveal any clear differences.

Furthermore, the statistical analysis methods used by Adang were not the most appropriate. The data should have been analysed by means of an analysis of variance for repeated measurements, in which all time points, including the unreported baseline values, should have been included.

The raised monocyte content in all groups of rats (including the sham group) might possibly indicate an infection in the entire laboratory population.

Finally, the literature data about comparable studies provide no support to the hypothesis that there might be effects on the blood picture.

Design of behavioural experiments

The behavioural experiments were only carried out on the group that was exposed to a pulsed 970 MHz signal. They are insufficiently elaborated to allow conclusions to be drawn about the effects of this on behaviour.

Analysis of survival data

According to the Committee, the analysis Adang carried out on the survival data is incorrect and incomplete. Adang's conclusion that there is an effect on survival from exposure to 9.70 GHz electromagnetic fields is untenable: an analysis carried out on the entire set of survival data at the Committee's request demonstrated no significant differences among the four groups. Histopathological analysis was only conducted on a few animals and has merely illustrative value. It cannot be determined to what any higher mortality percentage might be attributed. Neither do the data from an updated literature search offer any support to the hypothesis that long-term exposure to radiofrequency electromagnetic fields might have an effect on survival.

4.2 Response to questions in the request for advice

The first question in the request for advice reads:

Could you provide a response with regard to the cited research?

Despite the fact that the hypothesis behind Adang's study is interesting and relevant, the study itself and the analysis of the data contain too many flaws to allow valid scientific conclusions about health effects of long-term exposure to radio-frequency electromagnetic fields to be drawn based on this research.

In the questions from the House of Representatives that form the basis of the request for advice, the conjecture is expressed that Adang's research shows that rats die faster than normal from GSM radiation. This conclusion is erroneous. Firstly, Adang only found an increased mortality in the group exposed to 9.70 GHz, and not in the group exposed to a GSM-like signal. But Adang conducted an incomplete analysis of the mortality data. The full analysis that the Committee had carried out leads to the conclusion that there is no statistically significant difference in survival among the various groups.

The Committee further indicated that it is unclear for exactly how long the rats in the 9.70 GHz group were exposed, since the generator broke down after a few months and could not be repaired. The Committee considers the fact that this piece of information and its consequences were only very summarily reported in the thesis, and not at all in the publication, to be a serious omission.

The second question in the request for advice reads:

Do you expect that the results of this research will cause you to modify your earlier conclusions with regard to possible health effects of mobile telephony?

In earlier advisory reports, the Committee concluded, based on the current state of scientific development, that no causal link had been demonstrated between health problems and exposure to the electromagnetic fields originating from mobile phones or base stations for mobile telephony. Neither Adang's research nor the updated literature study give the Committee any cause to modify this conclusion.

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A	The request for advice
B	The Committee
C	The blood analysis
D	Data from long-term exposure studies

Annexes

Annex **A**

The request for advice

On 2 July 2009, the Minister for Housing, Spatial Planning and the Environment sent the following letter to the President of the Health Council of the Netherlands (ref. RB/2009043028):

Dear President,

Several months ago you sent me the report entitled “Electromagnetic fields: Annual Update 2008”. I wish to thank you and your Committee for this.

Through the Annual Updates you keep me informed about scientific developments concerning the possible health effects of exposure to electromagnetic fields. The Annual Updates thus fulfil an important role socially speaking. In the 2008 Annual Update, you provided a comprehensive explanation of the procedure and methods you use to analyse data. In addition to this, you considered the effect of radiofrequency electromagnetic fields on brain activity and the association between exposure to such fields and the incidence of health problems. I am most grateful to you for this.

On 25 June 2008, MP Van Dam made a request to me and my colleague in Economic Affairs about an appraisal of a scientific study in Belgium that would show that rats die more quickly from GSM radiation.

In our reply to the House of Representatives, we wrote that the government is being advised on the current state of scientific development with respect to health aspects of electromagnetic fields by

your Electromagnetic Fields Committee. At the same time, however, we indicated that the Belgian research did not comply with the criterion for analysis by the Health Council, namely publication in a peer-reviewed journal.

