

Risk evaluation of the health effects
of mobile phone communication.
Results of a scientific dialogue

Presentation and discussion of the topic areas

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Preface

The present study documents a dialogue between scientists whose goal it was to produce a risk evaluation for the issue of "mobile phone communication and health".

Participating experts included: PD Dr. Peter Achermann, Prof. Dr. Maria Blettner, Prof. Dr. Clemens Dasenbrock, Prof. Dr. Thomas Eikmann, Dr. Rudolf G. Fitzner, Dr. Richard Gminski, Prof. Dr. Konstantin-Alexander Hossmann, Prof. Dr. Karl-Heinz Jöckel, Prof. Dr. Alexander Lerchl, Dipl. Psych. Sabine Regel, Dr. Martin Röösl, Prof. Dr. Andreas Stang, Dr. Dr. Kathrin Schlatterer, Dr. Heike Seitz, PD Dr. Myrtill Simkó, Dr. Doris Stinner, Prof. Dr. Florian Stögbauer and Dr. Peter Ullsperger.

In addition, the advisory expert panel included: Prof. Dr. Wolfgang Dekant, Prof. Dr. Rainer Meyer, Prof. Dr. Wolfgang-Ulrich Müller, Prof. Dr. Dr. Heiner Raspe, Prof. Dr. Thomas Penzel und PD Dr. Gerhard A. Wiesmüller.

The Program Group "Mensch Umwelt Technik (MUT)" [Humans, Environment, Technology] of the Research Center Jülich led and moderated the scientific dialogue and summarized the expert opinions and discussions. The focus was directed towards an easily comprehensible characterization of the findings and conclusions for the evaluation of the relationship between mobile phone communication and health. The report presented here aims to help the public and policy makers to better understand the current state of the scientific evidence as well as the risk evaluation.

The present report is the English language version of the first part of the original German report which is comprised of a two part series containing this report as well as the individual expert opinion reports and their appendices. The latter are presently only available in their original German language version.[†] Cited passages from excerpts of various sources were translated for the purposes of this report. Whenever possible, we of course used official or approved translations but those were not always available. Thus, although we took great care in our translations of cited passages, they should not be considered to be official or approved translations and should not be cited or excerpted from this report as such.

We thank all participants for their extraordinary commitment. We also thank the T-Mobile Germany, who supported this study financially.

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[†] Online available: http://www.emf-risiko.de/projekte/ergeb_bewlit.html

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1. Summary

Procedures and results of the risk dialogue on "mobile phone communication and health"

The program group Mensch Umwelt Technik (MUT) [Humans Environment Technology] of the Research Center Jülich conducted a scientific dialogue from September 2003 to April 2005. The goal was to develop a dialogue process for a transparent risk evaluation of the "mobile phone communication and health" topic.

Twenty-five subject matter experts from Germany and Switzerland, recognized for having their own research programs, were won as experts or advisory expert panelists. The selection of the experts through the program group MUT was to ensure that the spectrum of different expert opinions on each issue was represented. Six topic areas were the focus of the risk dialogue:

1. Genotoxic (DNA-damaging) effects from radio-frequency electromagnetic fields,
2. Laboratory animal cancer studies,
3. Epidemiological studies on cancer,
4. Effects on the central nervous system as well as on cognitive functions and sleep,
5. Impairment of well-being and
6. Effects on the blood-brain-barrier.

For each of these topic areas, at least two experts who themselves are active researchers in that field selected the most important studies and evaluated their findings. Research from the years 2000 until 2004 was examined. For each topic area, a workshop was conducted with the experts and additional advisory expert panelists. In a subsequent collective workshop, the resulting conclusions were discussed.

Thus, an evaluation of six important topic areas on "mobile phone communication and health" can be presented here. This evaluation is based on a broad expert knowledge base and presents its underlying rules of evaluation clearly and transparently. Only through the prerequisite of a transparent and balanced presentation can laypeople arrive at their own risk-aware judgment.

Results

The results of the dialogue pertain on the one hand to procedural issues, and on the other hand to the results of these procedures, i.e. the evaluations.

First, the procedures that MUT developed and enhanced for the risk evaluation. This includes the initiation of a risk dialogue as well as instruments for the characterization of the evaluations of individual research studies.

The most important innovation is the aptly named "evidence framework", that allows for a transparent summarization of the experts' line of reasoning. As always, the summarization of individual studies into an overall evaluation is dependent upon their interpretation. Consequently, it is not surprising that subjective assessment meas-

ures are apparent since there exist no unambiguous rules or evaluation-standards as to the approach and implementation of how very different studies with at times contradictory findings are to be summarized into an overall picture.

To address this shortcoming of the risk evaluation process, MUT has developed the "evidence framework" with which the most crucial arguments for as well as against a risk suspicion, the conclusions of the experts, and the remaining uncertainties can be better understood.

For several issues, clarifications of content could be achieved through the dialogue process. In other areas, contradictions and ambiguity remain, which signifies a demand for future research. Consequently, according to the assessment of the experts, the present research studies provide no indication that radio-frequency electromagnetic fields of mobile phone communication cause cancer in animal experiments or promote cancer growth. The studies of the blood-brain-barrier also find no indications of effects from electromagnetic fields by mobile phone communication.

Furthermore, the experts concluded that the experimentally determined effects of mobile phone communication on the central nervous system do not pose a recognizable health disadvantage. The same applies to the indications of genetic damage. Since this does not result in damage to the cells, it does not support the derivation of a health endangerment, according to the opinion of the experts.

For most impairments of well-being – the exception being headaches – the experts view the weight-of-evidence as so weak, that an evaluation is hardly feasible. However, from the perspective of the experts, the few existing research findings don't indicate a link to exposure with RF-EMF. Admittedly, the experts see an indication of a link between headaches and mobile phone usage. However, it remains uncertain whether this proves a relationship between electromagnetic fields and headache, or whether the cause could simply be telephone stress.

The issue of a special sensitivity (electromagnetic hypersensitivity) of certain persons to the EMF of mobile phone communication could not be conclusively clarified. Admittedly, no findings that speak in favor of the existence of such a special sensitivity could be found, but it can also not be ruled out with certainty. For the same reason, it cannot be evaluated whether effects may possibly manifest themselves in sick or health-impaired individuals.

The findings regarding epidemiological cancer studies are in part contradictory. Consequently, the experts arrived at different evaluations: on the one hand they evaluated that a cancer-promoting effect is likely not to be expected, but on the other hand they evaluated that there is a vague initial suspicion. The scientists agreed, however, that after a few years of use of mobile phones, an increased risk of tumors is not to be expected.

Altogether, in light of the six topic areas investigated, support for the hypothesis that EMF of mobile phone communication exhibits unhealthy effects was not strengthened.

2. Introduction

In the summer of 2003, the program group Mensch Umwelt Technik (MUT) [Humans Environment Technology] of the Research Center Jülich began to conduct a scientific dialogue of the risk evaluation of mobile phone communication. This project was supported by the T-Mobile Germany and builds upon the results of the first risk dialogue "*Mobile phone communication and health— Risk evaluation in a scientific dialogue*" that MUT conducted in 2001 to 2002 (see Wiedemann, Schütz & Thalmann 2003).

In contrast to the previous risk dialogue project, in which the dialogue only began after completion of the expert opinion reports, the new dialogue already started with the selection of the experts and thus included all steps of the expert opinion preparation up to the concluding discussions.

The subject matter of the project is the set of new scientific studies on biological effects of radio-frequency electromagnetic fields (RF-EMF) of mobile phone communication, which were conducted in the years 2000 until 2004. Six topic areas that currently are at the center of the scientific – but also public – debate are focused upon:

- Genotoxic effects from radio-frequency electromagnetic fields.
- Laboratory animal experimental studies of cancer from radio-frequency electromagnetic fields.
- Epidemiological cancer studies from radio-frequency electromagnetic fields.
- Effects of mobile phone communication fields on the central nervous system in the awake - and sleep states.
- Impairments of well-being from radio-frequency electromagnetic fields.
- Effects of mobile phone communication fields on the blood-brain-barrier.

Aim of the project was to further develop the risk dialogue process presented by us (Wiedemann et al. 2003), as well as (1) to identify how experts evaluate the current scientific evidence in the chosen six topic areas, (2) what conclusions in regards to the risk potential they reach, (3) which arguments are employed in the justification, and (4) which consensus and disagreements exists among the experts.

3. Course of the project

The project was initiated in September 2003 and was completed in April 2005. The project path was divided into several steps: (1) the selection of the experts and advisory expert panelists, (2) the preparation of the expert opinion reports, (3) the discussion of the expert opinion reports in workshops, (4) the possibility for reworking the expert opinion reports, and (5) a collective final workshop.

3.1 Selection of the experts and advisory expert panelists

Each topic area was addressed by two experts. An essential criterion for the selection of the experts was that they themselves are engaged in scientific research in the area of EMF and in the respective topic area, as documented by publications in recognized specialty journals. This was to ensure that the experts would have both the contextual-theoretical background as well as the methodological knowledge for pre-

paring an expert opinion report. Knowledge gained from performing one's own experimental studies as well as empirical expertise with the investigation methods, is crucial for the critical evaluation of the scientific evidence presented in the primary studies on possible health effects from RF-EMF.

The critiques and discussions of the expert opinion reports during the workshops were to be supported by advisory expert panelists. For their selection as well, the criterion of scientific expertise in the respective topic area was essential. However, it was not required that the scientific research of the advisory experts focuses specifically on the EMF field (although this was for the most part the case). Rather, the selection depended on their ability – for the respective topic area – to critically review the expert opinion reports and line of reasoning of the experts in regards to the contextual-theoretical and methodological basis.

The selection of the experts and the advisory expert panelists was performed by MUT. An attempt was made to find experts that are representative of the spectrum of scientific opinion for each topic area. In some cases, the scientists selected by MUT opted to prepare the expert opinion reports together with their colleagues. Table 1 presents the experts as well as expert groups and the advisory expert panelists for the six topic areas.

Table 1: Experts and advisory expert panelists for the six topic areas

Topic area	Experts	Advisory expert panelists
Genotoxic Effects	<ul style="list-style-type: none"> • Dr. Rudolf G. Fitzner, Dr. Dr. Kathrin Schlatterer und Dr. Richard Gminski (Institute for Clinical Chemistry and Pathobiochemistry, Charité–University Medicine, Berlin) • PD Dr. Myrtil Simkó (Institute for Cell Biology and Biosystems Technology, University of Rostock) 	Prof. Dr. Wolfgang-Ulrich Müller (Institute for Medical Radiobiology, University clinics of Essen)
Cancer Epidemiology	<ul style="list-style-type: none"> • Prof. Dr. Maria Blettner (Institute of Medical Biostatistics, Epidemiology and Informatics, Johannes Gutenberg University of Mainz) • Prof. Dr. Karl-Heinz Jöckel und Prof. Dr. Andreas Stang¹ (Institute for Medical Informatics, Biometry and Epidemiology, Medical School, University Duisburg-Essen) 	Prof. Dr. Dr. Heiner Raspe (Institute for Social Medicine, University Clinics Schleswig-Holstein)
Laboratory animal cancer studies	<ul style="list-style-type: none"> • Prof. Dr. Clemens Dasenbrock (Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover)² • Prof. Dr. Alexander Lerchl (International University Bremen, School of Engineering and Science) 	Prof. Dr. Wolfgang Dekant (Institute for Toxicology, University Würzburg)

¹ Contact information: Since summer 2004 he is with the Institute for Medical Epidemiology, Biometrics and Computer Science [IMEBI], Medical faculty, Martin-Luther-University Halle-Wittenberg.

² Contact information: Since Summer 2004 he is with Boehringer Ingelheim Pharma GmbH &CoKG, Biberach an der Riss.

Topic area	Experts	Advisory expert panelists
CNS / sleep	<ul style="list-style-type: none"> • PD Dr. Peter Achermann und Dipl. Psych. Sabine Regel (Institute of Pharmacology and Toxicology, University of Zurich) • Dr. Peter Ullsperger (Federal Institute for Occupational Safety and Health, Berlin) 	Prof. Dr. Thomas Penzel (Marburg University Medical Center)
Impairment of well-being	<ul style="list-style-type: none"> • Dr. Martin Rösli (Department of Social and Preventive Medicine, University of Berne) • Dr. Heike Seitz, Dr. Doris Stinner und Prof. Dr. Thomas Eikmann (Institute of Hygiene and Environmental Medicine, Justus-Liebig-University Gießen) 	PD Dr. Gerhard A. Wiesmüller (Outpatient Unit of Environmental Medicine (UEM) of the Institute of Hygiene and Environmental Medicine, University Hospital Aachen, Medical Faculty of the Rheinisch-Westphalian Technical University (RWTH) Aachen)
Blood-brain-barrier	<ul style="list-style-type: none"> • Prof. Dr. Konstantin-Alexander Hossmann (Max-Planck-Institute for Neurological Research in Cologne) • Prof. Dr. Florian Stögbauer (Dept. of Neurology, University Hospital Münster) 	Prof. Dr. Rainer Meyer (Institute for Physiology, School of Medicine, University of Bonn)

The prerequisite for the selection of the experts – namely to actively research and publish in the topic area itself – led in some cases to the situation that the experts had to evaluate their own work. This applies to Achermann, Jöckel, Fitzner, Rösli, Simkó, Stang, Stögbauer and Ullsperger. Since each topic area, however, was always addressed by two experts and the line of reasoning presented in the expert opinion reports was critically reviewed by the advisory expert panelists, this circumstance should not result in a bias in the evaluation of the overall state of scientific knowledge.

3.2 Preparation of the expert opinion reports

The experts were given their tasks by MUT in the autumn of 2003. They were allowed sufficient time for the preparation of their expert opinion reports. For each topic area, a workshop was conducted with the experts and the advisory expert panelists. The expert opinion reports could then again be revised based on the workshop discussions. The results of the expert opinion reports were then presented again in a collective final workshop and discussed as a group.

In order to ensure the greatest amount of uniformity – and consequently comparability – of the presentation of the state of scientific knowledge, MUT suggested a structure for the preparation of the expert opinion reports that was adopted by all the experts.³ The expert opinion reports were to address the following points:

³ The suggestion of MUT for the structured presentation of the expert opinion reports was guided by the Cochrane Review (see http://www.cochrane.dk/cochrane/handbook/3_1_rationale_for_protocols.htm) and (http://www.cochrane.dk/cochrane/handbook/appendix_2a_guide_to_the_format_of_a_cochrane_review.htm), (<http://www.cochrane.dk/cochrane/handbook/hbook.htm>).

1. Aim of the expert opinion report

- Characterization of the topic area (especially in regards to the relevance of the findings from this topic area for the evaluation of potential health risks).
- Selected endpoints and rationale behind their selection.

2. Selection of the studies to be considered from the period 2000 to 2004

- Criteria for the selection of the considered studies (if necessary, also mention of the selected field strengths, frequency range and signal shape).
- Search strategies for the selection of primary research studies (personal bibliographic lists of references/ databases; Medline, etc.).
- Information on the quality of method for each study.

3. Presentation of the state of scientific knowledge

- Discussion of the findings and method of the studies for each individual endpoint.
- Evaluation of the scientific weight-of-evidence for the individual endpoints.

4. Overall evaluation for the topic area

- Summarizing evaluation of the scientific evidence for the topic area.

5. List of the considered studies and the references used

The experts were asked to closely coordinate the first two work steps among them, so that the expert opinion reports for each topic area would pertain to the same endpoints and be based on the evaluation of the same set of primary studies. In several cases, however, the experts realized during the coordination that there exists such an extent of overlap – even for the evaluation of the evidence – that they decided to develop a joint expert opinion report and individually point out the possible evaluation differences within the joint report. Although originally two separate expert opinion reports for each topic area were called for, the suggestion by the experts was accepted to avoid redundancy and to improve the readability of the expert opinion reports.

For the topic areas "genotoxic effects", "experimental laboratory animal cancer studies", "epidemiological cancer studies" and "blood-brain-barrier" there are joint expert opinion reports available, while for "CNS/sleep" and "impairment of well-being" separate expert opinion reports were prepared. The preparation of separate expert opinion reports, however, does not mean that the differences in the evaluation of the evidence among the different experts were in any way greater than those for the jointly developed expert opinion reports. All of the expert opinion reports can be found in Part 2 of this report.

3.3 Workshops

After the preparation of the expert opinion reports, each topic area was discussed during a one-day workshop with the experts and the advisory expert panelist. An overview of the workshops, which were conducted from June 2004 until November 2004, is given in Table 2. The authors of this report participated in all of the workshops.

Table 2: Overview of the workshops

Topic Area	Date	Location	Participants
Impairment of well-being	01.06.2004	Gießen	<ul style="list-style-type: none"> • Seitz, Stinner, Eikmann • Rössli • Wiesmüller
Experimental laboratory animal cancer studies	03.06.2004	Hannover	<ul style="list-style-type: none"> • Dasenbrock • Lerchl • Dekant
Blood-brain-barrier	16.06.2004	Cologne	<ul style="list-style-type: none"> • Hossmann • Stögbauer • Meyer
CNS / sleep	23.06.2004	Berlin	<ul style="list-style-type: none"> • Achermann, Regel • Ullsperger • Penzel
Genotoxic effects	09.07.2004	Berlin	<ul style="list-style-type: none"> • Simkó, • Fitzner, Gminski, • Müller, Obe⁴
Cancer epidemiology	03.09.2004	Hannover	<ul style="list-style-type: none"> • Blettner • Stang • Raspe
Collective final workshop	03.11.2004	Berlin	<ul style="list-style-type: none"> • Experts • Advisory expert panelist • T-Mobile • BMU

The workshops for the topic areas had the following structure: first, the experts introduced their opinion reports, and then questions of understanding were clarified. Then followed the assessment of the expert opinion reports by the advisory expert panelists, wherein the advisory experts were to specifically address the following points:

- Based on the presented scientific documentation (primary studies), are the conclusions drawn in the expert opinion reports regarding the influence of radio-frequency electromagnetic fields on the endpoint or rather effect for each topic area plausible?
- Did the primary studies use appropriate methodology (study design, exposure measurement, effect measurement, evaluation procedures, etc.)?
- Were alternative explanations for positive as well as negative findings considered?
- How is the consistency or rather inconsistency of the overall scientific picture to be judged?
- Based on the presented scientific studies, are the conclusions regarding the relevance to health of the discussed effects plausible?

While only the experts, the advisory expert panelists, and the authors of the report participated in the topic area-specific workshops, representatives of the funding organization for the project – T-Mobile Germany – as well as representatives of the German Federal Ministry of Environment also participated in the final workshop held in Berlin on 3.11.2004 as observers.

⁴ Prof. Dr. Günther Obe (Professor emeritus, University Duisburg-Essen, FB-9, Genetics), as an associate member of the working group of Dr. Fitzner, also participated in this workshop and also in the final workshop. However, he is not a coauthor.

In the final workshop, one of the experts first presented the central results for each topic area. Then MUT presented the weight-of-evidence for the respective topic area offered in the expert opinion report in the form of an evidence framework. In this framework the evaluation of the weight-of-evidence by the experts is summarized in the form of "Pro and Con" arguments. Afterwards the evidence frameworks as well as cross-linkages between the six topic areas were discussed.

The topic area-specific workshops as well as the collective final workshop provided valuable insights for the following presentation and discussion of the topic areas.

4. Presentation and Discussion of the Topic Areas⁵

The same structure for the presentation and discussion of the six topic areas is employed:

- First, a short introduction is given into the topic area and its significance for the risk evaluation.
- For each respective topic area, this is followed by an assessment of the state of knowledge up until the year 2000 by two expert committees, whose prior assessments of the possible risks of mobile phone communication enjoyed much resonance especially in the public: the German Radiation Protection Commission (SSK 2001), and the English Independent Expert Groups on Mobile Phones (IEGMP 2000).
- Then, the results of the expert opinion reports and the discussions are presented. This presentation takes the shape of a Pro- and Con-argumentation that is visualized with the help of the evidence framework. The content of the Pro- and Con-arguments are based on the respective expert opinion reports and workshop discussions. The evidence frameworks were presented and discussed during the collective final workshop. For a comprehensive understanding of the Pro- and Con-arguments, the "supporting" as well as "attenuating" arguments (also shown in the evidence frameworks) play a significant role. This is because the Pro- and Con-arguments frequently are based only on the fact that (a certain number of) studies found something. Only through the qualifying arguments does it become obvious to what extent one can judge these findings to be reliable.
- Subsequently, the conclusions for the evaluation of the evidence and for the risk evaluation are presented.
- In another section, the remaining uncertainties for the evaluation of the evidence and the risk evaluation are identified.
- The presentation concludes with an assessment by MUT in which the points we see as specifically essential for the evaluation of the evidence and risk are once more discussed.

⁵ A first draft of the presentation of each topic area was made available to the respective experts and advisory expert panelists for comments and correction of factual errors. We sincerely thank the experts and advisory expert panelists for their many comments and suggestions for corrections.

4.1 Genotoxic effects

Starting point

The focus of this topic area is the possible damaging effect of radio-frequency electromagnetic fields on the genotype (DNA). Such DNA damages include, for example, strand breaks, i.e. breaks in one or both of the polynucleotide strands of DNA. Such alterations in the genotype (genetic mutations) appear spontaneously to a certain extent and can be corrected through cellular repair mechanisms. The correctly repaired genetic mutations present no consequential damage to the organism. If the cellular repair mechanisms fail however, this can lead for example to disruption of the cellular communication, to changes in the rate of cell division or lead to apoptosis (programmed cell death). Possibly, this could result in damage to the whole organism, for example as neurodegenerative illness or cancer.

Significance for the risk evaluation

If it could be shown that the exposure to radio-frequency electromagnetic fields induces damages to the genotype, this would certainly be a serious indication for a health risk. Conversely, negative results for the investigation would contradict the notion that radio-frequency electromagnetic fields are responsible for diseases in which cellular damage plays a role.

The experts for this topic area, however, expressly point out that for the risk evaluation the changes or damages to the genotype are not as significant in themselves, as is the relevance of the changes or damages for influencing the cell cycle and cell proliferation. For only if cell damages affect the cell cycle, for instance through an accelerated rate of cell proliferation, is this indication of a health risk, for example a tumor development.

