European Commission

Scientific Committee on Health, Environmental and Emerging Risks

SCHEER

Opinion on the need of a revision of the annexes in the Council Recommendation 1999/519/EC and Directive 2013/35/EU, in view of the latest scientific evidence available with regard to radiofrequency (100kHz - 300GHz)

Scientific Committees
on Consumer Safety
on Health, Environmental and Emerging Risks

The SCHEER adopted this document by written procedure on 16 August 2022

ABSTRACT

The SCHEER has considered meta-analyses, systematic reviews, and, when necessary, narrative or scope reviews and single research papers published after and including 2015 on radiofrequency electromagnetic fields (100 kHz to 300 GHz).

The SCHEER could not identify moderate or strong level of evidence for adverse health effects resulting from chronic or acute RF EMF exposure at levels below the limits set in the annexes of Council Recommendation 1999/519/EC and Directive 2013/35/EU.

The SCHEER advises positively on the need of a technical revision of the annexes in Council Recommendation 1999/519/EC and Directive 2013/35/EU with regard to radiofrequency electromagnetic fields (100 kHz to 300 GHz), because there is a need to recognize the recently introduced dosimetric quantities and establish limits for them.

Keywords: Radiofrequency, Electromagnetic Fields, Health effects, Biological effects, Interaction mechanisms

Opinion to be cited as:

SCHEER (Scientific Committee on Health, Environmental and Emerging Risks), Preliminary Opinion on the need of a revision of the annexes in Council Recommendation 1999/519/EC and Directive 2013/35/EU, in view of the latest scientific evidence available with regard to radiofrequency (100kHz - 300GHz), adopted by written procedure on 16 August 2022

ACKNOWLEDGMENTS

Members of the Working Group are acknowledged for their valuable contribution to this opinion. The members of the Working Group are:

The SCHEER members:
Teresa Borges
Demosthenes Panagiotakos
Ana Proykova
Theodoros Samaras
Marian Scott

External experts:
Clemens Dasenbrock
Heidi Danker-Hopfe
Olga Zeni

The additional contribution of the following experts is gratefully acknowledged:
Fiorella Belpoggi
Alexander Lerchl

All Declarations of Working Group members are available at the following webpage:
Register of Commission expert groups and other similar entities (europa.eu)

About the Scientific Committees (2022-2026)

Two independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Safety (SCCS) and the Scientific Committee on Health, Environmental and Emerging Risks (SCHEER). The Scientific Committees review and evaluate relevant scientific data and assess potential risks. Each Committee has top independent scientists from all over the world who are committed to work in the public interest.

In addition, the Commission relies upon the work of other Union bodies, such as the European Food Safety Authority (EFSA), the European Medicines Agency (EMA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCHEER

This Committee, on request of Commission services, provides Opinions on questions concerning health, environmental and emerging risks. The Committees addresses questions on:

- health and environmental risks related to pollutants in the environmental media and other biological and physical factors in relation to air quality, water, waste and soils.

- complex or multidisciplinary issues requiring a comprehensive assessment of risks to consumer safety or public health, for example antimicrobial resistance, nanotechnologies, medical devices and physical hazards such as noise and electromagnetic fields.

SCHEER members

Thomas Backhaus, Roberto Bertollini, Teresa Borges, Wim de Jong, Pim de Voogt, Raquel Duarte-Davidson, Peter Hoet, Rodica Mariana Ion, Renate Kraetke, Demosthenes Panagiotakos, Ana Proykova, Theodoros Samaras, Marian Scott, Emanuela Testai, Marco Vighi, Sergey Zacharov

Contact
European Commission
DG Health and Food Safety
Directorate C: Public Health
Unit C2: Health information and integration in all policies
Office: HTC 03/073, L-2920 Luxembourg
SANTE-C2-SCHEER@ec.europa.eu

© European Union, 2022

The Opinions of the Scientific Committees present the views of the independent scientists who are members of the committees. They do not necessarily reflect the views of the European Commission. The Opinions are published by the European Commission in their original language only.

http://ec.europa.eu/health/scientific_committees/policy/index_en.htm

TABLE OF CONTENTS

1 MANDATE FROM THE EU COMMISSION SERVICES

The following part is provided by the requesting Commission service.