Because there is much interest in society in this subject I wish to ask you nevertheless to advise me on Dr Adang's thesis.

With reference to the above, I wish to put the following questions to you:

1 Could you provide a response with regard to the cited study?
2 Do you expect that the results of this research will cause you to modify your earlier conclusions with regard to possible health effects of mobile telephony?

I look forward to receiving your response.

Yours faithfully,
The Minister for Housing, Spatial Planning and the Environment,
(signed)
Dr Jaqueline Cramer

Annex **B**

The Committee

The membership of the Electromagnetic Fields Committee at the time of preparation of this advisory report was as follows:

- Dr G.C. van Rhoon, *chair*
  physicist, Erasmus University Medical Centre Rotterdam
- Dr L.M. van Aernsbergen, *observer*
  physicist, Ministry of Housing, Spatial Planning and the Environment, The Hague
- Prof. A. Aleman
  professor of Cognitive Neuropsychiatry, University of Groningen
- Dr G. Kelfkens, *advisor*
  physicist, Netherlands Institute for Public Health and the Environment, Bilthoven
- Prof. H. Kromhout
  professor of Occupational Hygiene and Exposure Characterisation, Institute for Risk Assessment Sciences, University of Utrecht
- Prof. F.E. van Leeuwen
  professor of Cancer Epidemiology, Free University of Amsterdam,
  epidemiologist, Netherlands Cancer Institute, Amsterdam
- Dr H.K. Leonhard, *observer*
  physicist, Ministry of Economic Affairs, Groningen

- Prof. H.F.J. Savelkoul
  professor of Cell Biology and Immunology, Wageningen University
- Prof. W.J. Wadman
  professor of Neurobiology, University of Amsterdam
- D.H.J. van de Weerdt, physician
  toxicologist and specialist in environmental medicine, Central Gelderland Municpal Health Services (GGD), Arnhem
- Prof. A.P.M. Zwamborn
  professor of Electromagnetic Effects, Eindhoven University of Technology, physicist, TNO (Netherlands Organisation for Applied Scientific Research), The Hague
- Dr E. van Rongen, s*ecretary*
  radiobiologist, Health Council of the Netherlands, The Hague

The Kaplan-Meier analysis of the mortality data was carried out by Dr W.L.J. van Putten, statistician at the Erasmus University Medical Centre in Rotterdam.

The Health Council and interests

Members of Health Council Committees – which also include the members of the Advisory Council on Health Research (RGO) since 1 February 2008 – are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the President and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist involved. During the establishment meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Annex **C**

The blood analysis

The Committee searched Adang's thesis for the mean values and associated standard deviations of the various parameters investigated in the blood. In most cases, these are given in the text, but in some cases the standard deviations had to be calculated from the error bars in the graphs.

In the figures below, the upper and lower limits of the baseline values are shown by means of two horizontal lines. These are derived from the data for a large number of control animals published in a report on the animal supplier's website.[6] The values shown are those of one standard deviation above and one standard deviation below the mean.

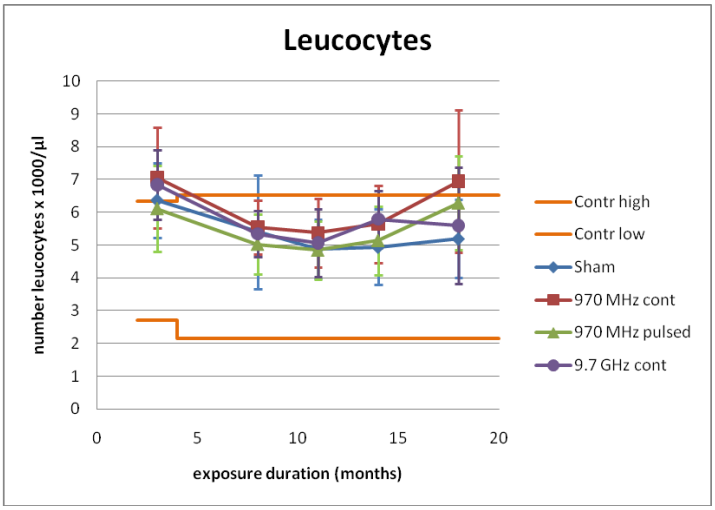

Figure C1 Time line of the number of white blood cells during the study. Means and standard deviations are shown. The horizontal lines represent the values for one standard deviation both above and below the mean for a large group of control animals (as provided by the supplier). The age is the duration of exposure + 4 months.