4.1.1 State of the knowledge in the year 2000

The German Radiation Protection Commission (SSK 2001) elaborated on the state of knowledge in the year 2000 with respect to genotoxic effects:

Die Untersuchungen zu genetischen Schäden durch hochfrequente Felder sind kaum untereinander vergleichbar, weil unterschiedliche Expositionsparameter wie Frequenz, Modulation und Feldstärke verwendet wurden. Die Ergebnisse mit Feldstärken deutlich oberhalb der Grenzwerte sind nicht einheitlich. Es ist festzuhalten, dass Untersuchungen in Feldern, die durch den Mobilfunk (kontinuierliche, amplituden- und frequenzmodulierte Felder) entstehen, keinen Hinweis auf ein genotoxisches Potential ergaben. (p. 13) [*The investigations of genetic damage from high(radio)-frequency fields can hardly be compared to one another because different exposure parameters such as frequency, modulation, and field intensity were used. The findings from field intensities clearly above the limit values are not uniform. It should be noted that investigations for fields created by mobile phone communication (continuous, amplitude- and frequency-modulated fields) did not provide indications for a genotoxic potential. (p. 13)][†]*

The assessment of the Independent Expert Group on Mobile Phones (IEGMP 2000) stated:

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

Several different assays of genotoxicity have failed to produce clear evidence that RF radiation is genotoxic at non-thermal levels. The most consistent results come from observations of micronucleus formation, but these are not simple to interpret and have uncertain implications for health. (p. 73)

4.1.2 Results of the expert opinion report and discussion

The two expert/groups, Dr. Gminski, Dr. Dr. Schlatterer, Dr. Fitzner and Dr. Simkós submitted a joint expert opinion report. The advisory expert panelist for this topic area was Professor Dr. Wolfgang-Ulrich Müller (Institute for Medical Radiobiology, University Clinics of Essen).

Basis of evidence (studies since the year 2000)

In the expert opinion report, three groups of studies are distinguished: (1) studies in which human cells and the cell proliferation were examined, (2) studies in which human cells without consideration of the cell proliferation were examined, and (3) studies in which animal cells were used.

Only studies out of group 1 are explicitly drawn upon for the risk evaluation. Table 3 lists the studies considered in the expert opinion report and their grouping.

Table 3: Studies on genotoxic effects since the year 2000

Studies Group 1	Studies Group 2	Studies Group 3
D'Ambrosio et al. (2002)	Maes et al. (2000)	Bisht et al. (2002)
Hook et al. (2004)	Maes et al. (2001)	Koyama et al. (2003)
McNamee et al. (2003)	Mashevich et al. (2003)	Lagroye et al. (2004)
Miyakoshi et al. (2002)	McNamee et al. (2002)	Li et al. (2001)
REFLEX (2004)	McNamee et al. (2002)	Park & Kim (2002)
Tice et al. (2002)	Miyakoshi et al. (2002)	
Vijayalaxmi et al. (2001a)	Rüdiger et al. (2003)	
Vijayalaxmi et al. (2001b)	Unknown (WHO 2001)	
Zeni et al. (2003)	Vijayalaxmi et al. (2000)	
	Zhang et al. (2002)	
	Zotti-Martelli et al. (2000)	

Pro- and Con-arguments for genotoxic effects

The evidence framework for the topic area of genotoxic effects shows that there are two central Pro-arguments and one Con-argument (see Figure 1 and Figure 2).

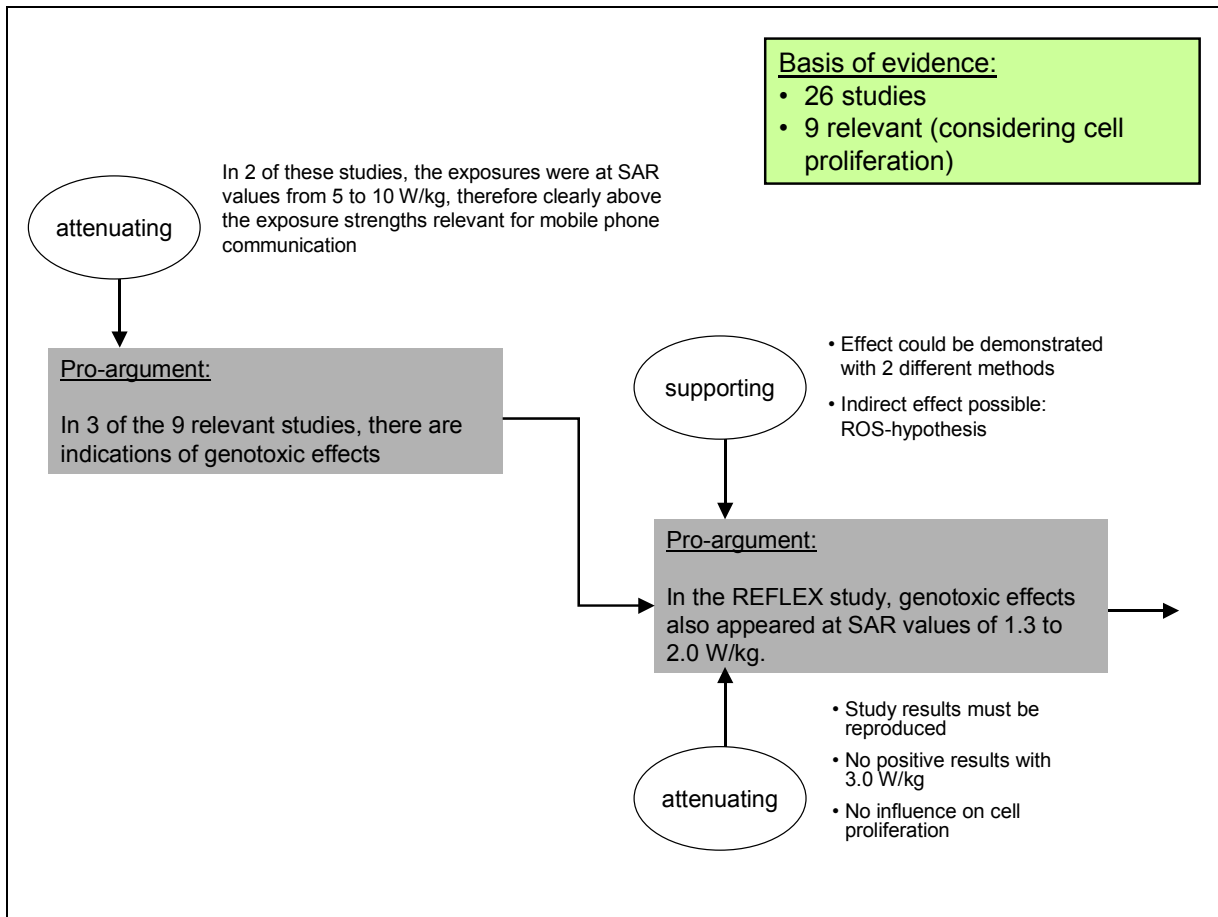


Figure 1: Evidence framework for genotoxic effects (Part 1)

Pro-argument:

The first Pro-argument refers to the finding that in three of the nine conducted studies (D’Ambrosio et al. 2002, Tice et al. 2002, REFLEX 2004) in which human cells were used and cell proliferation was investigated, indications of genotoxic effects were observed (see Figure 1). However, in none of the studies could changes to the cell proliferation be observed that were regarded by the experts as decisive for the risk evaluation.

The Pro-argument is further attenuated by the very high exposures in two of the studies: the SAR values ranged from 5 to 10 W/kg and therefore clearly above the relevant exposure strengths for mobile phone communication (D’Ambrosio et al. 2002; Tice et al. 2002). In this respect, these results are not meaningful for a risk evaluation of mobile phone communication.

The second Pro-argument refers to the REFLEX study⁶ in which genotoxic effects are shown even at SAR values from 0.3 to 2.0 W/kg – therefore in the relevant range for mobile phone communication. The relevance refers to the utilization of mobile

⁶ The REFLEX study (Risk evaluation of potential environmental hazards from low-energy electromagnetic field (EMF) exposure using sensitive *in vitro* methods) is an international project comprised of multiple component studies in which not only radio-frequency but also low-frequency electromagnetic fields were investigated with respect to their effects on cells and the genotype.

phone units whose limit values lie at 2W/kg. For mobile phone communication base stations the limit values are at 0.08 W/kg. Here, the REFLEX study showed no effects at 0.1 W/kg.

This argument is strengthened by the fact that in the REFLEX study an influence from exposures to 1800 MHz fields was observed with not just one but two different methods: DNA strandbreaks (single- and double-strandbreaks) as well as increased micronucleus formation could be determined. The ROS-hypothesis supports these findings because, for the first time, it allows for a possible explanation of how RF-EMF could result in DNA damage. Up to now, the challenge for the interpretation of positive results was that no mechanism was known by which such fields could cause genotype damage. For example, the energy of radio-frequency electromagnetic fields is too weak to break the atomic bonds of DNA and thus result in damage. In RF-EMF experiments of the REFLEX study on HL-60 cells—a cell line from human leukemia cells—an increase of reactive oxygen species (ROS) was observed. Thus, it appears possible that DNA breaks are caused by the formation of free radicals. This hypothesis does not only appear plausible from the perspective of the experts, who admittedly participated in the development of the hypothesis, but also appeared plausible to the advisory expert panelist Prof. Müller.

The results of the REFLEX study are attenuated by three points: (1) To date the results have not yet been reproduced, i.e. confirmation of the results from other studies. (2) Despite the observed genotoxic effects, no influence of the RF-EMF exposure on cell proliferation and cell cycle could be detected. (3) There is no plausible dose-response relationship for the observed increase of micronucleus formation with RF-EMF exposure in HL-60 cells: for exposures to 0.2 W/kg and 1.0 W/kg the micronucleus formation does not differ significantly from the control (sham exposed) group HL-60 cells. The micronucleus formation increases dramatically for exposure to 1.3 W/kg and then slowly decreases again for 1.6 W/kg and 2.0 W/kg – whereby all three exposure levels differ statistically significantly from the control (sham exposed) group. At an exposure of 3.0 W/kg, however, there is again to difference to the control (sham exposed) group. This issue was discussed in the project's final workshop. The experts argued that in light of the ROS-hypothesis such a non-monotonic dose-response relationship is entirely plausible if one assumes that the ROS-effect reaches an optimum at approximately 1.3 W/kg. Thereby, diverging effectiveness optima for both genotoxic effects as well as cellular repair mechanisms could play a role, which could result in a complex and non-linear dose response relationship.

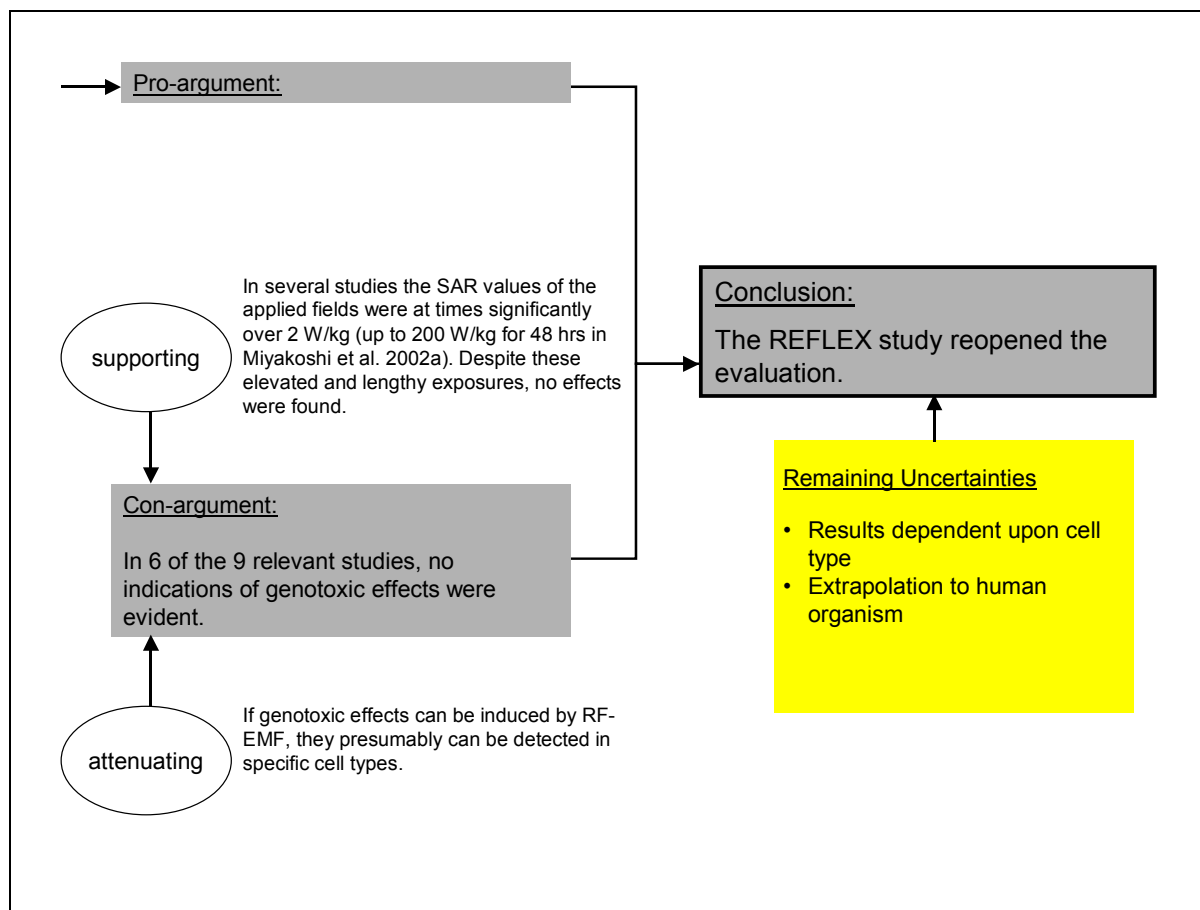


Figure 2: Evidence framework for genotoxic effects (Part 2)

Con-argument:

The Con-argument is that in six of the nine conducted studies, in which human cells were used and cell proliferation was investigated, no indications for genotoxic effects were observed (Hook et al 2004, McNamee et al. 2003, Miyakoshi et al. 2002a, Vijayalaxmi et al. 2001a, 2001b and Zeni et al. 2004). This argument is supported by the fact that in several studies the strength (SAR values) of the applied fields were at times significantly above 2 W/kg (up to 200 W/kg for an exposure duration of 48 hours in Miyakoshi et al. 2002a) and despite these elevated and lengthy exposures, no effects were found.

The Con-argument is attenuated, however, through the assessment of the experts that genotoxic effects from RF-EMF exposures will presumably only appear in specific cell types and not in cells of the peripheral blood system. In this respect, the negative findings in the studies with lymphocytes and leukocytes cannot be generalized.

4.1.3 Conclusions

The essential conclusion of the experts, which is also shared by the advisory expert panelist Prof. Müller, is that in light of the results of the REFLEX study, the evaluation of genotoxic effects from exposure to radio-frequency electromagnetic fields has been reopened. The up to now predominantly negative research findings and the resultant assessment that genotoxic effects from radio-frequency electromagnetic

fields (below the current limit values) are unlikely,⁷ must be re-examined in light of the contraindicative findings of the REFLEX study.

However, based on the experts' assessment, it cannot be concluded from this that health risks from RF-EMF due to genotoxic effects are therefore to be anticipated. As justification, they refer to a series of critical points, that are to be considered not only in the evaluation of the findings of the REFLEX study but in general for the risk evaluation regarding genotoxic effects:

- Even if *in vitro* investigations determine the presence of genotoxic effects, this doesn't inevitably signify an increased health risk, because living organisms possess a series of repair mechanisms and protective functions with which damages to the DNA can be remedied or "degenerated" cells can be neutralized.
- In general – according to the recommendation of regulatory commissions – the classification as non-genotoxic or genotoxic should not be made solely based on a single test method, rather different tests should be utilized. Only then, if all or the majority of the tests shows significant effects, should RF-EMF be classified as genotoxic.
- Finally, the results of *in vitro* studies cannot be simply transferred to humans *in vivo*.

In their assessment of the weight-of-evidence, the experts therefore determine (expert opinion report of Gminski et al., p. A-16):

Generell sollte aus diesem Gutachten geschlossen werden, dass es aus den aufgeführten Studien zur Genotoxizität der Jahre 2000 bis 2004 zur Zeit keinen gesicherten wissenschaftlichen Nachweis für die Annahme gibt, wonach eine Exposition von Zellen mit RF-EMF zytogenetische Veränderungen induzieren, die eine biologische Bedeutung für die menschliche Gesundheit haben könnten. [*In general, it should be concluded from this expert opinion report that for the mentioned studies on genotoxicity from the years 2000 to 2004 no confirmed scientific evidence exists, at present, for the assumption wherein cell exposure to RF-EMF induces cytogenetic changes which could have a biological relevance to human health.*][†]

4.1.4 Remaining uncertainties

Uncertainties in the evaluation of the evidence are especially recognized in regards to the question for which cell types the genotoxic effects from RF-EMF exposure are to be expected. Additionally, the ROS-hypothesis, which for the first time describes a mechanism for DNA damage by RF-EMF, requires further experimental validation.

4.1.5 Assessment by MUT

The differentiation made by the experts between genotoxic effects without consequence for cell proliferation and genotoxic effects with cell proliferation is essential for the understanding of the significance of genotoxic effects for the risk evaluation. Because only if alterations in cell growth, cell division and the programmed cell death (apoptosis) are manifested, will it be relevant to the risk. Since the REFLEX study did

⁷ In this respect, we refer to the above cited assessments of the SSK and the IEGMP.

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

not detect any such alterations, the issue of genotoxic effects maybe revived, but the risk evaluation seems less likely to be reopened. Thus, even the findings of the REFLEX study do not result in a new evaluation.

4.2 Experimental laboratory animal cancer studies

Starting point

To prove a causal relationship between exposure to radio-frequency electromagnetic fields and carcinogenicity, experimental studies are imperative. Only in experiments, can exposures be purposely varied and their effect on the cancer initiation (formation of cancer) as well as on the cancer promotion (advancement of cancer) be observed and associated confounding factors be eliminated or rather controlled. It goes without saying that such experiments cannot be conducted on human volunteers. Analogous to the examination of other potential non-physical toxins (e.g. chemicals), can experimental studies of carcinogenicity of radio-frequency electromagnetic fields only be performed in animal experiments.⁸

In several research fields, for example pharmaceuticals, industrial chemicals, plant pesticides, there exists international guidance for the conduct of such animal experiments (e.g. by the EU, OECD). For the EMF research field, there is no such guidance to date.

Significance for the risk evaluation

Although the use of animal experiment results for the assessment of health risks for humans always raises the issue of transferability of the results from animal to human, animal experimentation is successfully employed for the risk evaluation in many fields (e.g. drug permitting, classification of hazardous materials). It is assumed that especially between mammals and humans the similarities of cell- and organ-functions are so great that a transferability of the findings from animal to human is possible (see DFG 2004).

Especially when reliable results from human studies are still lacking or such investigations are principally prohibited on ethical grounds, must the risk evaluation depend on the results from animal experimentation. In this context, the International Agency for Cancer Research (IARC) for example states that:

Although this association cannot establish that all agents and mixtures that cause cancer in experimental animals also cause cancer in humans, nevertheless, in the absence of adequate data on humans, it is biologically plausible and prudent to regard agents and mixtures for which there is sufficient evidence of carcinogenicity in experimental animals as if they presented a carcinogenic risk to humans. The possibility that a given agent may cause cancer through a species-specific mechanism which does not operate in humans [...] should also be taken into consideration.⁹

⁸ For humane reasons (animal protection), but also from a cost perspective, can an increasing attempt towards replacement of animal experimentation with *in vitro* procedures be seen. At present, however, experimental animal studies are still imperative for the evaluation of the hazard potential of environmental health-relevant contaminants and similar toxins.

⁹ <http://www-cie.iarc.fr/monoeval/studiesanimals.html>

4.2.1 State of the knowledge in the year 2000

The state of knowledge from experimental animal studies on the effects of radio-frequency electromagnetic fields is assessed by the German Radiation Protection Commission (SSK 2001) as follows:

Untersuchungen zur Tumorbildung in Hochfrequenzfeldern sind nicht zahlreich und haben keinen wissenschaftlichen Hinweis auf einen entsprechenden Zusammenhang eines Feldeinflusses ergeben. Die Untersuchungen zu Krebs, ausgelöst durch kanzerogene Substanzen oder Implantation von Krebszellen haben keine neuen Hinweise gegeben, dass hochfrequente elektromagnetische Felder die Entstehung oder die Promotion von Tumoren negativ beeinflussen. Eine Einzelstudie, die eine erhöhte Lymphominzidenz bei genmanipulierten Mäusen zeigte, wird als wissenschaftlicher Hinweis auf mögliche Reaktionen gewertet. Derzeit werden Wiederholungsstudien durchgeführt. [p. 13] [*Investigations of tumor formation under high(radio)-frequency fields are not numerous and have provided no indication of a corresponding relationship for a field influence. The investigations on cancer, initiated by carcinogenic substances or by implantation of cancer cells, have provided no new indication that high(radio)-frequency electromagnetic fields will negatively influence the creation or promotion of tumors. A single study that showed an elevated lymphoma incidence for genetically manipulated mice is evaluated as scientific indication for possible reactions. At present, replication studies are performed. (p. 13).*][†]

The Independent Expert Group on Mobile Phones (IEGMP 2000) reaches a similar assessment:

Further, a variety of cancer studies using animals have sought evidence of an effect of RF exposure on spontaneous or natural cancer rates, the enhancement of the effects of known carcinogens or effects on the growth of implanted tumours. However, they have provided equivocal evidence for an effect on tumour incidence. [p. 77]

4.2.2 Results of the expert opinion report and the discussion

The two experts, Prof. Dasenbrock und Prof. Lerchl, decided to prepare a joint expert opinion report because it was discovered during the first phase of the preparation that was to be jointly undertaken (selection of the literature, establishment of quality criteria and the endpoints to be considered) that even the risk evaluation would result in extensive and overlapping agreements. The advisory expert panelist for this topic area was Professor Dr. Wolfgang Dekant (Institute for Toxicology, University Würzburg).