1.1 Background

Council Recommendation of 12 July 1999[1] (hereafter Recommendation) on the limitation of exposure of the general public to electromagnetic fields (0 Hz to 300 GHz) sets out basic restrictions and reference levels for the exposure of the general public to electromagnetic fields (EMFs). These restrictions and reference levels are based on the guidelines published by the International Commission on Non Ionizing Radiation Protection in 1998 (ICNIRP)[2]. In response to the Recommendation, all Member States have implemented measures to limit the exposure of the public to EMF, either by implementing the provisions and reference levels and limits proposed by the Recommendation, or by implementing more stringent provisions[3]. In particular, twenty (20) Member States follow the Recommendation/ICNIRP Guidelines, while seven (7) impose stricter limits than those of the Recommendation.

In relation to the protection of workers' health and safety, Article 153 of the Treaty on the Functioning of the European Union foresees that the European Parliament and the Council can adopt by means of directives minimum requirements for the improvement, in particular, of the working environment to protect workers' health and safety, in order to support and complement the activities of Member States. In this context, the Council and the Parliament adopted Directive 2004/40/EC of 29 April 2004[4] on the minimum health and safety requirements regarding their exposure to the risks arising from physical agents such as electromagnetic fields which was repealed by Directive 2013/35/EU[5]. Member States had to transpose Directive 2013/35/EU by 1st July 2016. It lays down minimum requirements including action levels and exposure limit values for electromagnetic fields. In accordance with Article 153 of the TFEU, Member States are allowed to maintain or adopt more stringent protective measures for the protection of workers.

The Recommendation also invites the Commission to "*keep the matters covered by this recommendation under review, with a view to its revision and updating, taking into account possible effects, which are currently the object of research, including relevant aspects of precaution (paragraph 4)".* The ICNIRP guidelines were endorsed by the Scientific Steering Committee (SSC)[6] in its Opinion on health effects of EMFs of 25-26 June 1998. The Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) prepared an update of the Scientific Steering Committee's Opinion and concluded in its Opinion on "*Possible effects of Electromagnetic Fields (EMF), Radio Frequency Fields (RF) and Microwave Radiation on human health", of 30 October 2001, that the information that had become available since the SSC Opinion of June 1999 did not justify revision of the exposure limits recommended by the Council*[7]*.* The Opinions delivered by the SCENIHR in March 2007[8], January 2009[9], July 2009[10] and January 2015[11] confirmed the earlier

1 (OJ. L 199/59, 30.7.1999)
2 http://www.icnirp.de/
3 http://ec.europa.eu/health/electromagnetic_fields/role_eu_ms/index_en.htm
4 https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32004L0040&from=en
5 https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:179:0001:0021:EN:PDF
6 http://europa.eu.int/comm/food/fs/sc/ssc/index_en.html
7 The main frequencies in the ELF frequency range are 50 Hz in Europe and 60 Hz in North America. The RF and lower microwave frequencies are of particular interest for broadcasting, mobile telephony. The 2.45 GHz frequency is mainly used in domestic and industrial microwave ovens
8 http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_007.pdf
9 http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_022.pdf
10 http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_024.pdf
11 https://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_041.pdf

conclusion of the CSTEE and again highlighted the need for additional data and research on this issue and recommended that specific research areas should be addressed.

The Commission relies on the SCHEER to periodically review new information that may influence the assessment of risks to human health in this area and to provide regular updates on the scientific evidence base to the Commission.

Since June 2014, the cut-off date for the previous review by the SCENIHR, a sufficient number of new scientific publications have appeared to warrant a new analysis of the scientific evidence on possible effects on human health of exposure to EMF.

In addition, ICNIRP has released new guidelines for the protection of humans exposed to radiofrequency electromagnetic fields in March 2020. While the 1998 guidelines already provide protection regarding EMF exposure in all frequency bands for existing technologies, and all bands currently envisaged for 5G, the new guidelines provide additional guidance on a set of issues relevant to the latest developments in 5G technology and cover the range 100 kHz to 300 GHz[12].

The full guidelines are published in the scientific journal Health Physics and are accessible at the website of ICNIRP[13].

Consequently, the SCHEER is being asked to examine this new scientific evidence and to address in particular the questions listed in the Terms of Reference.