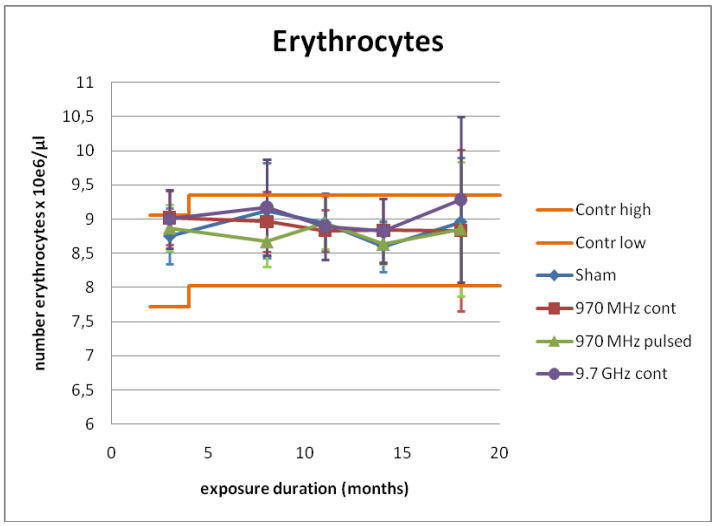

Figure C2 Time line of the number of red blood cells during the study; details as in Figure C1.

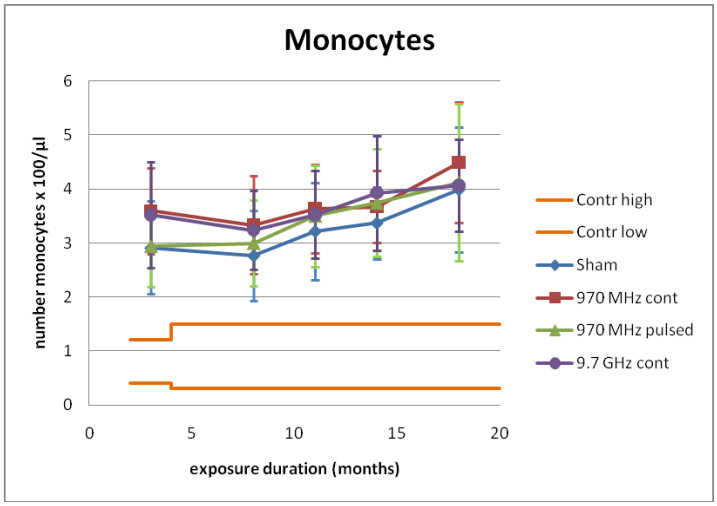

Figure C3 Time line of the number of monocytes, a certain type of white blood cell, during the study; details as in Figure C1.

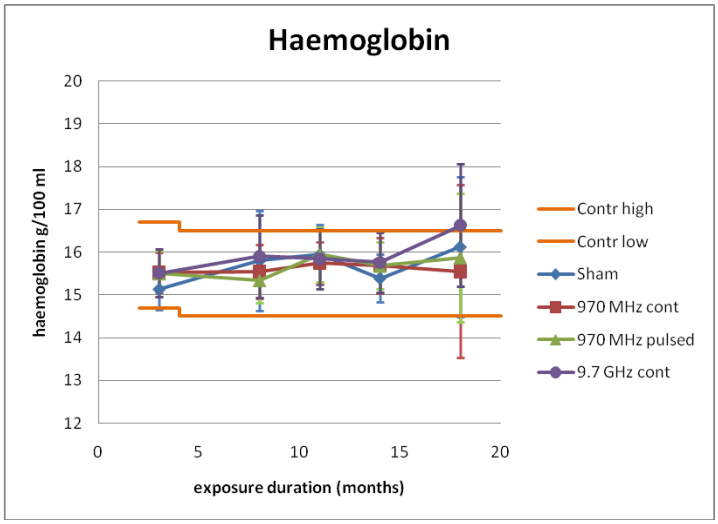

Figure C4 Time line of the haemoglobin content in the blood during the study; details as in Figure C1.