Basis of evidence (since 2000)

The literature search yielded ten new studies, which met the selection criteria of the experts (see Table 4). However, in one of these studies (Jauchem et al. 2001), highly energetic ultra-wideband EMF pulses were investigated that do not share any characteristics of mobile phone communication.

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

Table 4: Experimental animal studies on carcinogenicity since the year 2000

Authors	Species
Adey et al. (2000)	Rats
Anane et al. (2003)	Rats
Bartsch et al. (2002)	Rats
Heikkinen et al. (2003)	Mice
Heikkinen et al. (2001)	Mice
Imaida et al. (2001)	Mice
Jauchem et al. (2001)	Mice
La Regina et al. (2003)	Rats
Utteridge et al. (2002)	Mice
Zook & Simmens (2001)	Rats

These ten studies form the basis of evidence for the assessment of whether radio-frequency electromagnetic fields from mobile phone communication demonstrate a carcinogenic or cancer-promoting effect in animal experiments.

Pro- and Con-arguments

The results of the experimental animal research presented here allow for the derivation of the following arguments for as well as against the assumption that a carcinogenic effect from mobile phone communication is evident. Figure 3 presents the evidence framework.

Pro-argument:

None of the ten studies evaluated by the experts found a relationship between exposure of the experimental animals to radio-frequency EMF and cancer initiation or promotion. Thus, no argument that speaks for the presence of a carcinogenic effect in animal experiments from such fields can be derived.

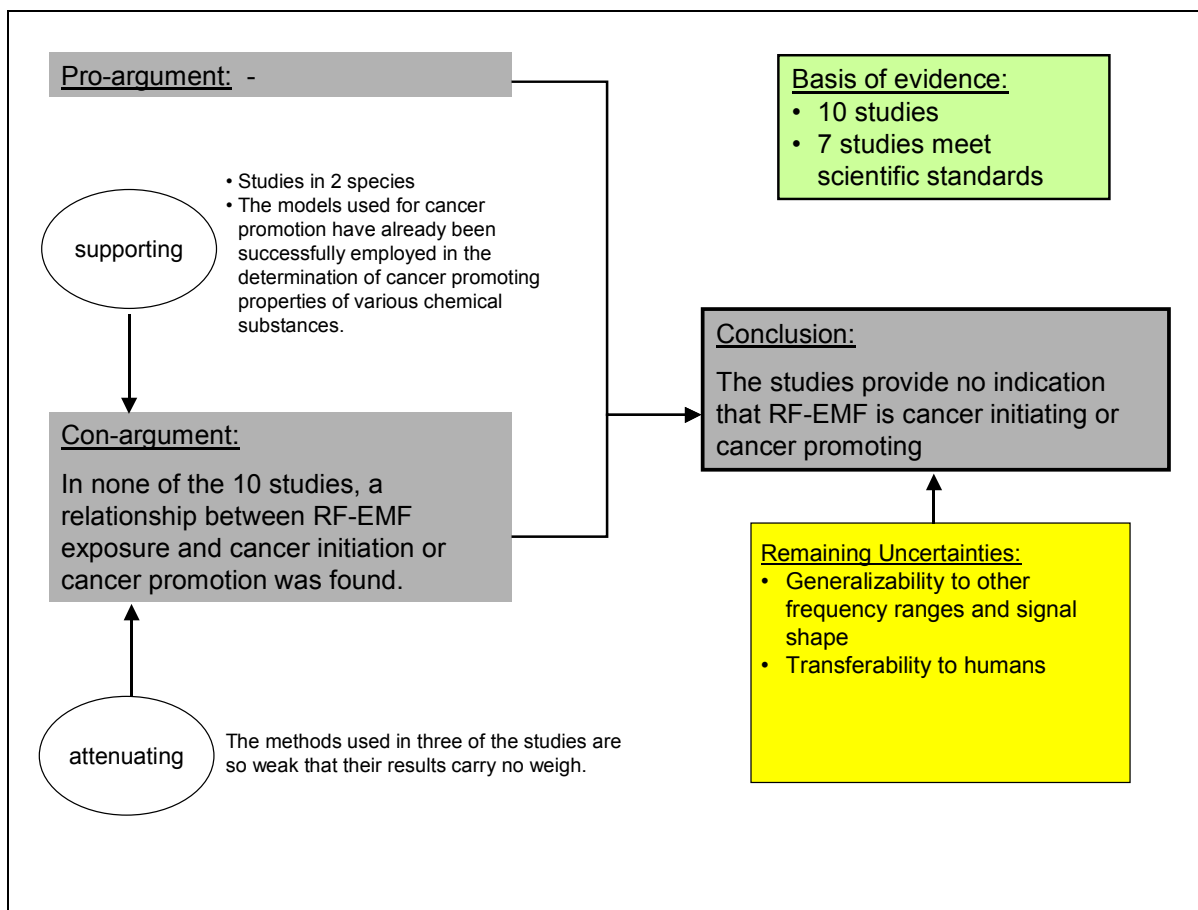


Figure 3: evidence framework to animal-experimental studies cancer

Con-argument:

In none of the ten studies evaluated by the experts could a relationship between exposure of the experimental animals to radio-frequency EMF and cancer initiation or promotion be seen. Although these negative results cannot *prove*¹⁰ that radio-frequency EMF will never show a carcinogenic effect in animal experiments, they do, however, speak against the existence of such effects.

This argument is supported by the fact that the employed models for cancer promotion have already been successfully used in the determination of carcinogenic properties of various chemical substances. This demonstrates that the models will work in principle. Therefore, if a carcinogenic effect from electromagnetic fields of the mobile phone communication exists, these models should be able to determine it.

The negative findings receive additional weight because they are available not only for one but for two species. Thereby one of IARC's criteria for the classification of "*evidence suggesting lack of carcinogenicity*" is met.¹¹

¹⁰ Logic dictates that it is impossible to scientifically prove the non-existence of an effect. No matter the number of negative findings, this cannot prove that the effect is not actually present – because the very next investigation could (e.g. with a different method) find the effect

¹¹ "*Evidence suggesting lack of carcinogenicity*: Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent or mixture is not carcinogenic. A conclusion of evidence suggesting lack of carcinogenicity is inevitably limited to the species, tumour

The Con-argument is weakened because – according to the assessment of the experts – not all ten studies meet the scientific quality criteria. The methods of three of the studies are assessed to be so weak that their results carry no weight. Thus, the basis of evidence for the timeframe from the year 2000 on is decreased to seven studies. In addition, it is uncertain whether in all studies the number of experimental animals was sufficiently large to discover a carcinogenic effect – assuming it was there – with an adequate probability. In order to ensure this, the number of animals needed for the verification of the hypothesis would need to be calculated already during the planning for the study with the aid of a power analysis. Such an analysis was, however, only conducted in one of the ten studies evaluated. Still, from the view of the experts, seven of the ten studies used quantities of experimental animals that were sufficiently large to achieve a reliable result (see the overview table in Dasenbrock & Lerchl, p. B-19).

4.2.3 Conclusions

The conclusion of the experts is unambiguous. According to their assessment of these studies from the year 2000 on (until April 2004), there is no indication that radio-frequency electromagnetic fields of mobile phone communication is cancer-initiating nor cancer-promoting in animal experiments.

4.2.4 Remaining uncertainties

It is uncertain whether the negative findings can be generalized without modification. That involves, on the one hand, both the frequency range and the signal shape. Since nine of the ten experiments were conducted with GSM or GSM-like signals, statements on UMTS will have associated uncertainties. On the other hand, the extrapolation from animal models to humans is always associated with uncertainties.

4.2.5 Assessment by MUT

The experimental animal studies that were considered provided no indication for cancer initiation or cancer promotion from RF-EMF. During the final workshop, however, Prof. Dasenbrock drew attention to the fact that at present a series of investigations on this topic were underway – among others within the frame of the PERFORM-A project¹². Their results will determine whether the assessment provided herein will have to be revised.

4.3 Cancer epidemiology

Starting point

Epidemiology examines the incidence, prevalence, and distribution of diseases in a

sites and levels of exposure studied.“ (<http://www-cie.iarc.fr/monoeval/eval.html>)

¹² In this international project, animal models (rat and mouse) are to shed light on whether mobile telephony presents a carcinogenic risk. Results are to be presented during the year 2005. More information on the internet at: http://www.item.fraunhofer.de/de/medien/newsreports/Januar_2002/1.html

population with the goal of description, explanation, and prevention of these diseases. In risk evaluation, epidemiology plays an important role because it attempts to determine the disease causes and influence parameters. However, complex exposure conditions as well as multi-factorial cause-and-effect relationships can make the proof of causation for environmental health related diseases considerably more difficult. On the other hand, epidemiological studies nevertheless possess the advantage that they avoid the uncertainties that are inherent with the extrapolation of animal models to humans, because they directly test “in humans.”

Without question, especially serious endpoints like carcinogenic diseases are of particular significance in risk evaluation. Therefore, carcinogenic diseases shall be the central focus of subsequent discussions hereforth.

With one exception – the study of Baumgardt-Elms et al. (2002) on testicular cancer – the studies evaluated by the experts examined tumors in the head region. This selective focus is based on the assumption that tissues and organs are exposed to fields from mobile phone communication in different ways and that the tumors are induced at those body positions at which the radiation is at its maximum deposition (direct effect). Furthermore, the different organ sensitivities are also taken into account. Therefore, primary consideration is given to tumors in the head region. Since mobile phones are worn in a powered-on state on the body, other organs can also receive local exposures. However there also exist hypotheses for an indirect effect wherein irradiation of a body location results in a systemic effect that induces a tumor distant from the position of maximal exposure by way of blood or lymph factors (cf. expert opinion report of Blettner et al., p. C-7). Such a “long-distance effect” or “systemic effect” is extremely difficult to evaluate.

Significance for the risk evaluation

A causal relationship between exposure to radio-frequency electromagnetic fields and carcinogenicity can only be demonstrated by epidemiological studies up to a certain degree. This limitation is a consequence of specific methodological characteristics as well as confounding factors that are inherent to epidemiological studies: they concern the determination of exposures, the causality models, the numerous tumor identities, the various biases and confounders, the different possibilities for data interpretation, the event measure, etc. (Blettner et al., expert opinion report, pp. C-6 to C-9). Nevertheless, as long as there is no clear biological hypothesis for a carcinogenic effect of electromagnetic radiation from mobile phone communication available, can epidemiological studies that are qualitatively good and conducted for a wide population base provide important indications for possible cancer diseases. On this basis, changes that are observed are termed “associations indicative of an effect.” For example, the relationship of smoking to lung cancer observed in the epidemiological research is now undoubtable, even though the effect mechanism has yet been fully resolved in detail.

4.3.1 State of the knowledge in the year 2000

On the state of the knowledge in the year 2000 for epidemiological studies, the German Radiation Protection Commission (SSK 2001) states:

Epidemiologische Studien, die einen Zusammenhang zwischen bestimmten Erkrankungen und der Exposition durch Sendeanlagen oder durch Mobiltelefone untersuchten, sind nicht zahlreich. Die vorhandenen Studien haben keine statistisch nachweisbare Assoziation zwischen Krebs im Kopfbereich und Nutzung eines Mobiltelefons gezeigt.

Die Studien weisen insgesamt dosimetrische Mängel auf. Ohne relevante Angaben zur Exposition ist die Aussagekraft der Studien jedoch gering. Es ist kein Mechanismus bekannt, wie die Felder der Mobiltelefone eine Krebserkrankung beeinflussen könnten. Aus den derzeitigen Erkenntnissen lassen sich weder ein wissenschaftlich begründeter Verdacht noch Hinweise auf einen negativen Einfluss auf die Gesundheit ableiten. [p. 14] *[Epidemiological studies that investigated a relationship between diseases and the exposure from base stations or from mobile phones are not numerous. The available studies have shown no statistically-proven association between cancer in the head region and usage of a mobile phone.*

Overall, the studies demonstrate dosimetry deficits. Without relevant information on exposure, the studies carry little weight. There is no mechanism known, how the fields of mobile phones could influence cancer. From the current insights, neither a scientifically founded suspicion nor an indication for a negative influence on health can be derived. (p. 14)][†]

The assessment of the Independent Expert Group on Mobile Phones (IEGMP 2000) is:

The epidemiological evidence currently available does not suggest that RF exposure causes cancer. This conclusion is compatible with the balance of biological evidence, which suggests that RF fields below guidelines do not cause mutation, or initiate or promote tumour formation. However, mobile phones have not been in use for long enough to allow comprehensive epidemiological assessment of their impact on health, and we cannot, at this stage, exclude the possibility of some association between mobile phone technology and cancer. In view of widespread concern about this issue, continued research is essential. [p. 102]¹³

4.3.2 Results of the expert opinion report and the discussion

The two expert/groups involved (Blettner and Stang/Jöckel) submitted a joint expert opinion report. Advisory expert for this topic area was Professor Dr. Dr. Heiner Raspe (Institute for Social Medicine, University Clinics Schleswig-Holstein).

The experts evaluate the prior knowledge up to the year 2000 as follows (expert opinion report by Blettner et al., p. C-5):

Bis Ende 1999 gab es nur eine epidemiologisch-analytische Studie (Hardell et al., Int J Oncol 1999), die insgesamt keinerlei Risikoassoziation zwischen Mobilfunkgebrauch und Hirntumorrisiko (Odds Ratio 0.98) zeigte. Erst die seitengetrenten Analysen unter Berücksichtigung der vorwiegenden Seite des Mobiltelefongebrauchs und der betroffenen Gehirn-Hälfte (Hirntumor) ergab für die ipsilateralen Analysen ein deutlich erhöhtes Hirntumorrisiko, was mathematisch aufgrund des insgesamt fehlenden Zusammenhangs zwangsläufig bedeutete, dass das Hirn-

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

¹³ On the epidemiological investigations of RF-EMF exposure at the workplace the IEGMP elaborates: „In summary, the overall balance of evidence from epidemiological occupational studies does not indicate that RF radiation affects the risk of cancer in people. However, the types of exposure investigated have varied between studies and are not identical to those associated with mobile phone technology. Also, many of the studies have had low statistical power and some have suffered from methodological deficiencies. Therefore, the absence of consistently positive findings does not establish firmly that RF radiation from mobile phones carries no important risk of cancer.“ (p. 97)

tumorrisiko auf der kontralateralen Seite einen protektiven Effekt hat. Aufgrund dieses Sachverhalts wird diese Studie von den Gutachtern als Studie eingestuft, die keinen Zusammenhang zwischen Hirntumorrisiko und Mobilfunk zeigt. [*Until end of 1999 there was only one epidemiological-analytical study (Hardell et al., Int J Oncol 1999), which overall showed no risk association between mobile phone communication use and brain tumor risks (Odds Ratio 0.98). Only when a separate analysis for the brain sides was performed respective of the predominant side for mobile phone use and the affected brain half (brain tumor) was there a significantly increased brain tumor risk for the ipsilateral analysis. On the basis of the absent overall relationship, this means that mathematically-speaking there must be a protective effect for brain tumor risk on the contralateral side. Due to this fact, the study is evaluated by the experts as a study that shows no relationship between brain tumor risk and mobile phone communication.*][†]

For the evaluation of the original studies, the experts used a modified version of the checklist “Kriterien zur Bewertung strahlenepidemiologischer Studien” [*Criteria for evaluation of radiation-epidemiological studies*] (German Radiation Protection Commission from 12. April 2002, see Appendix 9 of the expert opinion report by Blettner et al.). The checklist was completed by Blettner and Jöckel / Stang independently of each other. The comparison between the evaluations demonstrated only minor differences. Therefore, the experts agreed to develop a joint expert opinion report and to point out differences in the evaluations within the expert opinion report.

Basis of evidence (since 2000)

Only analytic studies that allow for a measurement of the relationship between exposure and disease to be determined were considered relevant for the risk evaluation. This includes cohort-studies, case-control-studies and cross-sectional studies (however, no relevant cross-sectional study was published within the considered time period).

Altogether, 30 publications were taken into account. All studies refer to exposures to electromagnetic fields from mobile telephone units. In the period from 2000 to April 2004, no scientifically valid studies were published on the electromagnetic fields from mobile phone communication base stations.

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

Table 5: Primary epidemiological findings since the year 2000

Authors	Type	Endpoint
Auvinen et al. (2002)	Case-control study	Brain tumor
Baumgardt-Elms et al. (2002)	Case-control study	Testicular tumor
Christensen et al. (2004)	Case-control study	Acoustic neuroma
De Roos (2001)	Case-control study	Neuroblastoma
Hardell et al. (1999-2003) #1	Case-control study	Brain tumor
Hardell et al. (1999-2003) #2	Case-control study	Acoustic neuroma
Hardell et al. (1999-2003) #3	Case-control study	Brain tumor
Inskip et al. (2001)	Case-control study	Brain tumor
Johansen et al. (2001)	Cohort-study	Brain tumor
Muscat et al. (2000)	Case-control study	Brain tumor
Muscat et al. (2002)	Case-control study	Acoustic neuroma
Stang et al. (2001)	Case-control study	Uveal melanoma
Warren et al. (2003)	Case-control study	Facial nerve tumor

The studies presented in Table 5 received different weights in the subsequent evaluation. On the basis of methodological deficits, the experts were especially cautious in their consideration of the research of Hardell et al. and Warren et al. (2003).

Pro- and Con-arguments for epidemiology

The evidence framework in figure 4 shows that there is both a central Pro- and a Con-argument. Both arguments, however, are attenuated above all by methodological deficits of the studies.

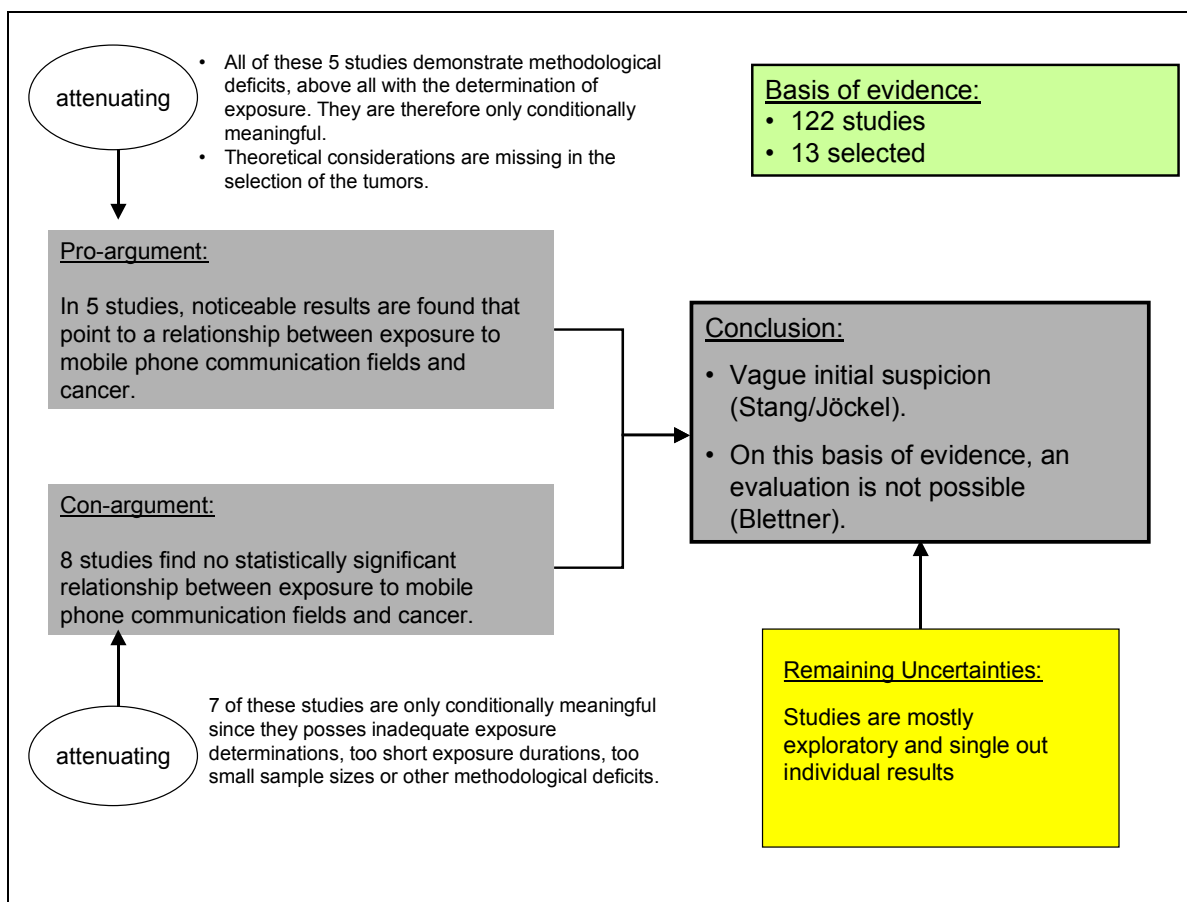


Figure 4: Evidence framework for epidemiology of carcinogenic diseases

Pro-argument:

In five studies, noticeable results are found that point to a relationship between exposure to mobile phone communication fields and cancer. One of those is the study by De Roos et al. (2001) on neuroblastoma. For the fathers of toddlers with neuroblastoma, no increased risk is found; in the mothers an increased odds ratio of 1.8 (95% CI 0.5-6.0) from occupational exposure to mobile phone communication in the last two years preceding the pregnancy is determined. A methodological deficit of this study is the imprecise estimation of the effect based on the low number of exposed study participants. The data collection on mobile phone utilization was conducted with little detail and referred merely to the workplace. Nevertheless, the noticeable maternal result cannot be simply explained as a result of confounding (private mobile telephone usage), because then the confounder *per se* would be responsible for the health risk. Despite the study's serious methodological deficits, the experts view the results as "noticeable findings" and "first indications of a relationship between mobile phone communication exposure and risk of neuroblastoma" (expert opinion report of Blettner et al, p. C-14). To no small extent, this is because there was no prior knowledge present of a relationship between mobile phone communication and neuroblastoma and because even in the future a study of this size for such a rare tumor can hardly be expected. In the discussions during the workshops it became evident, however, that this reflects above all the assessment of Stang and Jöckel. Contrary, Blettner and the advisory expert panelist Raspe view the methodological weaknesses of this study to be too serious to place so much weight in the findings.

The study of Stang et al. (2001) on uveal melanoma shows for test subjects that are classified as likely exposed for at least half a year to mobile phone communication an increased odds ratio—the pooled estimate being 4.2 (95% CI 1.2-14.5). This finding was weighted by Stang and Jöckel as noticeable but not as a strong indication for a relationship between mobile phone communication and risk of uveal melanoma because the study allows for only imprecise effect estimation due to the small case number and because the determination of exposure was not detailed enough.

While the Auvinen et al. (2002) study on brain tumors shows several methodological peculiarities (no selection bias, no recall bias), Stang and Jöckel identify individual results as "noticeable". For instance, an OR of 2.4 (95% CI 1.2-5.1) is seen for people with mobile phone contract duration of 1-2 years for analog phones. The weak points of the study are the missing induction and latency time periods and the poor determination of exposure. There is disagreement between the experts (cf. Blettner et al., expert opinion report, p. C-17) in regards to this study. Stang and Jöckel evaluate the finding as a first initial suspicion, which Blettner rather does not because of the presumably high misclassification (a "private subscriber" is not synonymous with a "private user").

The second and third case control studies for analog mobile phones of Hardell et al. (2002a,b; 2003) evaluated in the expert opinion report show "noticeable findings" (expert opinion report by Blettner et al, p. C-20) for the overall group of tumors and for the group of acoustic neuroma. The methodological deficits of this study (not enough exposed subjects, no investigation of dose-response relationship, suspiciously high response proportions in the population control group, ambiguous descriptions of the tumors, etc.) weigh heavily in the evaluation of the experts and

therefore the findings of this study cannot be judged as providing an indication of risk.

Con-argument:

The Con-argument for risk is supported by the population-based case control study into testicular cancer by Baumgardt-Elms et al. (2002). The exposure to “radiofrequency emitters” shows no effect. This study, however, is judged to provide neither “evidence of no effect” nor “no evidence of effect”, since the determination of exposure was not detailed enough.

The study of brain tumors by Muscat et al. (2000) demonstrates no overall relationship between the usage of analog mobile phones and the risk of brain tumors. This statement is limited, however, to a mean cumulative exposure duration of only two to three years. Furthermore, the study did not consider latency periods. In the assessment of the experts, the fractional analysis of the data on acoustic neuroma (Muscat et al. 2002) provides only little information because of the small case numbers and, therefore, the resultant very imprecise effect estimation.

The study of brain tumors by Inskip et al. (2001) provides no indication of a hazard from usage of analog mobile phones for a few years. Persons with longer exposure hardly occur in the study. The latency period is not considered. The study’s interpretation of the data looks at too many and too small sub-groups. In addition, multiple (but only potential) risk factors are drawn upon in the model development whereby the results are possibly biased. For these reasons, Jöckel and Stang assess this study as having limited reliability and only to a limited extent as a null result. Contrary, Blettner considers it one of the qualitatively better and more reliable studies, whose conclusion in reference to the brain tumor risk is negative.

The Danish data from the international *Interphone*¹⁴ study on acoustic neuroma (Christensen et al. 2004) shows overall no increased risk. It should be noted that an OR of 0.26 was found for persons whose first mobile phone service contract was for an analog mobile phone. These persons presumably have used mobile phones for the longest period of time. The value of 1.57 for the upper bound of the confidence interval of the ever/never-analysis for mobile phone communication contradicts the idea that mobile phone usage is associated with a significantly increased risk for acoustic neuroma.

The Con-argument is also supported by the retrospective cancer incidence study of Johansen et al. (2001). However, the result of a strongly decreased relative risk for lung cancer (male RR=0.65, 95% CI 0.58-0.73) is not to be judged reliable since both a selection bias and a confounder were present (expert opinion report by Blettner et al., p. C-23). For brain tumors, selection bias and confounders have no significance; here no increased risk is shown (null result). This, however, is only valid for exposures to digital mobile phone communication with duration of usage of a few years (92% under 3 years).

¹⁴ *Interphone* is an international, multi-center case-control study on brain tumor risks that is coordinated by the World Health Organization (WHO). It is conducted according to a jointly developed study protocol in identical manner in thirteen (13) countries with more than 7000 patients. Besides Germany, the Scandinavian countries, Great Britain, France, Italy, Israel, Australia, New Zealand, Japan, and Canada are participants. Results from the overall study are expected for the year 2005. Further information can be found in the Internet under: <http://info.imsd.uni-mainz.de/interphone.html>

The experts Jöckel and Stang find this study to be conditionally reliable because the exposure data are inadequate (exposure was only estimated based on the data from the mobile phone service contracts). In addition, the Danish general public was an unsuitable control group since a good part of it was already “exposed” in the time period under investigation (cf. Godward et al. 2001).

The studies of Hardell et al. (case-control study #1) and Warren (2003) also show no relationship (see expert opinion report by Blettner et al., pp. C-19 to C-22, as well as p. C-16), but because of methodological reasons are evaluated by the experts as unreliable (pp. C-25 to C-26).

4.3.3 Conclusions

According to the opinion of the experts, an overall evaluation is quite difficult since most studies exhibited methodological deficits and the room for interpretation of epidemiological studies is inherently wide.

The partially different interpretations of the results lead to different overall assessments. Blettner believes that above all the qualitatively good studies of Muscat, Inskip, and the Danish data of the Interphone study allow the conclusion to be reached that a carcinogenic effect is rather not to be expected. However, this evaluation must be restricted to the comparatively few tumor types that have been examined until now.

The overall evaluation of Stang/Jöckel is that a “vague initial suspicion” for a cancer risk from electromagnetic fields of mobile phone communication exists. The experts view this standpoint supported by results of the studies from De Roos et al., Auvinen et al., Stang et al. and others. However, most of the positive test results refer to the analog mobile phone technology, which is hardly used anymore. On the basis of these data, Stang cautiously concludes that if – at all – a cancer-promoting effect on the part of mobile phone communication is present, that it refers to analog mobile phone technology.

A consensus between the experts is found in the assumption that persons exposed to digital mobile phones for short durations (i.e. a few years) do not show an increased risk of brain tumors.¹⁵

¹⁵ At present, the *Interphone* study enjoys special attention. In the final workshop, the results of the Swedish component study on acoustic neuroma (Lönn et al. 2004) were discussed (the study was only just published in October 2004 and therefore could not be included in the expert opinion reports). The unique facet of the study is that it includes for the first time mobile phone communication users that have been exposed for ten (10) years or longer. With an exposure duration of ≥ 10 years the odds ratio (OR) increases to 1.9. While not significant, Stang labeled this value in the final workshop as „noticeable” with the justification that the lion’s share of the confidence interval falls within the increased-risk region and only a minor part in the reduced-risk region (95% CI 0.9 to 4.1). In addition, for the ipsilateral analysis (tumor is situated on the same side as mobile phone usage) the OR climbs to 3.9 (95% CI 1.6 – 9.5) for an exposure duration of ≥ 10 years. The normal usage of DECT telephones results in an OR of 0.7 (95% CI 0.4 – 1.2). However, additional data from the Swedish Interphone study have meanwhile been published that show no relationship of brain tumors to usage of mobile phone communication (Lönn 2004).

4.3.4 Remaining uncertainties

The experts have repeatedly presented very diverse uncertainties that widen the room for interpretation of epidemiological studies as well as those that constrain the value considerably (see expert opinion report by Blettner et al., p. C-6). The controversy of “significance versus estimation accuracy” belongs to the first category while the second category includes the small case study numbers for subgroup comparisons as well as the assumptions of induction and latency periods. In particular, Blettner also highlighted the problematic situation of exploratory studies – which should not be used for the validation of hypotheses

4.3.5 Assessment by MUT

Prior to the year 2000, there was only one epidemiological-analytical study on the relationship between mobile phone communication and risk of brain tumors (Hardell et al. 1999). Therefore, one could hope that for this topic – which is especially important for the public discussion of mobile phone communication risks – that the studies conducted since 2000 would yield a clearer assessment of the hazard potential. This hope was only partially fulfilled. Because most of the studies demonstrate methodological deficits according to the assessment by the experts, their conclusions regarding the hazard potentials are rather guarded. The experts agree that the studies provide no indication for brain tumor risks with short duration exposures (i.e. exposures of a few years) to the EMF from digital mobile phones. However, the actually interesting question – whether exposure to EMF from mobile phone communication can even cause cancer or more precisely in this case brain tumors (which possibly may only manifest itself in the long term) – could not be satisfactorily answered on the basis of these studies.

For epidemiology, the answer to this question is linked to two fundamental problems. On the one hand is the difficulty that the causality of epidemiological findings can actually only be interpreted if experimental animal and mechanistic studies are also consulted. On the other hand, there are a number of diverse influence factors that must be taken note of in the evaluation of epidemiological studies of the relationship between mobile phone communication usage and cancer and which are explicitly pointed out by the experts (see Chapter 6 of the expert opinion report of Blettner et al., p. C-6ff). The methodological problems referred to above are essentially a result of the difficulty of controlling these diverse possibilities for influence during the performance of the study. To what extent the study is successful will vary and can be assessed – in part – differently. Thus, there remains room for diverging interpretations in the evaluation of the different study results.

4.4 CNS / cognitive functions / sleep

Starting point:

In the topic area CNS / cognitive functions / sleep, different aspects are examined that play a role in the discussion of possible health risks from mobile phone communication. Common to them is their focus on the functioning of the central nervous system (CNS). Specifically, the focus is on the influence of mobile phone communication fields on cognitive performance, on the waking-EEG, and on sleep whereby the sleep quality (i.e. the subjective evaluation of sleep by the affected persons) as well as the sleep architecture (which can be determined by sleep-EEG measurements) is con-

sidered. Furthermore, for the measurement of changes in the CNS under EMF exposure, the regional cerebral blood flow (rCBF) is also assessed.

Significance for the risk evaluation:

If impairments of cognitive performances (e.g. degradation of memory performance or elongation of reaction times) through exposure to RF-EMF were to be found, these would *per se* not necessarily represent health damages, but they could certainly be considered undesirable effects.¹⁶ As to the question whether such impairments should already be evaluated as indications for possible health damages is, on the one hand, dependent upon whether they remain in the normal range of variability. On the other hand, it must be taken into account that such impairments could also be the result of many daily situations, e.g. sleep deficit, alcohol consumption, noise pollution. In this respect, it should be questioned why electromagnetic fields as a cause are afforded special significance.

Changes of the sleep architecture as well as impairment of the sleep quality also do not necessarily represent a health impairment by themselves. Likewise, the question here is at which point should such changes or rather impairments be seen as an indication of a health risk. Ongoing sleep disturbances can lead to health problems, e.g. by way of a weakening of the immune system (cf. Bryant, Trinder & Curtis 2004).

To an even larger extent, the problems of interpretation of the changes in the waking-EEG resulting from EMF exposure are an issue. The waking-EEG is known to react extremely sensitively to internal as well as external stimuli. Therefore, changes of the waking-EEGs based on exposure to radio-frequency EMF are first without significance for the risk evaluation. However, even in the waking-EEG certain patterns (e.g. spikes) are known to be interpreted as indications for acute pathologies (e.g. for epilepsy). If such patterns would be found in the waking-EEG upon exposure to EMF, this would certainly be of significance for the risk evaluation.

Changes of the regional cerebral blood flow (rCBF) by exposure to EMF are again by themselves not an indication of health damage. Similar to the EEG, rCBF first of all only demonstrates that radio-frequency electromagnetic fields can influence the activity of the brain. Only if the changes of rCBF would be outside their normal range because of exposure to EMF, would this be an indication of possibly harmful health effects.

4.4.1 State of the knowledge in the year 2000

The German Radiation Protection Commission (SSK 2001) elaborates on the state of knowledge from the year 2000 regarding the effects to the CNS from exposure to electromagnetic fields of mobile phone communication:

[Schlaf]

In diesem Zusammenhang werden oft die Abschlussberichte der „Schwarzenburg-Studie“ erwähnt. Mit mehreren Versuchsansätzen wurde die Bevölkerung in Schwarzenburg (Schweiz), die seit Jahrzehnten z.B. über Schlafstörungen als Folge eines Kurzwellensenders klagte, untersucht [...]. Wiederholt konnte in Querschnittsstudien in der gleichen Population gezeigt werden, dass

¹⁶ This is of course also dependent upon the definition of health that is used.

Durchschlafstörungen in Bevölkerungsgruppen, die näher an dem Sender wohnten, häufiger auftraten als in Bevölkerungsgruppen im Umland. Diese räumliche Assoziation lässt sich auch in kurzen Zeitreihen bestätigen. Die Aussagekraft dieser Studie ist geringer als die der o.g. kontrollierten Laborexperimente, da die Studie nicht doppelblind durchgeführt wurde und die Befindlichkeitsstörungen nur anhand einer Fragebogenaktion erfasst wurden. Es existieren keine individuell korrelierten Messungen, was zu einer Missklassifizierung, einer Über- oder Unterschätzung der effektiven Exposition, führen könnte. Deshalb sind die o.g. Ergebnisse der Einzelstudie allenfalls als unbestätigte Hinweise einzustufen. Zur Abklärung, ob es Schlafstörungen durch hochfrequente Felder gibt, sind kontrollierte, doppelblind durchgeführte Schlafexperimente geeigneter, um zwischen physischen und psychischen Ursachen der Störung unterscheiden zu können. [p. 33]

[EEG]

Es kann zusammengefasst werden, dass die bisherigen Studien nicht im Ergebnis übereinstimmen, aber dennoch Hinweise auf expositionsbedingte Änderungen neurophysiologischer Prozesse geben. Insgesamt sprechen die Experimente zu Ruhe-EEGs eher gegen eine Beeinflussung der spontanen Hirnaktivität. Die beschriebenen Veränderungen bei den komplexeren evozierten Potentialen sind im Einzelnen noch nicht wiederholt und bestätigt. Daher sind weitere Untersuchungen notwendig. [p. 32f.]

[Kognitive Funktionen beim Menschen]

Ziel dieser Studien ist es, einen vermuteten Einfluss elektromagnetischer Felder auf kognitive Funktionen zu untersuchen. Mit Verhaltensexperimenten kann ein Feldeinfluss auf die aktive intellektuelle Informationsverarbeitung (kognitive Leistung) untersucht werden.

[...]

Die Vielzahl an untersuchten, unterschiedlichen Reaktionszeittypen, die bei Exposition zum Teil verkürzt, aber andere auch verlängert waren, lässt keine eindeutige Bewertung zu, gibt aber Hinweise auf eine mögliche Beeinflussung von physiologischen Prozessen. Es ist weitere Forschung notwendig, um zu klären, ob bei der Nutzung von Handys die Leistungsfähigkeit des Gehirns beeinflusst wird. [p. 33]

[/Sleep]

In this context, the final reports of the "Schwarzenburg-Study" are often mentioned. The population in Schwarzenburg (Switzerland), which for decades complained about e.g. sleep impairment in response to a high(radio)-frequency base station, was examined with several experimental approaches [...]. For the same population it could be shown repeatedly in cross-sectional studies that for population groups living closer to the base station, sleep impairments were more frequent than for population groups in the surrounding countryside. This spatial association was also confirmed in short time series. The study carries less weight than the above mentioned laboratory experiments because the study was not performed double-blind and the impairments of well-being were only surveyed with a questionnaire. No individually correlated measurements exist which could allow one to surmise a misclassification, an over- or underestimate of the effective exposure. Thus, the above mentioned findings of this single study are at best to be evaluated as unconfirmed indications. For the clarification whether sleep impairments resulting from high(radio)-frequency fields exist, are controlled, double-blindly performed sleep experiments more suitable in order to be able to differentiate between physical and psychic causes for the impairment. [p. 33]

[EEG]

It can be summarized that the studies to date do not agree in their findings, but, nevertheless, provide indications for exposure-related changes in neurophysiological processes. Overall the

experiments on resting-EEG speak against an influence of the spontaneous brain activity. The described changes for the more complex evoked potentials have individually not yet been repeated and confirmed. Therefore, further investigations are needed. [p. 32]

[Cognitive Functions in humans]

Goal of this study is to investigate a suspected influence of electromagnetic fields on cognitive functions. With behavioral experiments the influence of a field on the active intellectual information processing (cognitive function) can be investigated.

[...]

The multitude of different investigated types of reaction times, where some were shortened with exposure but others were lengthened, does not allow for an unequivocal evaluation but does provide indications for a possible influence of physiological processes. Further research is needed to clarify whether the cognitive abilities of the brain are influenced by the usage of mobile phones. [p. 33]†

The assessment of the Independent Expert Group on Mobile Phones (IEGMP 2000) is:

Together, the findings from electrophysiological studies suggest that exposure to mobile phone signals influences brain function. The evidence is sufficiently substantial to warrant further investigation, notably with respect to the influence of GSM-like signals on sleep and on event-related EEG changes during the performance of cognitive tasks. It should be emphasised, however, that neither the biological nor the clinical significance of the findings described above is clear at present, and the relevance of the findings to the question of the safety of mobile phone technology is uncertain. [p. 85]

4.4.2 Results of the expert opinion reports and the discussion

After the first phase of the preparation of the expert opinion report which was to be performed jointly by the experts (selection of the literature, establishment of quality criteria and the endpoints to be considered), the two expert/groups of Dr. Achermann / Dipl. Psych. Regel as well as Dr. Ullsperger, submitted each their own expert opinion report. Advisory expert panelist for this topic area was Professor Dr. Thomas Penzel (Marburg University Medical Center).

For the risk evaluation, the experts defined three endpoints. They are: (1) behavior¹⁷ / sleep variables, (2) effects on parameters of the EEG and the regional cerebral blood flow (rCBF) and, (3) acute health effects. The Pro- and Con-arguments for these three endpoints are considered separately.

Basis of evidence (studies since the year 2000)

29 studies, that satisfy the quality criteria set forth by the experts, form the basis of the evaluation. For the evaluation of the endpoint “cognitive functions / sleep variables” there are seventeen (17) relevant studies (see Table 6), for the endpoint “parameters of EEG / rCBF” nine studies are drawn upon (see Table 7), whereby four studies are used for both endpoints. Seven additional studies cannot be assigned to either of these endpoints, but rather form – together with the aforementioned studies

† Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

¹⁷ In this context, the term “behavior“ refers to the reactions of subjects in cognitive tests as well as spatial orientation (location positioning) reactions of experimental laboratory animals.

– the basis of the evaluation of the endpoint “acute health effects”.

Table 6: Original findings for the endpoint “cognitive functions / sleep variables” since the year 2000

Authors	Type	Effect on
Bornhausen & Scheingraber (2000)	Laboratory animal experiment	Operant learning
Dubreuil et al. (2002)	Laboratory animal experiment	Spatial learning
Dubreuil et al. (2003)	Laboratory animal experiment	Memory, object recognition
Freude, Ullsperger et al. (2000)	Human study	Waking-EEG, cognitive functions
Haarala, Aalto et al. (2003a)	Human study	Waking rCBF, cognitive functions
Haarala, Bjornberg et al. (2003b)	Human study	Cognitive functions
Huber, Graf et al. (2000)	Human study	Sleep, sleep-EEG
Huber, Schuderer et al. (2003)	Human study	Waking and sleep-EEG; heart rate / changes in heart rate
Huber, Treyer et al. (2002)	Human study	Sleep, sleep-EEG, rCBF
Koivisto, Revonsuo et al. (2000a)	Human study	Cognitive functions
Koivisto, Krause et al. (2000b)	Human study	Cognitive functions
Lass, Tuulik et al. (2002)	Human study	Cognitive functions
Sienkiewicz, Blackwell et al. (2000)	Laboratory animal experiment	Spatial learning
Wagner, Röschke et al. (2000)	Human study	Sleep, sleep-EEG
Wang & Lai (2000)	Laboratory animal experiment	Spatial learning
Yamaguchi, Tsurita et al. (2003)	Laboratory animal experiment	Spatial learning
Zwamborn et al. (2003)	Human study	Subjective well-being, cognitive functions

Table 7: Original findings for the endpoints EEG parameter / rCBF since the year 2000

Authors	Type	Effect on
Arai et al. (2003)	Human study	EEG (auditory)
Freude, Ullsperger et al. (2000)	Human study	Waking-EEG, cognitive functions,
Haarala, Aalto et al. (2003a)	Human study	rCBF (awake), cognitive functions,
Hietanen, Kovala et al. (2000)	Human study	Waking-EEG
Huber, Graf et al. (2000)	Human study	Sleep-EEG
Huber, Treyer et al. (2002)	Human study	Sleep, sleep-EEG, rCBF
Huber, Schuderer et al. (2003)	Human study	Waking - and sleep-EEG; heart rate / changes
Krause, Silanmäki et al. (2000a)	Human study	in heart rate
Krause, Silanmäki et al. (2000b)	Human study	Waking-EEG
Wagner et al. (2000)	Human study	Waking-EEG

Pro- and Con-arguments for the endpoint cognitive functions / sleep

As shown in the evidence framework in figure 5, for the evaluation of the endpoint “cognitive function / sleep” there is one Pro-argument which speaks for a potential health risk from electromagnetic fields of mobile phone communication and two Con-arguments, that speak against it.