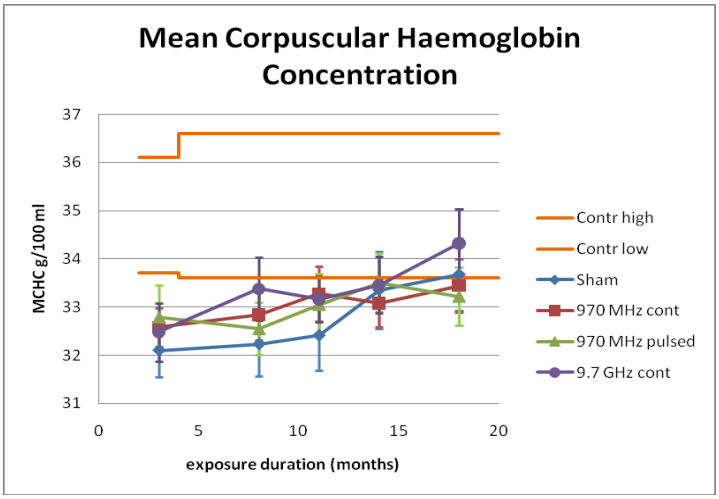

Figure C5 Time line of the MCHC, a measure of the haemoglobin content in erythrocytes, during the study; details as in Figure C1.

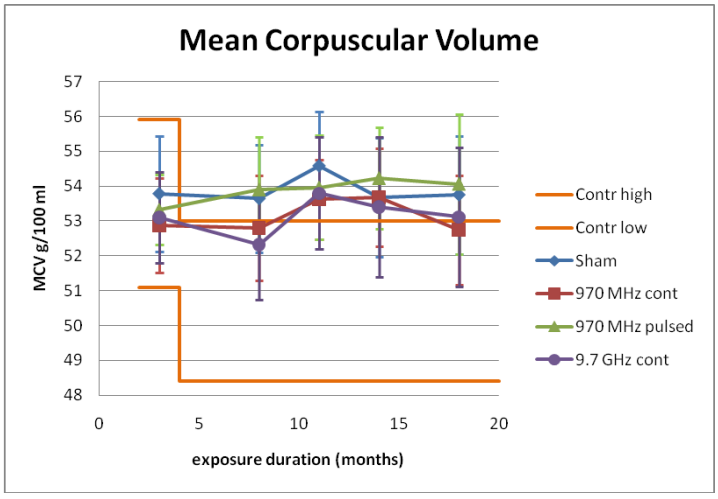

Figure C6 Time line of the MCV, a measure of the mean volume of an erythrocyte, during the study; details as in Figure C1.

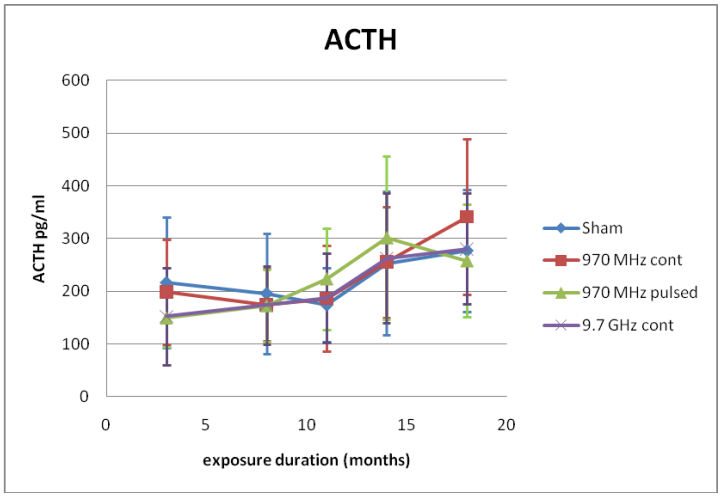

Figure C7 Time line of the concentration of adrenocorticotropic hormone in the blood during the study; details as in Figure C1.