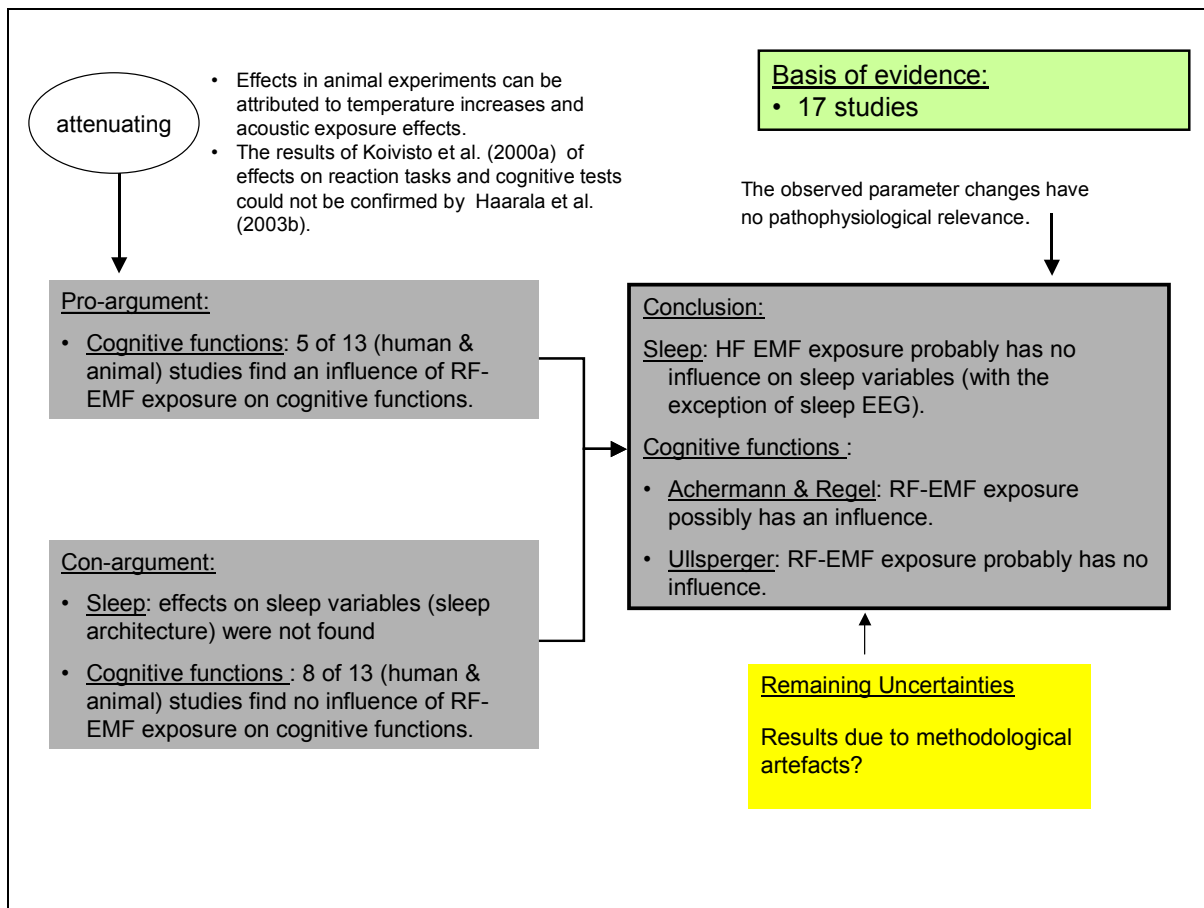


Figure 5: Evidence framework for the endpoint “cognitive functions / sleep”

Pro-argument:

The Pro-argument refers to the five studies that observed an influence of radio-frequency EMF on cognitive functions in human as well as animal experiments (Koivisto et al. 2000a, 2000b; Lass et al. 2002; Wang & Lai 2000; Zwamborn et al. 2003). The Pro-argument is attenuated by the fact that the influences of RF-EMF exposure on cognitive functions (learning) in animal experiments can be traced back to temperature increases and acoustic exposure effects. The observed effects of decreased reaction time in the human study by Koivisto et al. (2000a) could not be confirmed in the replicative study by Haarala et al. (2003b). Instead, it was shown that the positive findings of Koivisto et al. could be explained through noise that is not consciously perceptible and which emanates from the powered-on mobile phone during the exposure.

Con-argument:

Contrary to the assumption that the exposure to radio-frequency electromagnetic fields influences the endpoints “cognitive functions” and “sleep”, no effects on the sleep architecture (with the exception of sleep-EEG, see below) were found. Also, eight of the thirteen (13) studies in which cognitive functions were examined found no relationship to RF-EMF exposure (Freude et al. 2000; Bornhausen & Scheingraber 2000; Dubreuil et al. 2002, 2003; Haarala et al. 2003a, 2003b; Sienkiewicz et al. 2000; Yamaguchi et al. 2003).

Conclusion

On the basis of the considered studies, the experts reach an unambiguous evaluation for the endpoint “sleep”: Influences from radio-frequency electromagnetic fields on sleep– with the exception of the observed effect on sleep-EEG, see below – are thought to be unlikely. The experts, however, reach different conclusions for the endpoint “cognitive functions”. While in the assessment of Ullsperger here too the state of the observations makes an influence on cognitive functions from exposure with RF-EMF appear unlikely, Achermann and Regel regard such an influence as possible. However, in the discussions of the final workshop it became apparent that it was more about nuances of expression: the experts are in agreement that there are hardly any reliable studies that provide an indication for such a relationship.

The existing differences of evaluation result from Ullsperger assigning more weight to the influence of uncontrolled confounding factors on cognitive functions found in most of the studies, than do Achermann and Regel. On the one hand, Ullsperger refers to the influence of imperceptible auditory signals emitted by mobile phones¹⁸ on the subjects’ cognitive functions, which, for example, was shown by Haarala et al. (2003a) in an elaboration of the study by Koivisto et al. (2000a). Ullsperger elaborates on this in the workshop discussion that it is known from the occupational physiology field that auditorily discernible static and noise can at first improve cognitive functions. On the other hand, he notes that effects can often be traced back to repetitions because especially with cognitive tests the influence of training or rather habituation can play an essential role. In his opinion, these circumstances raise doubt about the role of RF-EMF exposure on cognitive performance. They lead him to conclude that an unambiguous proof of the EMF related systemic changes of parameters of behavior and of bioelectric brain activity is still missing.

Despite this evaluation difference, the experts and the advisory expert panelist Prof. Penzel are in agreement that changes to the parameters for the endpoint “cognitive functions / sleep” found in the studies, have no pathophysiological relevance. In the workshop discussion they specifically point out that the investigation on the influence of RF-EMF on cognitive functions do not represent a suitable approach for demonstrating health burdens from RF-EMF.

Remaining uncertainty

It remains unclear to what extent the observed effects can be traced back to methodological artefacts. In their expert opinion reports, the experts point out a series of methodological weaknesses in the studies of the influence of RF-EMF on cognitive functions and sleep variables, which could explain the observed effects.

Pro- and Con-arguments for the endpoint “EEG & rCBF”

The evidence framework in figure 6 shows that there is a Pro- and a Con-argument for this endpoint.

¹⁸ An explanation is found in the section on EEG and rCBF.

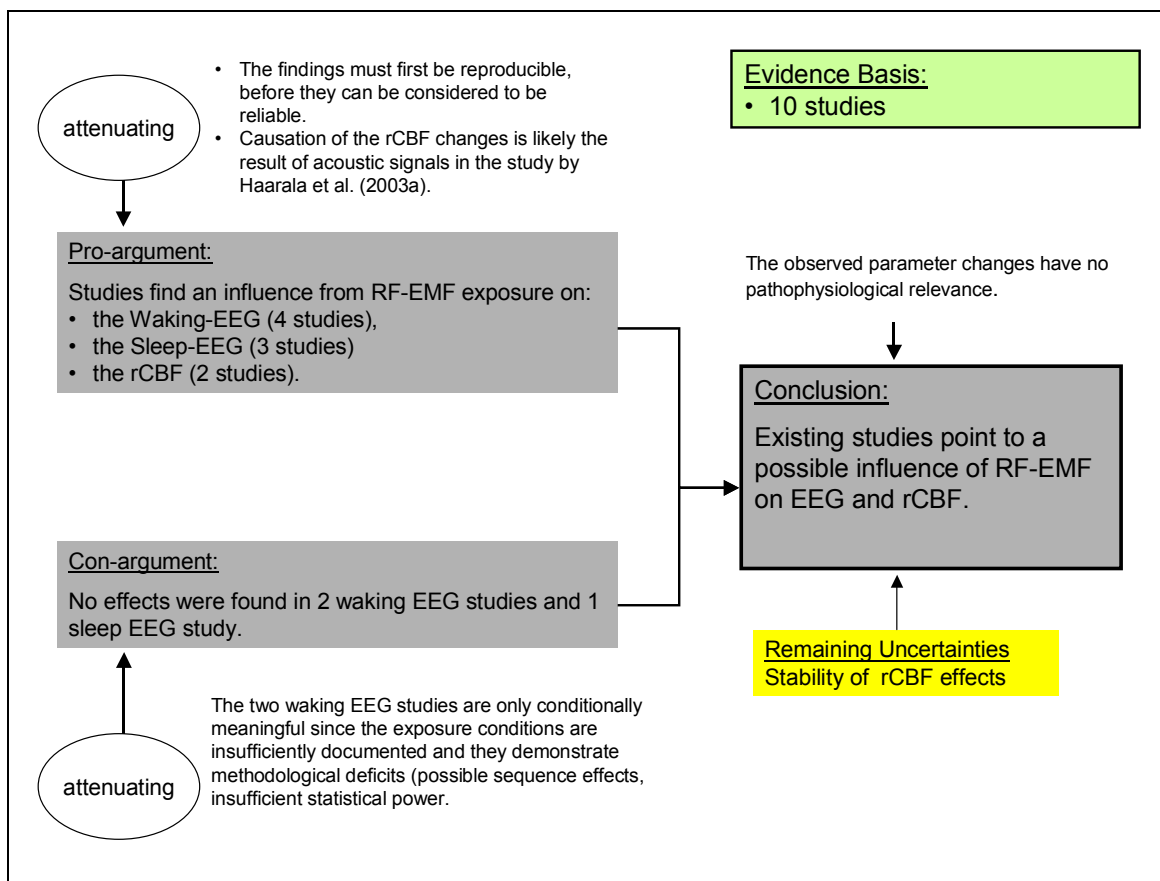


Figure 6: Evidence framework for the endpoint “EEG / rCBF”

Pro-argument:

The Pro-argument refers to the finding that in four studies an influence from RF-EMF exposure on the waking-EEG (Freude et al. 2000; Huber et al. 2003; Kraus et al. 2000a, 2000b) and in three studies on the sleep-EEG (Huber et al. 2000, 2002, 2003) was observed. Both studies that investigated regional cerebral blood flow during the time period considered in the evaluation, also showed an effect for exposure from radio-frequency EMF (Haarala et al. 2003a; Huber et al. 2003). This argument is attenuated by the fact that the findings of the investigations must first be reproduced before they can be judged to be reliable. In addition, a further point of attenuation is that the observed effect in the experiment by Haarala et al. (2003a) is explained by the authors themselves as a methodological artefact. Here, the mobile phone used in the investigation – or more precisely the rechargeable battery – generated a high-pitched sound when turned on which was not consciously perceived by the subjects, but nevertheless registered by them and could have led to the observed effect.

Con-argument:

The Con-argument refers to the two waking-EEG studies (Arai et al. 2003; Hietanen et al. 2000) and the sleep-EEG study by Wagner et al. (2000), in which no influence on EEG from exposure with RF-EMF was found. This argument is attenuated, however, in that the exposure conditions for both waking-EEG studies were insufficiently documented and the investigations demonstrate methodological deficits (possible sequence effects, insufficient statistical power). In the study by Hietanen et al.

(2000), male and female subjects were examined under six different exposure conditions (five variations of exposure, one control), which precludes the use of a balanced experimental design. Thus, sequence effects cannot be ruled out. The study by Arai et al. (2003), included only fifteen subjects which raises the question whether a relationship, if present, could even be detected with sufficient statistical probability (insufficient statistical power). Both studies, therefore, possess only conditional significance.

Conclusion

The experts conclude from the findings of the studies available in the evaluation time-frame that an influence from radio-frequency electromagnetic fields on the EEG as well as the regional cerebral blood flow is possible. The experts are, however, also in agreement that the changes in the parameters observed in the studies for the endpoint "EEG / rCBF" have no pathophysiological relevance. The parameter changes are minor, in part already at the limit of what can be measured, and thus within the range of normal variability. In comparison, the blinking of the eyes will result in greater parameter changes than the exposure to RF-EMF.

Remaining uncertainty

Uncertain is the extent to which the effects observed up to now are stable. This especially concerns the regional cerebral blood flow (rCBF). The role that modulation of the EMF signals plays is also still open.

Pro- and Con-arguments for the endpoint “acute health effects”

The evidence framework, see figure 7, shows that for this endpoint there is only one Con-argument and no Pro-argument.

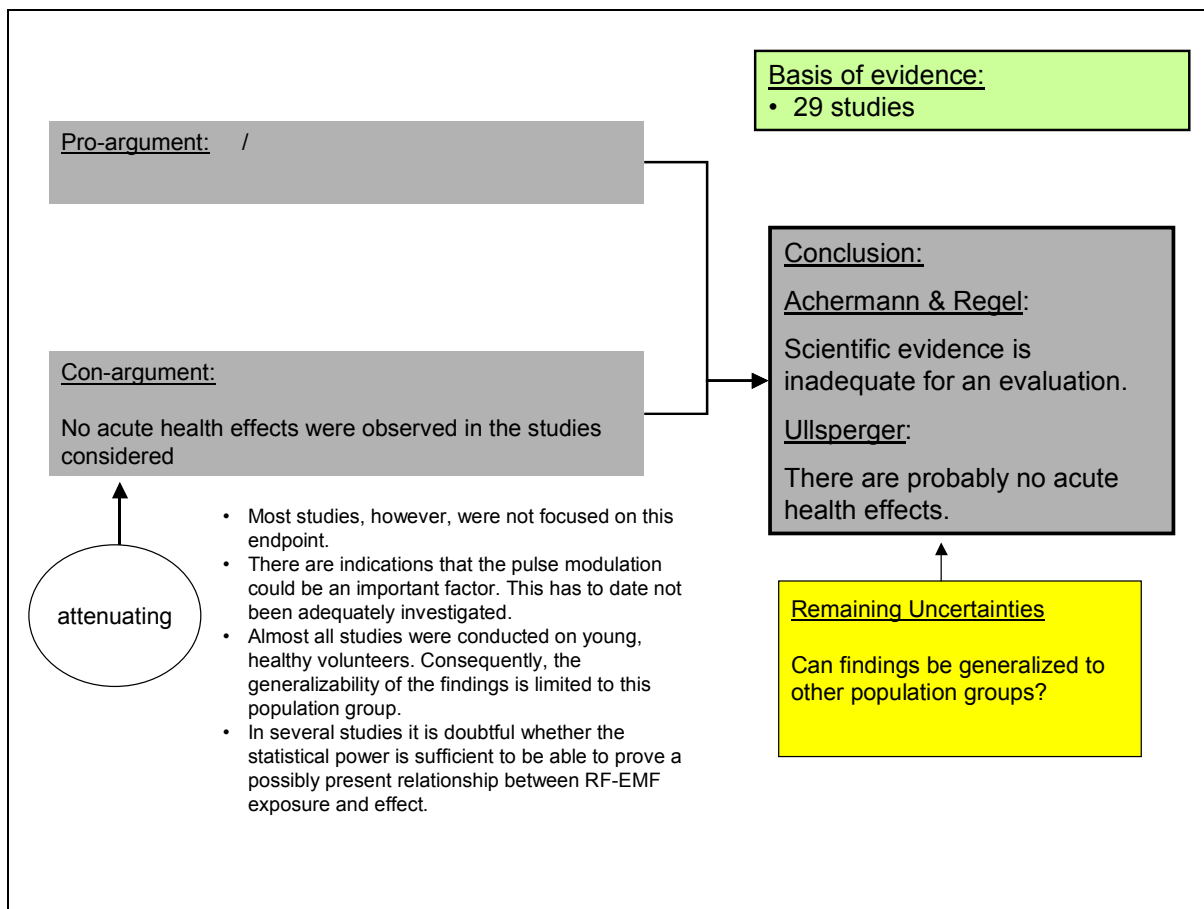


Figure 7: Evidence framework for the endpoint “acute health effects”

Pro-argument:

None.

Con-argument:

The Con-argument refers to the observation that in none of the studies considered was an acute health outcome found. In light of the number and diversity of the investigative approaches, this first of all speaks clearly against an acute health-damaging effect from RF-EMF for the CNS / sleep endpoint. This argument is attenuated, however, in that most of the considered studies were also not focused on discovering acute health effects. In addition to the limitations (e.g. statistical power) mentioned above in the discussion of endpoints, attention must also be paid to the fact that all studies considered here were conducted with healthy and in some cases young subjects. Thus, the results can only be generalized for this population group. This attenuates the Con-argument as well.

Conclusion

The experts are in agreement that acute health effects from radio-frequency electromagnetic fields cannot be deduced from the results of the studies considered. However, Achermann and Regel point out that effect mechanisms leading to health damage – beyond acute damages – from RF-EMF for the CNS / sleep endpoint are not known. In this regard, the experts believe that given the current state of knowledge it cannot be evaluated whether the observed effects are relevant to health. For Ullsperger the findings observed to date rather speak against a relationship between RF-EMF exposure and health outcomes.

Remaining uncertainty

Remaining uncertainties involve the role of the modulation of the EMF signals and, above all, the validity of the previous results for potentially sensitive subpopulation groups, for example children, disabled or electro-(hyper)sensitive people. In addition, persons with sleep impairments (insomniacs) may possibly react to RF-EMF in a distinctive manner.

4.4.3 Assessment by MUT

The experts' evaluation of the various studies for the endpoints cognitive functions, sleep variables, parameters of the EEG, and regional cerebral blood flow (rCBF) differ slightly. The assessment of the findings for a risk evaluation is unambiguous, however. That is, independent of whether the observed effects will be confirmed or not: they do not show a health risk from radio-frequency electromagnetic fields.

In addition, the experts are unanimous in that no clues can be found for acute health effects in the studies considered.

Nevertheless, the above mentioned limitations are valid for all the examined endpoints: up to now investigations were only performed on essentially healthy (and mostly young) adults. It is, however, possible that there are sensitive subpopulations for whom health relevant effects may be demonstrable.

4.5 Impairment of well-being

Starting point:

Environmental impairment of well-being is understood to represent the afflicted persons' perceived and negatively viewed environmental burden (cf. Bullinger & Guski 1997). It is frequently expressed in the form of unspecific symptoms (i.e. symptoms not attributable to a specific cause), such as fatigue, sleep disturbances, headaches, difficulties in concentrating, or nervousness. Impairment of well-being primarily involves subjective experiences. Their measurement is therefore dependant upon the self-appraisal by the afflicted. Ideally, psychometrically-proven and standardized questionnaires are available for the self-appraisals.

In the context of the overall symptoms, the question is whether there are sensitive groups in the population that are more likely to suffer such impairments of well-being because they react especially sensitively to EMF (cf. Bergqvist et al. 1997). The term "electromagnetic hypersensitivity" has been coined to describe this concept.

Significance for the risk evaluation:

The question whether impairments of well-being are even relevant for a risk evaluation essentially depends on whether they should be viewed as a disease or at least as an indicator for health damage, or whether they should only receive the status of an annoyance, that may be unpleasant but is not relevant to health.

Given the definition of health in accordance to the World Health Organisation ("Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" WHO 1948), then impairments of well-being are undoubtedly to be judged a diminishment of health. Even if this very widely reaching definition is not fully agreed to, there exists at least for the serious impairments of well-being a relationship to health damages. For example, ongoing sleep disturbances can lead to a reduction of the immune system functions (cf. Bryant, Trinder & Curtis 2004). Therefore, it appears reasonable to also consider impairments of well-being in the risk evaluation of mobile phone communication.

4.5.1 State of the knowledge in the year 2000

The topic of impairment of well-being is not dealt with in the expert opinion report the German Radiation Protection Commission (SSK 2001).

The assessment of the Independent Expert Group on mobile phones (IEGMP 2000) is:

Apart from the risks associated with the use of mobile phones while driving [...] there is no persuasive epidemiological evidence that exposure to RF radiation in general – or to the limited extent that it has been investigated, mobile-phone-related exposures in particular – causes disease in people. Although the epidemiological research that has been carried out to date does not give cause for concern, it has too many limitations to give reassurance that there is no hazard. A substantial number of people report symptoms such as fatigue, headache and feelings of warmth behind the ear that occur during or shortly after the use of mobile phones. However, it is unclear to what extent, if any, these symptoms are caused by RF radiation. (p. 99)

4.5.2 Results of the expert opinion reports and the discussion

The two expert/groups, Dr. Seitz, Dr. Stinner, Prof. Dr. Eikmann (Gießen) and Dr. Rösli (Berne) submitted separate expert opinion reports. The advisory expert panelist for this topic area was PD Dr. Wiesmüller (Outpatient Unit of Environmental Medicine (UEM) of the Institute of Hygiene and Environmental Medicine, University Hospital Aachen, Medical Faculty of the Rheinisch-Westphalian Technical University (RWTH) Aachen).

For the risk evaluation, the experts defined eleven endpoints (see Table 8) and agreed on a list of studies that were drawn upon for the risk evaluation. In most of these studies, as seen in Table 9, multiple endpoints were examined. Almost all investigations looked at the exposure from mobile telephones; only Hutter et al. (2002), Navarro et al. (2003), and Zwamborn et al. (2003), examined the exposure from base stations.