Table C1 shows the differences presented by Adang (expressed as percentages) between sham and actual exposure for all parameters investigated in the blood. Statistically significant differences are shaded.

Table C1 The differences presented by Adang (expressed as percentages) between sham and actual exposure for all parameters investigated in the blood. Significant differences are shaded.

	970 MHz continuous					970 MHz pulsed					9.70 GHz continuous				
month	3	8	11	14	18	3	8	11	14	18	3	8	11	14	18
WBC	+10.9	+2.6	+9.9	+14.1	+33.6	-4.0	-7.0	-0.9	+4.0	+21.0	+7.5	-1.2	+3.6	+17.2	+7.7
RBC	+3.0	-1.8	-1.3	+2.7	-1.4	+1.4	-4.0	-0.1	+0.3	-1.1	+2.9	+0.4	-0.6	+2.6	+3.6
HBC	+2.6	-1.7	-1.3	+1.9	-3.6	+2.5	-2.9	0.0	+1.9	-1.6	+2.6	+0.6	-0.6	+2.4	+3.1
HCT			-3.4	+2.7	-3.3			-1.6	+1.4	-0.7			-2.6	+2.1	+0.8
MCV	-1.7	-1.5	-1.8	-0.02	-1.9	-0,8	+0.4	-1.1	+1.0	+0.6	-1.3	-2.5	-1.4	-0.5	-1.2
MCHC	+1.5	+1.9	+2.7	-0.8	-0.7	+2.2	+1.0	+2.0	+0.5	-1.3	+1.2	+3.6	+2.3	+0.3	+1.9
LYM					-13.0					-11.6					-15.1
NEUT					+27.9					+26.4					+34.7
EOS	-16.8	-4.6	-11.9	-15.6	+19.4	-7.4	-12.6	-11.5	-14.8	+8.1	-11.9	-8.2	-8.0	-11.1	+2.5
MOC	+23.5	+20.6	+13.0	+9.0	+12.5	+1.0	+8.4	+8.8	+14.1	+3.3	+21.1	+17.1	+9.6	+16.6	+2.1
RETIC		+6.2	-2.5	+11.0	+1.3		+14.0	-0.8	+5.0	+15.5		+5.3	-12.9	+6.3	+1.3
ACTH	-8.1	-11.2	+6.9	+1.1	+23.2	-31.1	-12.0	+28.4	+19.2	-6.9	-29.5	-11.3	+7.1	+3.8	+1.3
CORT			-2.1	-1.8	-17.4			+20.6	+7.5	-8.8			-6.2	-4.3	-3.3

WBC: white blood cells; RBC: red blood cells; HBC: haemoglobin content; HCT: haematocrit; MCV: mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; LYM: lymphocytes; NEUT: neutrophils; EOS: eosinophils; MOC: monocytes; RETIC: reticulocytes; ACTH: adrenocorticotropic hormone; CORT: cortisol

Annex **D**

Data from long-term exposure studies

The Committee carried out a literature study of investigations in which rodents were exposed long-term (for more than 6 months) to radiofrequency electromagnetic fields. Investigations in which exposure took place simultaneously with other factors, or in which tumours were induced using chemical agents, were not included.

In the first instance, a search was made in the WHO International EMF Project Research Database, with search criteria: Study Type=In Vivo; Freq Range=100 kHz - 300 GHz (RF/MW/mmW); Study Subtype=Long Term Rodent Bioassay. Thereafter, a search was conducted in PubMed with the following search terms: ((chronic OR life-time OR bioassay) AND (rats OR mice)) AND (radiofrequency OR radiowaves OR radio-waves OR radiofrequent OR cellphone OR mobile phone) NOT (in vitro[Publication Type] OR in vitro[All Fields]). The literature search took place on 19 August 2009; a repeat on 9 April 2010 revealed no new results.