Table 8: Endpoints for the risk evaluation of impairment of well-being

1. Fatigue, sleep disturbances (insomnia)
2. Dizziness, nausea
3. Headaches
4. Difficulties concentrating, memory impairment
5. Pain, besides headaches
6. Nervousness
7. Depressive state, low-spirited
8. Skin problems: itching, tingling, redness
9. Skin sensations of warmth: burning, behind/on ear
10. Tinnitus (diagnosis), noise in ear
11. Electromagnetic hypersensitivity and perception of electromagnetic fields

Table 9: Studies on impairment of well-being (based on the two expert opinion reports)

Authors	Type	Endpoints (explanations see table 8)											Evaluation ^(a)		
		1	2	3	4	5	6	7	8	9	10	11	Quality	Evi- dence of causality	
Chia et al. (2000)	Cross-sectional	X	X	X	X	X					X			+	-
Croft et al. (2002)	Crossover											X		+	+
Frick et al. (2002)	Cross-sectional	X	X	X	X	X	X	X	X	X				+	-
Hietanen et al. (2002)	Crossover											X		-	+
Hillert et al. (2001)	Experimental	X												+	-
Huber et al. (2000)	Crossover	X												+	+
Hutter et al. (2002) ^(b)	Cross-sectional	X												+	-
Koivisto et al. (2001)	Crossover	X	X	X	X						X			+	+
Navarro et al. (2003)	Cross-sectional	X	X	X	X	X		X			X			-	-
Ofteidal et al. (2000) Sandström et al. (2001) Wilén et al. (2003)	Cross-sectional	X	X	X	X	X					X			+	-
Ozturan et al. (2002)	Crossover										X			-	+
Raczek et al. (2000)	Crossover											X		+	+
Röösli et al. (2004)	Cross-sectional	X	X	X	X	X	X	X	X		X			+	-
Santini et al. (2001a) Santini et al. (2002) Santini et al. (2003)	Cross-sectional	X	X	X	X	X		X			X			-	-
Santini et al. (2001b)	Cross-sectional	X		X	X	X					X			+	-
Tahvanainen et al. (2004)	Crossover											X		+	+
Zwamborn et al. (2003)	Crossover			X				X				X		+	+

(a) Quality of study: + = good; - = insufficient.

Evidence of causality: + = study design useful for demonstrating a causal relationship; - = study design not useful.

(b) This study was only considered by Röösli.

Basis of evidence (studies since the year 2000)

The coordinated literature search by the two expert-groups yielded altogether seventeen (17) studies that are contextually relevant for the evaluation of the endpoints.¹⁹ However, in the assessment of the experts not all studies are equally suitable for the risk evaluation. First of all, several investigations demonstrate considerable quality deficits, and secondly, because of their study design not all studies are suitable for establishing a causal relationship between exposure to RF-EMF and impairment of well-being.²⁰ The evaluation of the quality of the investigations as well as their suitability for demonstrating causality is shown in Table 9, wherein we follow the assessment by the experts.

The following evidence framework summarizes the most important Pro- and Con-arguments, the conclusions, as well as the remaining uncertainties from the viewpoint of the experts. Three groups of endpoints are distinguished:

- (1) the endpoint *headache*, for which – in the assessment of the experts – the largest overlap of findings is present,
- (2) endpoints, for which either no causal relationship was found, or the existing studies are methodologically questionable. The endpoints here are: *fatigue / sleep disturbances, dizziness / nausea, pain (besides headaches), depressive state / low-spirited, skin problems, tinnitus / noise in ear, nervousness* as well as *difficulties in concentrating / memory impairment*, and
- (3) endpoints, for which probably no relationship to RF-EMF exposure exists. These endpoints are about *field perception, hypersensitivity and heat sensations of the skin*.

The following discussion presents these three groups of endpoints separately.

Evidence framework for endpoint 1:

In the evaluation of the endpoint *headache* seven studies are relevant. Their findings form the basis of the Pro- and Con-argument (see figure 8).

¹⁹ The multiple publication of the same studies or rather of the same data by Santini et al. as well as by Offendal/ Sandström/Wilen were assessed for each set of authors as a single study.

²⁰ See the chapter „Judgement of quality” in the expert opinion reports by Rööfli and Seitz, Stinner & Eikmann.

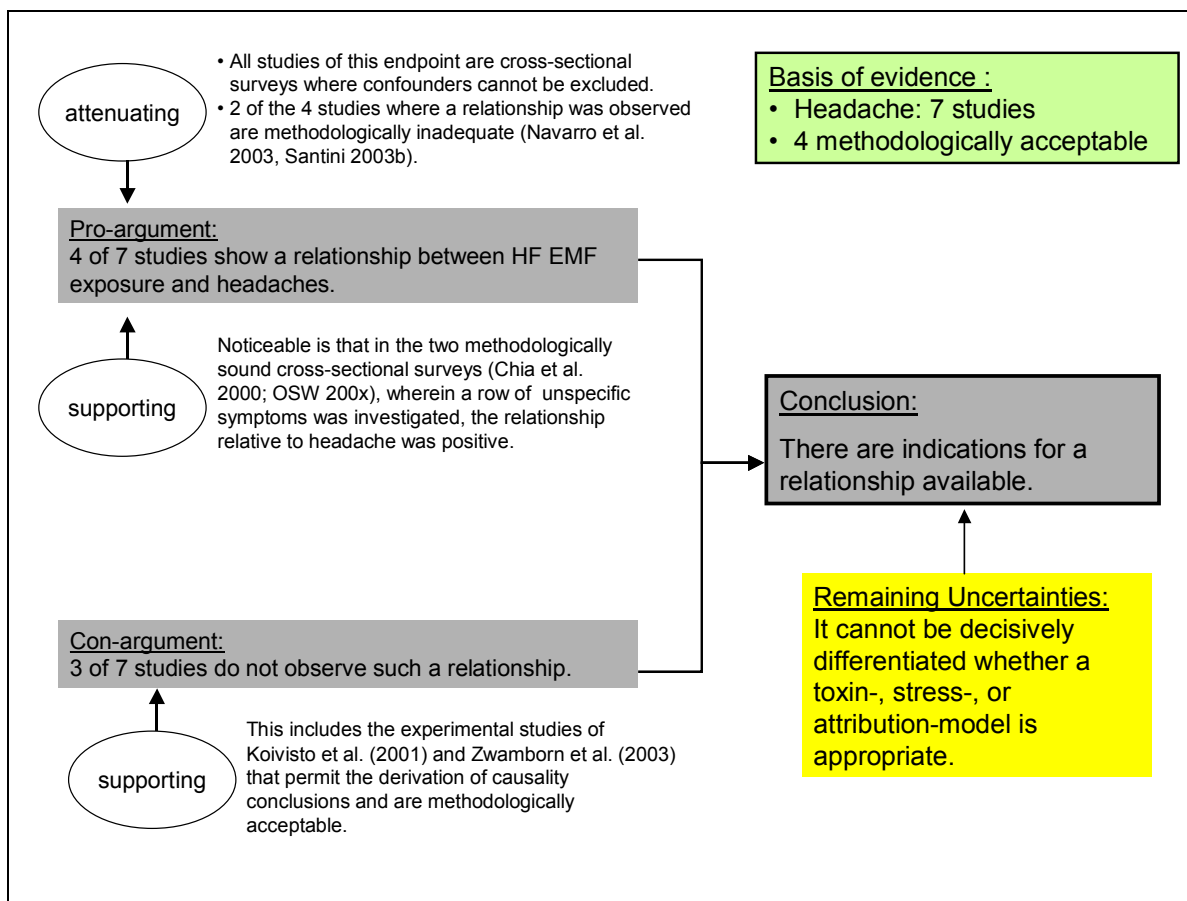


Figure 8: Evidence framework for endpoint 1

Pro-argument:

For the endpoint headache, four of the seven studies demonstrate a relationship with RF-EMF exposure. These include the following studies: Chia et al. (2000); Navarro et al. (2003), OSW (200x)²¹, Santini (2003b). The Pro-argument is supported by the fact that for both methodologically acceptable cross-sectional surveys (Chia et al. 2000; OSW 200x), which investigated a series of unspecific symptoms, the relationships relative to headache were positive.

The Pro-argument is attenuated by the fact that since all of the studies are cross-sectional surveys, the presence of confounders cannot be excluded. In addition, the two other studies that showed a relationship (Navarro et al. 2003, Santini 2003b) are methodologically inadequate to the extent that they cannot be considered in the evaluation.

Con-argument:

Three of seven studies find no relationship between headaches and RF-EMF exposure (Koivisto et al. 2001; Santini 2001b, Zwamborn et al. 2003). This argument is supported by the fact that this group of studies includes the investigation of Koivisto et al. (2001), which is the only study of the endpoint headache that not only satisfies the scientific requirements for quality but also has a study design that would be suit-

²¹ The different studies by Oftedal/Sandström/Wilen are collectively abbreviated herein as OSW 200x.

able for the evaluation of a causal relationship.

Conclusions

The experts are in agreement for the evaluation of the endpoint “headache” that the scientific studies provide indications of a relationship between headache and exposure with electromagnetic fields.

Remaining uncertainties

It is not clear however how these indications of a relationship are to be interpreted. Bullinger & Guski (1997, 51f.) discuss three models of effect mechanisms for environmental impairment of well-being: toxin-, stress-, and attribution-model. Is it indeed the actual electromagnetic fields themselves that are responsible for the headaches (toxin-model)? Are the exposure circumstances associated with stress and does this stress cause the headaches (stress-model)? Or do the afflicted persons simply attribute their headaches to EMF exposure (attribution-model)?²²

Evidence framework for endpoint group 2:

This group includes the endpoints *fatigue / sleep disturbances, dizziness / nausea, pain (besides headaches), depressive state / low-spirited, skin problems, tinnitus / noise in ear, nervousness* as well as *difficulties in concentrating / memory impairment*. For their evaluation, seventeen (17) studies are relevant. In the opinion of the experts, there are two studies that are both suitable for the evaluation of a causality hypothesis as well as simultaneously satisfying the methodological quality requirements. This includes the studies of Koivisto et al. (2001) and Zwamborn et al. (2003). The Pro- and Con-arguments are presented in figure 9.

²² For the latter case to be plausible, however, far-reaching assumptions would have to be made. For instance, in the study of Chia et al. (2000) the volunteer subjects were first asked if they suffer from headaches and then were requested to provide information on how frequently they use their mobile phone. Thus, the relationship observed by Chia et al. can only then be explained with the attribution-model if one assumes a selectively distorted memory (recall bias). This means that persons with headaches and that attribute their headaches to mobile phone usage would therefore maintain they have longer usage times than persons without headaches.

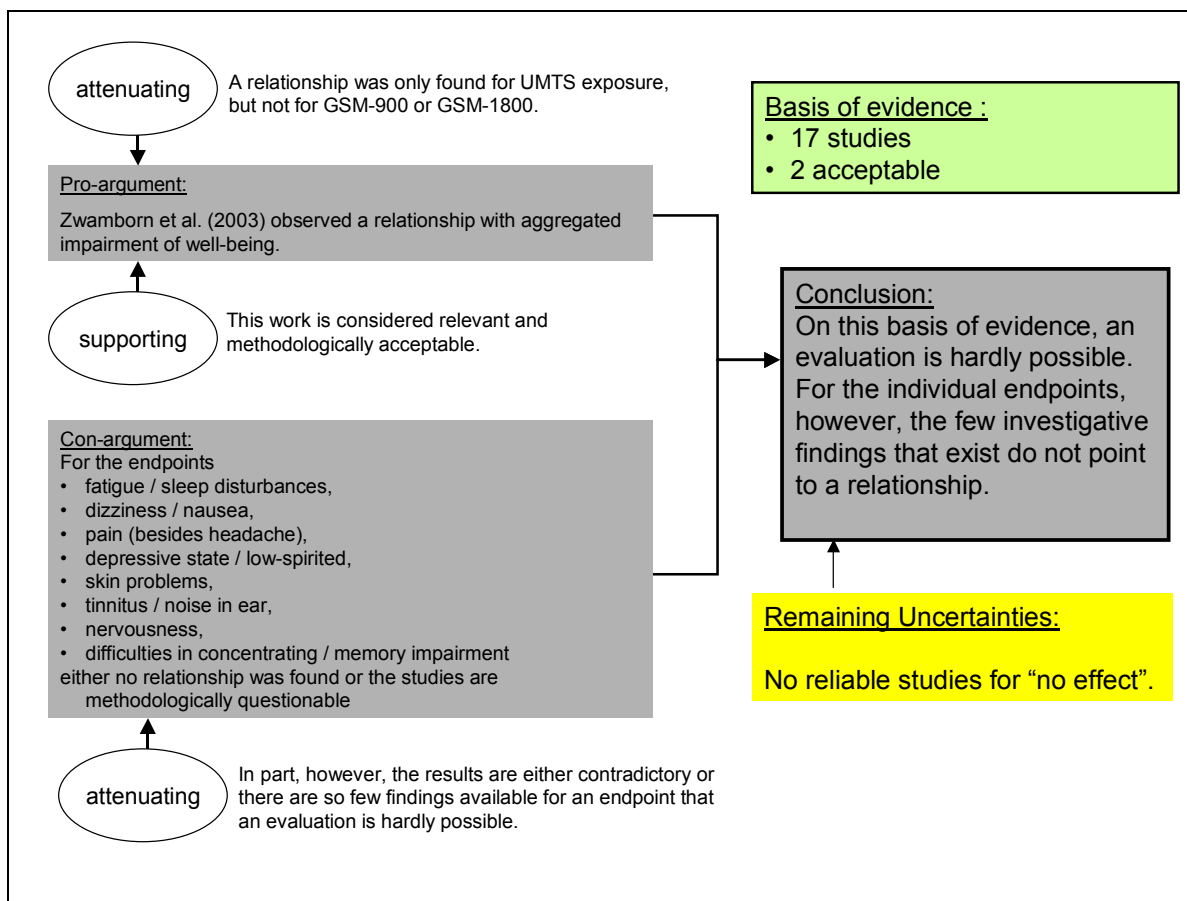


Figure 9: Evidence framework for endpoint-group 2

Pro-argument:

The Pro-argument is based on the results of the experimental investigation by Zwamborn et al. (2003), in which a series of very different symptoms of impairment of well-being were surveyed with a questionnaire and whose results were aggregated into cumulative values. In the experiment, a statistically significant relationship was then seen between exposure to EMF and the cumulative values. This argument is supported in that the experts assess the study by Zwamborn et al. to be one of the few studies that they count as a good study regarding its methodological quality as well as its usefulness for demonstrating causality.

The argument is attenuated because this relationship between EMF exposure and estimation of well-being was only observed with exposure to UMTS fields, but not GSM-900 or GSM-1800 fields. A plausible explanation for this selective effect is not available.

Con-argument:

The Con-argument is that for the endpoints *fatigue / sleep disturbances, dizziness / nausea, pain (besides headaches), depressive state / low-spirited, skin problems, tinnitus / noise in ear, nervousness* as well as *difficulties in concentrating / memory impairment* either no relationship was observed in the studies or the studies were of questionable methodology. The argument is attenuated in that either the findings are in part contradictory or that so few findings are available for an endpoint that a sound

evaluation is hardly possible.

Conclusion

For the endpoint group 2 (*fatigue / sleep disturbances, dizziness / nausea, pain (besides headaches), depressive state / low-spirited, skin problems, tinnitus / noise in ear, nervousness as well as difficulties in concentrating / memory impairment*), the experts view the state of the evidence as so weak that an evaluation is hardly possible. However, in the opinion of the experts, the few existing investigative results do not indicate a relationship with RF-EMF exposure.

Remaining uncertainties

Uncertainty in the evaluation remains because of the deficit of reliable studies. Thus, an observable effect cannot be ruled out.

Evidence framework for endpoint group 3:

This group includes three endpoints: feelings of warmth on skin, field perception, and hypersensitivity. Since the above Table 9 did not differentiate between hypersensitivity and perception of electromagnetic fields (field perception), Table 10 once again lists which studies examined which aspect.

It should be noted that in part considerable problems of terminology exist since the same terms are used to describe different concepts (cf. David et al. 2002, p. 9; Leitgeb 1998, p. 11):

- Hypersensitivity means the increased sensitivity to react symptomatically to EMF, compared to the normal population. To verify this concept of “hypersensitivity” it would need to be examined whether at low exposure levels impairments of well-being will be manifested in a specific population group while the same exposure level does not show effects in the normal population (the non-hypersensitive).
- A different frame of mind underlies the understanding of hypersensitivity as a self-diagnosis. Here, the afflicted attribute their impairments of well-being as having been caused by EMF. To verify this concept of “hypersensitivity” it would need to be examined whether the impairments of well-being only appear with corresponding exposures.
- Further differentiation should be given to studies that attempt to determine whether EMF exposure can in general cause impairment of well-being. Hereby, impairment of well-being can be determined by a set of different symptom measures.

The expert opinion reports discuss studies that fall within the latter two areas mentioned above under the topic “field perception / hypersensitivity”. Surprisingly, hypersensitivity – in the sense of a differentiation between hypersensitive and non-hypersensitive population groups – has not yet been examined, at least not in a sound methodological manner.

The majority of available studies address the question of whether EMF in general can cause impairment of well-being (see Table 10). These studies, however, are not further considered under the context of “hypersensitivity and field perception”.

Table 10: Studies on hypersensitivity and perception of electromagnetic fields

Study	Subjects	Field perception	Hypersensitivity	General impairments of well-being
Croft et al. (2002)	Healthy Volunteers	–	–	No differences between the exposure scenarios and subjective activation measurement (measured as mean for the scaling “tense, calm, excited, tired”).
Hietanen et al. (2002)	Self-diagnosis: electrosensitive	No effect	Sham exposure shows more symptoms; Study has deficits: no reliable statements	–
Koivisto et al. (2001)	Healthy Volunteers	–	–	No relationship between exposure and well-being (headache, dizziness, fatigue, skin redness, itching, feeling of warmth)
Raczek et al. (2000)	Diagnosed environmental sickness	No effect	–	–
Tahvanainen et al. (2004)	Healthy Volunteers	Was investigated in the experiment but results were not reported.	–	Presentation of results is not transparent – line of reason could not be followed. No differences between exposure scenarios for subjective symptoms
Zwamborn et al. (2003)	Healthy Persons +Self-diagnosis: electrosensitive	–	Comparison of the two groups not possible, since sampling characteristics are different.	Changes regarding well-being for the two groups only with UMTS signal

Only two studies (Hietanen et al. 2002; Zwamborn et al. 2003), examined whether the self-diagnosis “hypersensitivity” is applicable (also see the comments below in the section “Assessment by MUT”). The field perception was examined in three studies (Raczek et al. 2000, Tahvanainen et al. 2004, Hietanen et al. 2002).

The Pro- and Con-arguments are summarized in the following evidence framework (see figure 10).

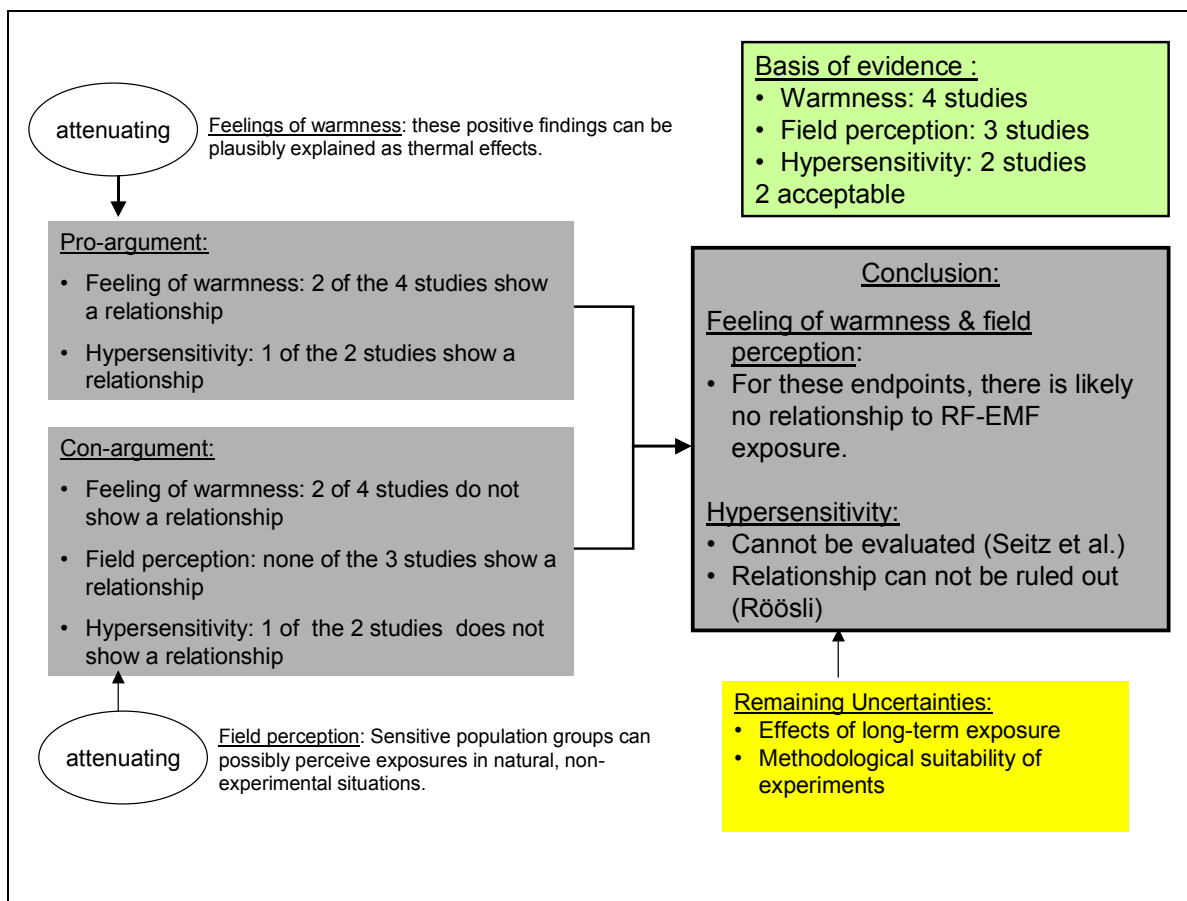


Figure 10: Evidence framework for endpoint group 3

Pro-argument:

For the endpoint *feeling of warmness* the Pro-argument refers to the fact that in two of the four studies a relationship with RF-EMF was found. The argument is attenuated in that these positive findings can be plausibly explained by the heat generated by the phone unit itself.

The Pro-argument for the endpoint *hypersensitivity* refers to the fact that – in the opinion of Rööslü (see opinion report p. G-29) – in one of the two relevant studies an indication for hypersensitivity is observed (Zwamborn et al. 2003).