The key data from the resulting investigations are summarised in the table below.

Animals	Exposure signal	Exposure duration/ blood sampling	SAR (W kg^{-1})	Restrained/ free	Effect tumor	Effect survival	Effect blood cells	Ref.
Rats								
Sprague-Dawley, male/female	860 MHz CW 860 MHz MiRS	6 h/d 5 d/wk 22 mo	Brain 0.8-1.2 WB 0.27-0.42	Restrained (carousel)	No effect on tumourigenesis	No effect	ND	[14]
F-344, male/ female	836.55 MHz NADC	2 h/d, 7.5 min on/ 7.5 min off 22 mo	Brain 0.3–0.5 WB 0.2-0.4	Restrained (carousel)	No effects on CNS/ brain tumour incidence	No effect	ND	[15]
F-344, male/ female	836.55 MHz FM	2 h/d 4 d/wk 23 mo	Brain 1.1-1.4 WB 0.3-0.7	Restrained (carousel)	No effects on CNS/ brain tumour incidence	No effect	ND	[16]
F-344, male/ female	835.62 MHz, FDMA 847.74 MHz, CDMA	4 h/d 5 d/wk 104 wk	Brain 1.3±0.5	Restrained (carousel)	No effects on tumour incidence	No effect	ND	[17]
F-344, male/ female	1.62 GHz Iridium	2h/d 5 d/wk 2 y At 2 y	Brain 0.11-0.18 or 1.1-1.8 WB ~0.02 or 0.2	Restrained (carousel)	No effects on tumour incidence	No effect	No effects on genotoxicity	[18,19]
Sprague-Dawley, male	435 MHz	22 h/d 6 mo At 1,2,3,4,6, 7,8, 10,11, 12,13,14,16, 17,18, 19,20 wk	WB 0.3-0.35	Freely moving	ND	ND	No effect on hematocrit, red, white blood cells, neutrophils, eosinophils, monocytes	[20]
Sprague-Dawley, male	2.45 GHz pulsed	21.5 h/d 7 d/wk 25 mo Every 6 wk,starting at wk 7	WB 0.15–0.4	Freely moving	No increase incidence individual tumour types. Four-fold increase combined primary malignancies, no increase combined primary benign tumours	No effect	Reduced eosinophils at 13 wk; reduced neutrophils at 13 & 19 wk	[9]
Wistar, male / female	902 MHz GSM or 1747 MHz DCS	2 h/d 5 d/wk 2 y At 6 & 12 mo	WB 0.44, 1.33 or 4.0	Restrained (Ferris wheel)	No effects on tumour incidence	No effect	No effect	[21]