For the endpoint *field perception* (i.e. the ability to “sense” radio-frequency electromagnetic fields), there is no Pro-argument since a positive result could not be observed in any of the studies in which this phenomenon was examined.

Con-argument:

For the endpoint *feeling of warmness* the Con-argument refers to the fact that in two of the four studies no relationship was found to the RF-EMF exposure.

The Con-argument for the endpoint *hypersensitivity* refers to the fact that in one of the two studies (Hietanen et al. 2002), no relationship was observed, but the study was classified as not reliable by the experts.

The Con-argument for the endpoint *field perception* is based on the evaluation that in none of the studies in which this phenomenon was examined were the test subjects able to “sense” an exposure to RF-EMF more frequently than simply by random chance. This argument is supported by the negative findings of the methodologically suitable and qualitatively good study of Raczek et al. (2000). The argument is attenuated because of the possibility that the experimental approach of the investigations for examining field perception could be unsuitable. Sensitive population groups could possibly sense exposure to electromagnetic fields under natural, non-experimental situations, but are unable to do so under laboratory settings (cf. expert opinion report by Rösli, p. G-29).

Conclusion

While the experts hold a relationship regarding the endpoint *feeling of warmth* with RF-EMF for unlikely and also assume there are no serious uncertainties associated, it is a somewhat different situation for the endpoints *field perception* and *hypersensitivity*. On the one hand, the experts observe that it is not entirely certain whether the disease state “hypersensitivity” even exists (expert opinion reports of Seitz, Stinner & Eikmann, pp. F-6 to F-8 , F-26 to F-30). On the other hand, it is questioned whether experimental studies can even capture long-term or cumulative effects. Therefore, the two expert(groups) arrive at different evaluations: while Seitz, Stinner & Eikmann believe that an evaluation is not possible on the basis of the available data, the opinion of Rösli maintains that a relationship cannot be ruled out, because there are still too few studies.

Remaining uncertainty

Above all, the uncertainties for the evaluation of the evidence result from two points: For one, the studies existing so far are unable to provide a statement about effects from long-term exposures. For the other, it should be questioned whether experimental studies are even capable of discerning differences among people regarding field perception or rather hypersensitivity.

4.5.3 Assessment by MUT

The evaluation of the endpoint “impairment of well-being” is especially difficult, since it deals with a concept that is distinctively vague. The separation into a row of more specific endpoints is only partially helpful. The presented symptoms are not only diffuse but also found frequently and, thus, make the evaluation of specific causes difficult.

Especially the different conceptual interpretations of the term hypersensitivity are unclear. Even if hypersensitivity is decoupled from the field perception, there is still conceptual fuzziness. Does hypersensitivity then come to represent the expression of symptoms, in general, in response to EMF exposure (see expert opinion report by Rösli, p. G-29), or is it rather a self-diagnosis by patients that attribute their ailments to EMF (this view is obviously shared by Seitz, Stinner & Eikmann in their expert opinion report, pp. F-26 to F-28). Or is hypersensitivity rather – as the prefix “hyper” indicates – an increased sensitivity towards EMF? Then differences between hypersensitive and non-hypersensitive people should be apparent. A reliable study that would have investigated this, however, does not yet exist (see above Table 10).

Furthermore, there are overall only 3 studies (Koivisto et al. 2001, Raczek et al. 2000, and Zwamborn et al. 2003) that could be drawn upon for the evaluation of hypotheses for causality under the aspects of suitability and quality. Wherewith the studies of Koivisto et al. and Raczek et al. provide negative results. However, the study of Zwamborn et al. (2003) finds selected relationships between well-being and RF-EMF exposures: not for GSM, but rather for UMTS exposures. It is unclear how this is to be evaluated.

The differences between the experts' evaluative standards for the various endpoints are also notable. For instance, with respect to the endpoint headache, indications for a relationship to mobile phone communication exposure are envisioned, even though none of the studies that are the basis of the claim are suitable for the evaluation of causality hypotheses. Such a pronounced conclusion is, however, not drawn from the studies of Koivisto et al. (2001) and Zwamborn et al. (2003), although they are among the few studies under the aspects of design and quality that could provide a test for a causal relationship.

In addition, the workshop discussions made clear why an unambiguous evaluation of a possible relationship between RF-EMF exposure and impairment of well-being is so difficult:

- The majority of the impairments of well-being appears very frequently in the general population and, therefore, could also have many other causes.
- Unspecific symptoms are strongly shaped by subjective characteristics and are methodologically very difficult to capture objectively. In the final workshop, different participants pointed out that in many studies the symptom "headache" was not even defined. There is, however, a large variety of possible expressions of this type of impairment (pressure in the eyes, tension pain, lasting or intermittent pain, etc). In examination questionnaires the subjects are frequently only asked whether they have headaches or not. The sensation of a headache is, however, very subjective and it is quite conceivable that the same phenomenon will be labeled as a "headache" by one, but as "no headache" by another.
- For examinations of impairment of well-being from RF-EMF exposure, the problem exists that the classic standardized survey instruments, which come from the psychosomatic field (e.g. SF-36), are too coarse to even detect relationships. It is questionable whether a relationship between RF-EMF exposure and impairment of well-being can even be unambiguously proven; to date such a proof is absent. For the endpoints impairments of concentration and field perception, the question is also whether the applied study designs are even suitable to test these endpoints.
- The actual exposure was not determined for any of the available studies. Especially problematic is the risk of misinterpretation of the exposure. To objectively determine the exposure both short-term as well as long-term exposure is necessary. A personal dosimetry is therefore desirable.
- For epidemiological studies, a large sample is necessary in order to ensure greater significance – the available studies only fulfill this requirement to a limited extent.
- Uncertainties for the evaluation also reflect the potential consequences from long-term exposure to RF-EMF, which has not yet been examined until now.
- A conclusive statement is therefore not possible for any of the endpoints since

the findings of the studies are quite contradictory. Without knowing an effect mechanism or having at least a hypothesis for it, the significance of discovered associations is weak.

At present, reliable statements whether impairments of well-being can be caused by RF-EMF can hardly be made. Therefore, the evaluation differences also reflect in significant fashion on the personal value system of the experts.

4.6 Blood-brain-barrier

Starting point

The blood-brain-barrier (BBB) is a brain-specific blood vessel barrier, which – in contrast to the blood vessels of all other organs of the body – prevents the free entry of proteins from the blood into the tissue. Thereby the BBB regulates the influx of energy and metabolic substrates required by the brain (especially glucose and amino acids), while simultaneously serving as a protective “shield” against the intrusion of potentially harmful substances from the blood in the capillaries into the brain fluid. The barrier effect is based on the fact that the endothelial cells of the blood vessels in the brain – in contrast to those of all other vessels of the body – are welded together through so-called tight junctions, which prevent the free exchange of substances between the lumen of the vessels and the extracellular space of the brain. Instead, all substrates that cross over from the blood into the brain or vice versa must pass through the endothelial cells and their membranes. For lipid-insoluble substances, brain-specific transport systems are required, which allow for a precise regulation of the metabolic exchange.

Disturbances of the blood-brain-barrier, i.e. changes of its permeability, can cause brain edemas that – if they exceed a certain magnitude – will result in an increase of the intracranial pressure and thus result in blood-flow disturbances. This in turn can lead to an impairment of the energy metabolism and to secondary biochemical disturbances. It is also conceivable that during a disturbance of the blood-brain-barrier toxic substances can intrude into the CNS and cause damage there. Such disturbances can, for example, be caused by heavy alcohol consumption or by a heat-shock.

Significance for the risk evaluation

Based on the functioning of the blood-brain-barrier it can be directly inferred that a disturbance of the BBB is potentially health-relevant. For high SAR values, different investigations have determined an elevated permeability of the blood-brain-barrier, which, however, can be traced back to thermal effects (cf. Hossmann & Hermann 2003). Disagreement exists over whether exposures to weak electromagnetic fields – like for example mobile phone communication fields – can evoke a disturbance of the blood-brain-barrier.

4.6.1 State of the knowledge in the year 2000

On the state of knowledge in the year 2000 of possible risks for a disturbance of the blood brain-barrier through electromagnetic fields from mobile phone communication, the German Radiation Protection Commission states (SSK 2001):

Es kann zusammengefasst werden, dass die Ergebnisse zu einer expositionsbedingten Permeabilitätsänderung der Blut-Hirn-Schranke kein konsistentes Bild ergeben und lediglich als Hinweise zu werten sind. Die offenen Fragen erfordern in Zukunft vorsorglich weitere Untersuchungen zu dieser Thematik. [p. 34] *[It can be summarized that the findings on exposure-related changes in the permeability of the blood-brain-barrier do not yield a consistent picture and are to be evaluated merely as indications. The open questions remaining will necessitate additional future examinations of this topic as a precaution. (p. 34)][†]*

The assessment of the Independent Expert Group on mobile Phones (IEGMP 2000) states

The available evidence for an effect of RF exposure on the blood-brain barrier is inconsistent and contradictory. Recent, well-conducted studies have not reported any effects. [p. 60]

4.6.2 Results of the expert opinion report and the discussion

It became apparent during the first phase of the preparation of the expert opinion report that was to be jointly undertaken by the experts (selection of the literature, establishment of quality criteria and the endpoints to be considered) that even in the risk evaluation broad overlap would exist. Thus, the two experts Prof. Dr. Hossmann and Prof. Dr. Stögbauer decided to prepare a joint expert opinion report. Advisory expert panelist for this topic area was Prof. Dr. Rainer Meyer (Institute for Physiology, School of Medicine, University of Bonn).

Basis of evidence (since 2000)

The literature search for the expert opinion report yielded thirteen publications that met the search criteria of the experts. Of those, however, only five turned out to be studies in which original research findings were presented (see Table 11).

Table 11: Original research findings since the year 2000 for the topic “disturbances of the blood-brain-barrier”.

Authors	Type of experiment
Finnie et al. (2001)	in vivo: mice
Finnie et al. (2002)	in vivo: mice
Salford et al. (2003)	in vivo: rats
Schirmacher et al. (2000)	in vitro: BBB model
Tsurita et al. (2000)	in vivo: rats

These five studies provide the basis of evidence on which the evaluation of possible health risks due to a disturbance of the blood-brain-barrier by electromagnetic fields of mobile phone communication is founded.

Pro- and Con-arguments

As the evidence framework in figure 11 shows, two arguments that speak for a potential health risk from electromagnetic fields of mobile phone communication can be

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

derived from the available research findings since the year 2000.

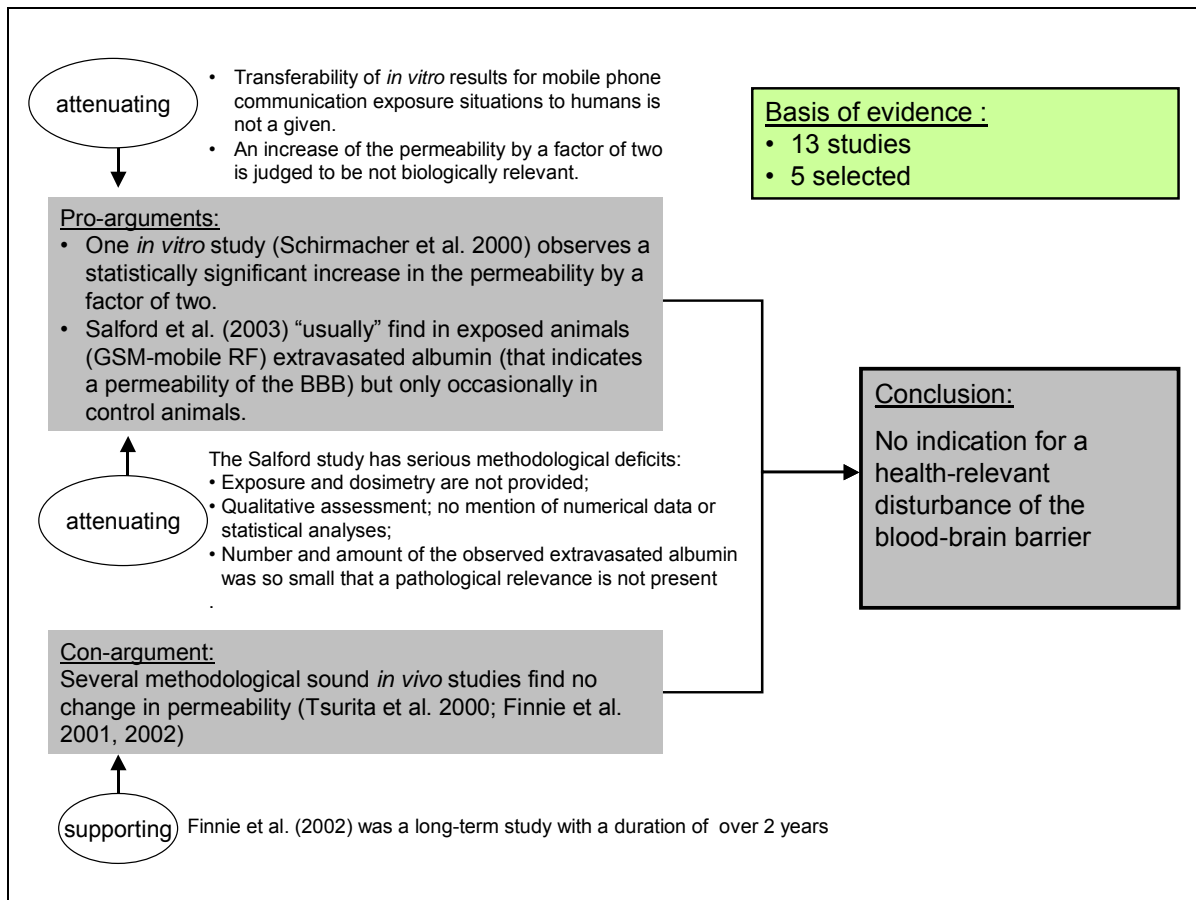


Figure 11: Evidence framework for disturbances of the blood-brain-barrier

Pro-arguments:

The first Pro-argument refers to the study by Schirmacher et al. (2000), which observed in their *in vitro* investigation of a cell model of the blood-brain-barrier an increase in permeability by a factor of two with a field typical of mobile phone communication and a SAR value of 0.3 W/kg. This can be understood to be an indication for a change in the BBB through exposure with mobile phone communication fields.

However, this argument is attenuated by two limitations: The increase in permeability by a factor of two is in the opinion of Hossmann and Stögbauer with highest probability biologically irrelevant, since in other *in vitro* investigations with BBB systems the positive controls, as for example heat exposure, showed an increase of permeability by a factor of 100. In addition, findings from *in vitro* investigations cannot be simply extrapolated to a whole organism and, therefore, also not to the mobile phone communication exposure situation in humans.

The second Pro-argument is based on the results of the study by Salford et al. (2003). In this investigation, young male and female Fischer rats were exposed to the electromagnetic field of a conventional GSM mobile phone. Salford et al. reported that in control animals (animals not exposed) extravasated albumin was "only occasionally" observed, but in exposed animals extravasated albumin was "usually" found

in the CNS. In principle, the observations of extravasated serum proteins such as albumin in the CNS indicate that the permeability of the blood-brain-barrier is increased with the exposure from mobile RF fields.

This argument is attenuated, however, through a series of methodological deficits: For instance, detailed information on exposure and dosimetry is missing and the assessment of the data is performed qualitatively with no mention of measured values or statistical analyses. In the first online version of their publication, the figure used as reference for the frequency of extravasated albumin had to be withdrawn by Salford et al., since it was taken from an older publication, which reported an investigation with higher exposure strengths above the limit values (3.3 W/kg). According to the experts, the visible number and amount of extravasated albumin in the corrected figure is so low, that it should not be assumed that a pathological relevance is given.

Con-arguments:

Speaking against the existence of a potential health risk is the fact that in three methodologically-sound, *in vivo* studies no permeability change under exposure with electromagnetic fields from mobile RF was observed. Herein, attention should especially be given to the study by Finnie et al. (2002) in which experimental animals were exposed over a duration of two years, so that here one can speak of a long-term exposure.

4.6.3 Conclusions

The conclusion of the experts is unequivocal: The scientific investigations published since the year 2000 provide no indication for a health relevant disturbance of the blood-brain-barrier from exposure with electromagnetic fields in the frequency- and intensity-range of mobile phone communication.

4.6.4 Assessment by MUT

Only a faint uncertainty factor remains which stems from the dose-effect question that has not yet been fully elucidated. The question is whether a *chronic* exposure to RF-EMF can cause a change in the blood-brain-barrier. The exposure durations of the majority of experiments – with the exception of the long-term study by Finnie et al. (2002) – are too short to be able to rule this out with certainty.

Contrary to ionizing radiation whose cumulative effect has been scientifically proven, there is no scientifically sound explanation (i.e. effect mechanism) for a cumulative effect of radio-frequency electromagnetic fields. Moreover, the experimental research (the long-term study by Finnie et al. 2002) provides no indication for a disturbance of the blood-brain barrier with prolonged exposure to electromagnetic fields of mobile phone communication.

5. Summary discussion

Here, the results of the expert opinion reports will be discussed. This chapter is divided into the following sections: the start of the chapter outlines how the evaluations of the studies from the six different topic areas are to be summarized into an overall risk evaluation.

Then the expert opinion reports are addressed: first, the changes to the data situation since the year 2000 is described: How should quality of the studies published since the year 2000 be evaluated? What are the improvements? What data gaps remain?

This is followed by a presentation once again of the most important evaluations of the experts on the six examined biological endpoints and shown if and how the state of the knowledge has changed in comparison to the evaluation by the SSK in 2001. Finally, conclusions for future risk dialogues are drawn.

5.1 Steps of the risk analysis

'Risk' is usually understood as possible health damage as a result of exposure to a hazardous substance.²³ A measure for this possibility is its likelihood (i.e. probability).

In accordance with this definition, risks can be distinguished by both their type and severity of the possible damage as well as by the likelihood of their occurrence. They can also be differentiated as to what extent it is proven that such a damaging effect even exists. Just to name two extremes: it can be truly proven or it can also be only suspected that a substance exerts a damaging effect.

For the best possible assessment of these conditions, four interrelated steps are necessary: (1) the hazard identification, (2) the assessment of the dose-response relationship, (3) the exposure assessment, and (4) the risk characterization.

Hazard identification: To be examined here is whether health damages even exist and if the agent²⁴ (i.e. the suspected hazardous substance) can cause these.

Therefore, a substantial task of the experts was to evaluate how well the existing studies can determine causal relationships. Thereby, the experts will enable a statement to be made whether the exposure to EMF of mobile phone communication will lead to specific effects, as well as how certain one can be of such causal relationships.

The second task of the experts involved the assessment of the effects: What significance to health do they have? Here, there is a whole set of possibilities: Effects can be obviously harmful to health, or they may only point to a possible detriment, or they

²³ E.g. the definition of the German Federal Institute for Risk Assessment [Bundesinstituts für Risikobewertung]: „The probability and severity of an adverse effect / event occurring to man or the environment following exposure, under defined conditions, to a risk source(s).” BfR, 2001, http://www.bfr.bund.de/cm/228/risiko_glossar.pdf

²⁴ The term „agent“ is used as a general term for a) substances (materials, chemicals), b) organisms, and c) physical impacts (e.g. sound waves, electromagnetic fields).

may represent a biological reaction, but which has no significance to health.

Therefore, for the *hazard identification* only those studies that involve an endpoint for which it is plausible that it is harmful to health can be drawn upon without restriction.

Dose-response relationship: the 15th century physician Paracelsus already knew that the dose makes the poison. In small quantities, a substance may be harmless. If it is administered in large quantities however, it may cause harm to health. The dose-response relationship is about the linkage between dose (amount, intake, exposure) on the one hand, and the magnitude and/or frequency of health disturbances on the other hand.

Frequently the dose-response relationship cannot be measured, but only estimated. Extrapolations, i.e. the transposition of estimations, are especially critical:

- from a short-term to chronic exposure duration;
- from the experimental animal to humans; and
- from population groups with average sensitivity to population groups with specific sensitivity.

For the conclusions of the expert opinion reports, all of these points are relevant. Thus, at present, there is no scientifically satisfactory basis to perform time extrapolations for EMF. This makes it more difficult to assess how a chronic, albeit low, exposure near base stations can be comparatively evaluated against short-term but much higher exposures from mobile RF telephones.

Furthermore, the findings from animal experiments cannot always be simply extrapolated to humans. Still, animal models are indispensable for the assessment of effects such as cancer.

Similar uncertainties exist regarding the transferability of the findings to different population groups, wherein the issue of a special sensitivity of certain subpopulations is the central question.

In general, the following limitation applies, which is decisive for the subsequent discussion: A dose-response relationship is only then applicable if an effect (response) is actually present. If, however, the very existence of an effect is uncertain, i.e. not proven, then a dose-response relationship can neither be determined not definitively rejected.

Exposure assessment: The exposure assessment is understood to be the qualitative and/or quantitative evaluation of the probable intake of biological, chemical, or physical agents (i.e. the hazardous substance).²⁵

Theoretically, it would be possible that no human being comes in contact with the hazardous substance. In this case, there would also be no risk. If, however, people will come in contact with the hazardous substance, then the magnitude of the risk depends upon who is exposed to what extent. Thereby the conditions of exposure must be considered, such as the level, the duration, the frequency, and the type of

²⁵ BfR (2001): http://www.bfr.bund.de/cm/228/risiko_glossar.pdf

exposure.

For the topic of EMF from mobile phone communication, such exposure assessments are only then necessary, if it is certain that a hazard is present. Is this not the case, an exposure assessment would not yield much insight. An illustrative example would be: the attempt to determine the sex of an unborn child, although one isn't even sure if a pregnancy has occurred.

Risk characterization is concerned about the summarizing, decision-making oriented presentation of the insights gained which form the basis of risk management²⁶ and that satisfy the needs and interests of the decision-makers and possible stakeholders. Such summarizing evaluations require special care since they are afforded particular significance in the public discussion.

5.2 State of the data

It is not surprising that – quantitatively seen – the state of the data for the risk evaluation of mobile phone communication has improved over the last years. Such a development was to be expected because of the numerous national and international research projects on mobile phone communication and health. This is especially true for the epidemiology of cancerous diseases where a series of studies on mobile phones and cancer have been published since the year 2000.