Animals	Exposure signal	Exposure duration/ blood sam-pling	SAR (W kg^{-1})	Restrained/ free	Effect tumor	Effect survival	Effect blood cells	Ref.
Wistar, male	970 MHz CW 970 MHz GSM 9.7 GHz CW	2 h/d 7 d/wk 21 mo At 3, 8, 11 14 18 mo	WB 0.08	Freely moving	Incomplete analysis	Increased mortality with 9.7 GHz	Variable effects	[1]
Mice								
RFM, female	800 MHz	2 h/d 5 d/wk 35 wk Weekly, after 4 wk ~monthly	WB 43 mW/cm^2	Restrained	ND	No effect	Variations, no sign effect on red, white blood cell counts, hematocrit, hemoglobin	[22]
CD-1, female	2.45 GHz	1 h/d 5 d/wk lifetime	WB 2 or 6.8	Restrained	ND	Decreased survival with SAR=6.8 W/kg	ND	[10]
DBA2 or Swiss,female	60 GHz	30 min/d 5 d/wk lifetime	WB 0.31	Restrained	No effect on L1210 or Lewis tumours in DBA2	No effect in Swiss up to 231 d	ND	[23]
C57BL/ 6Ntac mice	898.4 MHz GSM	1 h/d 5 d/wk 104 wk	WB 0.25, 1.0, 2.0 or 4.0	Restrained (Ferris wheel)	No effect on tumour incidence	No effect	ND	[24]
B6C3F1, male / female	902 MHz GSM or 1747 MHz DCS	2 h/d 5 d/wk 2 y At 12 mo	WB 0.4, 1.3 or 4.0	Restrained (Ferris wheel)	No effect on tumour incidence	No effect	No effects on various parameters	[25]
B6C3F1, male / female	902 MHz GSM or 1747 MHz DCS	2 h/d 5 d/wk 2 y	WB 0.4, 1.3 or 4.0	Restrained (Ferris wheel)	ND	ND	No effect on micronuclei in peripheral blood eryth-rocytes	[26]
C57BL, male / female	849 MHz or 1763 MHz	1 h/d 5 d/wk 6 or 12 mo	Head only 7.8	Restrained (carousel)	No effect on body weight or brain cellular parameters	ND	ND	[27]
Mice, tumour prone								
Eμ-*Pim1*, female	900 MHz GSM	2x 30 min/d 7 d/wk 18 mo	WB 0.13- 1.4	Freely moving (5/cage)	2-fold increase in lymphoma incidence	ND	ND	[28]
Eμ-*Pim1*	898.4 MHz GSM	1 h/d 5 d/wk 104 wk	WB 0.25, 1.0, 2.0 or 4.0	Restrained (Ferris wheel)	No effects on tumour incidence	No effect	ND	[24]

Animals	Exposure signal	Exposure duration/ blood sampling	SAR (W kg^{-1})	Restrained/ free	Effect tumor	Effect survival	Effect blood cells	Ref.
Eμ-*Pim1*, male / female	900 MHz GSM	1 h/d 7 d/wk 18 mo At 12 and 18 mo	WB 0.5, 1.4 or 4.0	Restrained (Ferris wheel)	No effects on lymphoma incidence Increased Harderian gland adenoma in males, not in females	Decreased, significant only for 0.5 W/kg	No effects on various parameters	12
AKR/J, female	900 MHz GSM	24 h/d 7 d/wk 10 mo Monthly as of 6 mo	WB 0.4	Freely moving (6-7/cage)	No effects on lymphoma	No effect	No effects on differential count of leucocytes	29
AKR/J, female	1.966 GHz UMTS	24 h/d 7 d/wk 35 wk Twice monthly as of 6 mo	WB 0.4	Freely moving (6-7/cage	No effects on lymphoma.	No effect	No effects on differential leucocyte count	30
C3H/HeA, female	2.45 GHz CW	2 h/d 6 d/wk 10.5 mo	WB ±2–3 or ±6–8	Freely moving (10/cage)	Accelerated tumor development	Decreased survival due to mammary tumorigenesis	ND	11
C3H/HeJ, female	435 MHz Pulsed	22h/d 7 d/wk 21 mo	WB 0.32	Freely moving (1/cage)	No effect on tumour incidence	No effect	ND	31
C3H/HeJ, female	2.45 GHz CW	20 h/d 7 d/wk 78 wk	WB 0.3	Freely moving (1/cage)	No effects on tumour incidence, except decreased incidence of alveolar-bronchiolar adenomas in lungs	No effect	ND	32
C3H/HeJ, female	2.45 GHz CW	20 h/d 7 d/wk 78 wk At 18 mo	WB 1.0	Freely moving (1/cage)	No effect on tumour incidence	No effect	No effect on micronuclei in peripheral erythrocytes	33,34
Ico:IFO(I.O. P.S. Caw), female	800 MHz GSM	1 h/wk 4 mo	WB SAR not determined	Freely moving	Acceleration of carcinogenesis	Acceleration of mortality	ND	13

CDMA: Code Division Multiple Access
CW: Continuous Wave
CNS: Central Nervous System
DCS: Digital Personal Communication System
FDMA: Frequency Division Multiple Access
FM: Frequency Modulation
GSM: Global System for Mobile Communication
MiRS: Motorola integrated Radio Services
NADC: North American Digital Cellular
ND: not detemined
SAR: Specific Absorption Rate