The quality of the studies differs, however, according to the endpoint topic area. Overall, the issue of quality can be shaped by a series of conditions, among others the dosimetry (How well was EMF measured as well as assessed?), the reliable measurement of endpoints, and the elimination of confounders. These issues of quality are extensively discussed in the expert opinion reports.

An improvement in quality was seen for the topic areas “genotoxic effects”, “laboratory animal experiments”, and “blood-brain-barrier”. In contrast, most of the available studies for the topic area “impairment of well-being” do not allow for reliable statements to be made on the basis of the quality of their research design as well their performance. This is of course also a reflection of the special complexity of this endpoint topic area.

Especially problematic is that impairment of well-being can only be measured by subjective input. Whether, for example, somebody suffers from headaches can hardly be measured objectively. It is also often difficult to avoid expectation and attitude effects of the examined subjects, which can influence the results of a study. Frick et al. (2002) showed how susceptible the determination of subjective symptoms is in particular to the survey techniques and conditions. Depending on how the question was posed, different symptoms are found. It is furthermore absolutely essential to control confounders that can falsify the results (such as e.g. consumption of coffee, cigarettes, stress, or the fluctuation of blood sugar levels after a meal).

²⁶“Risk characterization is the summarizing step of risk assessment. The risk characterization integrates information from the preceding components of the risk assessment and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers.” (EPA, Policy for Risk Characterization, 2000).

Other endpoint topic areas are by no means free of examination difficulties. In particular, they revolve around exposure assessments, error control and measurement problems.

5.3 Summary of the expert evaluations

The evaluations by the experts of the six endpoint topic areas are once again summarized in the following. As previously stated, the focus is on the health hazards of EMF from mobile phone communication. More detailed justifications for the evaluations are found in the expert opinion reports themselves, but also in our summary presentations for each individual endpoint.

Topic area genotoxic effects: The prevalent assessment up to now was that genotoxic effects are unlikely for radio-frequency electromagnetic fields (below the current limit values). This assessment is now put into question by the REFLEX study. In the opinion of the experts, it does not however follow from the REFLEX study that exposure-related health risks exist on the basis of genotoxic effects by RF-EMF, since no cell damage has been observed. Simply put: the effects observed in the REFLEX study obviously do not account for sufficient grounds for the formation of cancer.

Topic area laboratory animal cancer studies: In the evaluation of the experts, the available studies provide no indication that radio-frequency electromagnetic fields of mobile phone communication will initiate or promote cancer in animal experiments.

Topic area cancer epidemiology: The experts evaluate the state of the evidence in part differently. On the one hand, it is believed that a carcinogenic effect from exposure to EMF of mobile phone communication is rather not to be expected. On the other hand, a “vague initial suspicion” for a cancer risk is seen. The experts agree, however, that persons exposed to digital mobile telephones for short durations (i.e. a few years) do not have an elevated risk of brain tumors.

Topic area CNS / cognitive functions / sleep: On the basis of the considered studies, the experts come to the conclusion that radio-frequency electromagnetic fields of mobile phone communication do not influence the majority of the sleep variables. Effects are solely seen in the sleep-EEG. Still, they consider an influence on the waking-EEG as well as on the regional cerebral blood flow to be possible. Somewhat diverging conclusions are drawn by the experts for the endpoint “cognitive functions”.

While one expert, for this endpoint as well, evaluates the state of the evidence as showing that an influence on cognitive functions from exposure to RF-EMF is unlikely, the other two experts hold such an influence to be possible. The experts are, however, in agreement that the overall observed effects do not suggest an acute health endangerment.²⁷

Topic area impairment of well-being: The experts conclude in the evaluation of the endpoint “headache” that the scientific studies provide indications of a relationship

²⁷ It is, however, also conceded that “changes within the normal physiological range” do not necessarily lead to a conclusion of harmlessness of an effect. With certainty it can only be said that they are not acutely dangerous to health.

between mobile phone use and headache.

For the endpoint group fatigue / sleep disturbances, dizziness / nausea, pain (besides headaches), depressive state / low-spirited, skin problems, tinnitus / noise in ear, nervousness, as well as difficulties concentrating / memory impairment, and sensations of warmth is an evaluation on the basis of the weak state of the evidence hardly possible. However, from the experts' perspective the few available investigation results do not point to a relationship with RF-EMF exposure.²⁸

The endpoint "hypersensitivity" is evaluated by the two expert groups differently. While Seitz, Stinner & Eikmann believe on the basis of the state of the data, that an evaluation here is not possible, is the assessment of Rööfli that a relationship with RF EMF cannot be ruled out. This difference is, however, rather a reflection of different approaches of caution in the evaluation of scientific findings. On no account does it indicate serious differences.

Topic area blood-brain-barrier: The scientific investigations published since the year 2000 do not provide an indication for a health relevant disturbance of the blood-brain-barrier with exposure to electromagnetic fields in the frequency- and intensity-range of mobile phone communication.

5.4 Evaluation of the hazard by MUT

If viewed across all endpoint topic areas, the following picture emerges: The studies of the BBB and the experimental animal investigations on cancer are removed from further evaluation of the hazard of RF-EMF, since the available findings speak against exposure-related effects. Consequently, if there are no effects, then a hazard does not exist.

For the endpoints fatigue / sleep disturbances, dizziness / nausea, pain (besides headaches), depressive state / low-spirited, skin problems, tinnitus / noise in ear, nervousness, as well as difficulties concentrating / memory impairment, and sensations of warmth is an evaluation on the basis of the weak state of the evidence hardly possible, but the few available investigation results do not point to a relationship with RF-EMF exposure. Similarly, an influence by RF-EMF on sleep variables (except sleep-EEG) is held to be unlikely.

Therefore, the following endpoints remain for the evaluation of the hazard: (1) "cognitive functions", (2) "cancer epidemiology", (3) "headache", (4) "genotoxic effects". (5) "exposure-related changes in the waking- and sleep-EEG", as well as (6) "regional cerebral blood flow".

For the remaining endpoints of the evaluation, the following section will examine whether these effects can be drawn upon in the evaluation of the existence of a haz-

²⁸ The question of possible effects from UMTS exposure remains open. Here, the study of Zwamborn shows effects regarding impairment only for UMTS exposure, and not for GSM signals. How the positive findings for UMTS signals are to be classified is unclear (there are no hypotheses for a effect mechanism). Furthermore, there are effects seen in regards to animosity. How this is to be interpreted remains completely open.

ard. Because not every effect signifies a possible health detriment.

In particular, the SSK emphasized that not every effect automatically points to a “risk”. The SSK furthermore made it clear that one must distinguish between impact, effect, biological reaction and health impairment (SSK 2001). Only when it can be recognized that biological reactions will lead to health impairments – and this is not inevitable – will the biological reaction be relevant to risk. Only in this case will a hazard be present, i.e. “ein Faktor von biologischer, chemischer oder physikalischer Natur mit der Eigenschaft, eine Gesundheitsschädigung hervorrufen zu können” [*a factor of biological, chemical or physical nature with the characteristic to be able to elicit a health damage*][†] (BfR, 2001).

Of course, it is not always easy to clearly delimit when a damaging effect is present and when not. Herein, health- and disease-concepts, methods of detection, and societal conventions play a role (cf. Caplan et al. 2004, Englert 2004).

For a series of endpoints, the differentiation between effect and health impairment is trivial, because the endpoints are *per se* health-damages (e.g. cancer). For other endpoints, however, this does not apply, like for example for the blood-brain-barrier, EEG changes, changes in the cognitive functions and of the regional cerebral blood flow. Here effects do not automatically point to damage. Thereby it remains unanswered whether a hazard can even be assumed²⁹.

In the assessment of the experts, the observed effects for the endpoints “cognitive functions”, “EEG”, and “regional cerebral blood flow” are not to be evaluated as a hazard. Simply put, even though there are observed effects, they are not by themselves harmful. Therefore, since no unambiguous indications exist that the endpoints “changes in cognitive functions”, “EEG”, and “regional cerebral blood flow” can be evaluated as health disturbances, they will be dropped from further consideration

This assessment is also applicable to the observed genotoxic effects. In the opinion of the experts, the evaluation of the hazard must consider these effects in relationship to cell proliferation and programmed cell death (apoptosis).³⁰ This means that only when cell growth and cell division are affected does a hazard exist. Since such an influence was not seen in the REFLEX study, the observed genotoxic effects may represent a necessary but not yet sufficient evidence for the existence of a hazard.

For the evaluation of the hazard from EMF of mobile phone communication, only the endpoints “headache” and “cancer epidemiology” remain.

In regards to the epidemiological findings, two experts speak of a vague initial suspi-

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

²⁹ The inability to rule out the presence of damage is, by itself, not a sufficient argument for claiming a hazard. For it can never be definitively discounted, of course, that a biological effect could lead to damage. Without a scientifically plausible explanation why a biological effect can lead to damage, is such a claim at best speculation.

³⁰ Also see EPA (2003, p.2-25): “Both cell proliferation and programmed cell death are mandatory for the maintenance of homeostasis in normal tissues, and alterations in the level or rate of either are important elements of the carcinogenic process”.

cion. This assessment is not shared by the other expert, whose view it is that a cancer-promoting effect is rather not to be expected.

Indications of a relationship between “headaches” and usage of mobile phones are seen. Hereby it is uncertain whether the relationship between mobile phone use and headaches is caused by the exposure to EMF.³¹ The relationship could also reflect on the telephone usage itself, i.e. be related to telephone stress. In this case, however, the exposure to EMF would be completely irrelevant for the “headache” effect.

5.5 Comparison with the SSK evaluation of 2001

To help improve the classification of the state of the evidence, the suggestion of the SSK from 2001 on the evaluation of relationships is once again brought to mind here (see Textbox 1).

Wissenschaftlich nachgewiesen ist ein Zusammenhang zwischen einer Gesundheitsbeeinträchtigung und elektromagnetischen Feldern, wenn wissenschaftliche Studien voneinander unabhängiger Forschungsgruppen diesen Zusammenhang reproduzierbar zeigen und das wissenschaftliche Gesamtbild das Vorliegen eines kausalen Zusammenhangs stützt.

Ein **wissenschaftlich begründeter Verdacht** auf einen Zusammenhang zwischen einer Gesundheitsbeeinträchtigung und elektromagnetischen Feldern liegt vor, wenn die Ergebnisse bestätigter wissenschaftlicher Untersuchungen einen Zusammenhang zeigen, aber die Gesamtheit der wissenschaftlichen Untersuchungen das Vorliegen eines kausalen Zusammenhangs nicht ausreichend stützt. Das Ausmaß des wissenschaftlichen Verdachts richtet sich nach der Anzahl und der Konsistenz der vorliegenden wissenschaftlichen Arbeiten.

Wissenschaftliche Hinweise liegen vor, wenn einzelne Untersuchungen, die auf einen Zusammenhang zwischen einer Gesundheitsbeeinträchtigung und elektromagnetischen Feldern hinweisen, nicht durch voneinander unabhängige Untersuchungen bestätigt sind und durch das wissenschaftliche Gesamtbild nicht gestützt werden.

[Scientifically proven are relationships between health impairment and electromagnetic fields when scientific studies performed independently of each other by different research groups show reproducibly a relationship and the overall scientific picture supports the presence of a causal relationship.]

A scientifically founded suspicion of a relationship between health impairment and electromagnetic fields is present if the findings of confirmed scientific investigations show a relationship, but the totality of the scientific investigations does not sufficiently support a causal relationship. The extent of the scientific suspicion is dictated by the number and consistency of the available scientific studies.

Scientific indications are present if individual investigations point toward a relationship between a health impairment and electromagnetic fields, but are not confirmed by independent investigations and are not supported by the overall scientific picture.][†]

Textbox 1: Terminology of the German Radiation Protection Commission (SSK 2001, p. 7)

If the evaluation by our experts is compared to the summarizing evaluation of the scientific studies from 1998 to 2001 by the SSK, then it can be seen that individual findings for the exposure-related effects of mobile phone communication may have

³¹ Even the classification by the experts of „indications for a relationship“ was not without opposition in the workshop discussions in light of the fact that of the four reliable studies it was the two experimental studies (that allow for causal conclusions to be reached) that were negative. Only the cross-sectional surveys provided associations. That these are more heavily weighted than the experimental studies, is certainly not uncontroversial.

[†] Translated from German into English for the purposes of this report. This is not an official translation by the referenced authors and should not be cited or quoted as such.

changed, but the overall evaluation remains the same as in 2001.³²

The changes are:

- The indication seen by the SSK 2001 for cancer in experimental animal studies (on the basis of the study by Repacholi et al. 1997), is not confirmed by subsequent investigations (up to 2004).
- The indication for exposure-related changes in the blood-brain-barrier seen by the SSK in the expert opinion report of 2001, is not confirmed. This also applies to the study by Salford et al. (2003).
- The indications of changes in cognitive functions are weak and apparently hardly reliable. Compared to the evaluation of the exposure-related changes in cognitive functions from 2001 there is, therefore, no new basis for the evaluation. An influence on sleep variables (except sleep-EEG) is considered to be unlikely by our experts. Here, the SSK saw “at best unsubstantiated indications” [“allenfalls unbestätigte Hinweise”]. In regards to the EEG changes, the SSK still evaluated the available evidence in 2001 as an indication. Our experts hold an exposure-related change of the EEG and the regional cerebral blood flow for possible, but see therein no sign for an impairment of health.
- With reference to genotoxic effects, the SSK in the year 2001 speaks of individual, unreproduced indications. For the evaluation of the weight-of-evidence for 2004, the REFLEX study is above all essential, and for which genotoxic effects appear but no cell damage is observed. Therefore, it follows that no modified evaluation is offered based on the available findings up to 2004.
- In 2001, the SSK determined in regards to cancer epidemiological studies that there is no indication for a relationship between the use of mobile phones and the incidence of brain tumors. In our risk dialogue, two of the three experts see a “vague initial suspicion” – which in the meaning by the SSK is an indication. From the perspective of the third expert, cancer-promoting effects are rather not to be expected. Our experts are in agreement that elevated tumor risks are not to be expected from short-term exposures to digital mobile RF phones over a few years.
- Electromagnetic hypersensitivity was not evaluated by the SSK in 2001. In the discussion of electromagnetic hypersensitivity in regards to low-frequency fields, the SSK however determined that the available findings were not sufficient to represent a scientifically founded suspicion. They, however, also not allow for the electromagnetic hypersensitivity hypothesis to be rejected. Our experts reach a similar conclusion: They see no findings that confirm the electromagnetic hypersensitivity hypothesis. They, however, also point to the fact that the hypothesis cannot be rejected.
- The SSK did not evaluate impairment of well-being in 2001. Even today, the weight-of-evidence for many endpoints is insufficient. In the assessment of our experts, the available investigation findings let a relationship to RF-EMF exposure appear unlikely for the endpoints “fatigue / sleep disturbances”, “dizziness, nausea”, “pain (besides headaches)”, “depressive state”, “low-spirited”, “skin problems”, “tinnitus”, “noise in ear”, “nervousness and impairments of

³² However, for the next few years a whole series of new evaluations of health effects from RF-EMF are lined up. For one, already in 2005 the EU will reevaluate and perhaps modify its recommendations from 1999. In addition, the International Agency for Research on Cancer (IARC) of the WHO, the International Commission on Non-Ionizing Radiation Protection (ICNIRP), and the WHO will evaluate the EMF of mobile phone communication.

concentration". However, in the opinion of the experts, indications for exposure-related headaches can be determined.

Overall, the hypothesis that EMF from mobile phone communication has a harmful effect is not substantiated.

It should be noted that these statements refer to healthy persons. If and what effects are manifested in sick people can not be evaluated. The question of a special sensitivity (electromagnetic hypersensitivity) of certain persons to the EMF of mobile phone communication could not be completely answered. While the investigations do not provide evidence that speaks in favor of such a special sensitivity, it can also not be excluded with any certainty.

Finally, of course no statements can be made for endpoints that were not examined in the expert opinion reports.

5.6 Conclusions for future risk dialogues

At this point, a research program for the topic area "mobile phone communication and health" is not to be developed; a row of experts has anyway already been heard (see e.g. the German Mobile Telecommunication Research Programme)³³. Instead, we would like to restrict ourselves to the area of risk communication, which is the focus of our own research, and summarize our experiences with the risk dialogue and discuss its improvements.

For the present dialogue, we could already draw upon insights from a previous risk dialogue (Wiedemann, Schütz & Thalmann 2003). The crucial insights, which we also used in our planning, were:

- For the risk evaluation, research results from numerous, very specific thematic fields must be evaluated. This requires knowledge and abilities, that are best acquired through own research.
- Care must be given that for a risk assessment the spectrum of different scientific positions is represented.
- Similarly, it is essential that independent observers participate, which themselves are not part of the scientific dispute over the health effects of mobile phone communication, but that have received recognition as experts for each of the applied examination procedures. The inclusion of such consulting specialists is an important prerequisite for a competent risk evaluation free of prejudice.
- To simplify the comparison of risk evaluations within as well as across topic areas, the expert opinion reports should have a structure that is as uniform as possible. Thus, it was important to us to already determine the goals and boundaries of the examination in advance.

³³ See <http://www.emf-forschungsprogramm.de/forschung/?setlang=en>

- Only a careful and plausible selection of the scientific literature will ensure that the experts will draw upon the same database. Hereby, the standards established for the inclusion or rejection of scientific findings must be made clear in the expert opinion report.
- It is essential for the preparation of the risk evaluation that the assessments are plausibly justified. Therefore, it depends on the presentation of the measurement standards, with which contradictory findings are summarized into an overall picture, as well as to weigh fairly the Pro- and Con-arguments for the assessment.

While the first five points could be implemented in our risk dialogue without large difficulties, the last point remained critical.

Based on the positive experiences from the first risk dialogue, we again present – in agreement with the experts – the structure of the expert arguments in the form of Pro- and Con-arguments. Herein, however, in a more refined presentation where the essential Pro- and Con-arguments were supplemented by each of the supporting or attenuating qualifying arguments.

As a new element, the presentation of the conclusions together with the remaining uncertainties was added. Here, the possible existing evaluation differences between the experts was also pointed out.

To enable accessibility "in one glance" of the three core elements of the risk evaluation – the evidence basis, the Pro- and Con-arguments, as well as the conclusions with the remaining uncertainties – did we, for the first time, employ in our risk dialogue an evidence framework. This evidence framework can present the elements of the risk evaluation for a specific endpoint in a graphical manner. In the different workshop discussions, these evidence frameworks were considered useful instruments by our experts.

One problem, however, could not yet be solved satisfactorily. It is the characterization of the uncertainties, which makes the evaluation of the individual studies and particularly the summarizing overall evaluation (conclusions) more difficult.

If one looks at the expert opinion reports, it can be noticed that they contain a series of different idioms in order to describe uncertain and contradictory evidence. Among them are phrases such as "on the basis of this evidence an evaluation is not possible", "probably no relationship", "rather unlikely", "a relationship cannot be excluded", "not likely, but possible", or "vague initial suspicion". Evaluative phrases are also found such as "probability is judged to be between not likely and mid-level probable" and "...so that for a differentiation ... a somewhat higher, but still low probability ... can be concluded".

Such labeling – termed *hedging* phrases – may be indispensable if the hazard has neither been unequivocally proven nor can be unequivocally rejected (Hyland 1998)³⁴. They refer to the difficulties of the experts to take a stance in light of vague

³⁴ Such linguistic measures are used when a speaker interested in a communication free of conflict wishes to avoid making himself/herself vulnerable to attack. They are verbal protective shields.

and contradictory results. Since there are, however, practically no rules as to how such idioms are to be implemented, does it remain in the subjective judgment of every individual. Furthermore, vast room for interpretation exists in the meaning of these phrases. What e.g. "rather unlikely" means in contrast to "relationship can not be excluded" can be very differently interpreted. These circumstances will almost necessarily lead to different evaluations and conclusions for the recipients – politicians, journalists, and the public. Therefore, a scale would be useful that could show the strength of the evidence for or against a relationship between exposure and effect. There are already examples for such an evidence scaling, e.g. the evidence classification of the IARC³⁵ or the SSK (2001).

However, here too, there are at least two problems. On the one hand, the question is posed how a single (preferably across the different endpoints) consistent assignment of the evidence assessment can be accomplished by the experts. IARC, for example, uses a list of criteria that refers to the extent and the quality of the evidence for carcinogenicity from *in vitro* experiments, animal studies and epidemiological studies. Despite the at first glance transparent criteria for this already limited area is a uniform assignment apparently not easy (cf. Baines 2003). Within the framework of this risk dialogue, we actually tried different forms of evidence scaling together with the experts. Hereby, exactly this problem of a consistent assignment was seen. Apparently, another problem is that the evidence scaling must not only address the evidence area that speaks for the presence of a causal relationship between exposure and effect, but also covers the area that speaks against it. Thus, the IARC classification only offers a single, undifferentiated "Contra-category" while the SSK classification does not even address this area at all. If and how criteria for a consistent evidence scaling for such diverse topic areas such as genotoxic effects and impairment of well-being can be developed, is surely a worthwhile focus for future research.

On the other hand, it is doubtful, whether an evidence scaling will be understood as intended by the recipients of the risk evaluation – especially when they are not experts, but rather, for example, regulatory agencies, political decisionmakers, or the public. Results from risk communication research indicate that this, at the very least, cannot be simply assumed (Thalmann 2005).

Finally, a question is to be pointed out that addresses the communication of risk evaluations in general: How should indications for possible health effects – if they exist – be communicated so that on the one hand they do not scare the recipients excessively, but on the other hand also not suggest a false sense of security? Whether our evidence frameworks will also be suitable for the risk communication with laypeople remains to be evaluated in an appropriate manner.

Here, too, findings from risk communication research suggest that particular forms of result presentations can be more frightening than others (Purchase & Slovic 1999). Which (personality-specific, situative, contextual) factors are significant here, must also be addressed in future research.

³⁵ <http://www-cie.iarc.fr/monoeval/eval.html>

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