1.2 Terms of reference

The scientific committee SCHEER is consulted on the need of a (technical) revision of the Council Recommendation 1999/519/EC annexes and of the annexes of Directive 2013/35/EU in view of the latest scientific evidence available, in particular the ICNIRP guidelines updated in 2020[14] with regard to radio frequency (100 kHz to 300 GHz).

Opinion I

To advise on the need of a (technical) revision of the Council Recommendation 1999/519/EC annexes and of the annexes of Directive 2013/35/EU in view of the latest scientific evidence available, in particular that of the ICNIRP-guidelines updated in 2020, with regard to radio frequency 100 kHz to 300 GHz.

Opinion II

To update the SCENIHR Opinion of 2015 in the light of the latest scientific evidence with regard to frequencies between 1Hz and 100 kHz.

1.3 Deadline

Preliminary Opinion I: July 2022

Preliminary Opinion II: July 2023

[12] https://www.icnirp.org/en/publications/article/rf-guidelines-2020.html;https://www.icnirp.org/en/rf-faq/index.html

[13] https://www.icnirp.org/en/publications /index.html

[14] https://www.icnirp.org/cms/upload/publications/ICNIRPrfgdl2020.pdf

2 OPINION

- The SCHEER has considered meta-analyses, systematic reviews, and, when necessary, narrative or scope reviews and single research papers published after the (2015) SCENIHR Opinion on potential health effects of exposure to radiofrequency (RF) electromagnetic fields (EMF).
- The SCHEER notes that there is uncertain weight of evidence for interaction mechanisms in *in vitro* studies, involving oxidative balance, genetic and epigenetic effects, and calcium signalling, that can result in biological effects.
- The SCHEER could not identify moderate or strong level of evidence for adverse health effects resulting from chronic or acute RF EMF exposure at levels below the limits set in the annexes of Council Recommendation 1999/519/EC and Directive 2013/35/EU.
- The SCHEER has noted the technical progress achieved since the ICNIRP (1998) exposure guidelines in the areas of computational and experimental exposure assessment and dosimetry, allowing for an increased accuracy of human exposure evaluation.
- The SCHEER has alsonoted that new and emerging wireless applications using RF EMF tend to use higher frequencies and lower emitted power in closer vicinity to the human body. However, there are situations where beam focusing or intense pulsed radiation can increase exposure for short times.
- The SCHEER acknowledges that the latest (2020) ICNIRP exposure guidelines introduce new dosimetric quantities and limits to them, that can protect humans more effectively from emerging technological applications of RF EMF, and, therefore, advises positively on the need of a technical revision of the annexes in Council Recommendation 1999/519/EC and Directive 2013/35/EU with regard to radiofrequency electromagnetic fields (100 kHz to 300 GHz).

3 MINORITY OPINIONS

None

4 METHODOLOGY

4.1 Data/Evidence

The SCHEER, on request of Commission services, provides scientific opinions on questions concerning health, environmental and emerging risks. The scientific assessments carried out should always be based on scientifically accepted approaches, and be transparent with regard to the data, methods and assumptions that are used in the risk assessment process. They should identify uncertainties and use harmonised terminology, where possible, based on internationally accepted terms. In its scientific work, the SCHEER relies on the Memorandum on Weight of Evidence (WoE) and uncertainties (SCHEER, 2018), *i.e.*, the search for relevant information and data for the SCHEER comprises of identifying, collecting and selecting possible sources of evidence in order to perform a risk assessment and/or to answer the specific questions being asked. For each line of evidence, the criteria of validity, reliability and relevance need to be applied and the overall quality must be assessed.

4.2 Background

4.2.1 SCENIHR (2015) Opinion – Summary on biological and health effects

4.2.1.1 Introduction

The SCENIHR Opinion of 2015 on "Potential health effects of exposure to electromagnetic fields (EMF)" investigated the whole frequency spectrum from static fields to 300 GHz. Here we repeat only the main findings that pertain to the frequency range of 100 kHz to several GHz. In 2015, when that Opinion was published, there were very few studies investigating potential biological, non-thermal effects of sub-THz fields. *In vivo* studies in these frequencies indicated mainly beneficial effects but did not address acute and chronic toxicity or carcinogenesis. *In vitro* studies on mammalian cells differed greatly with respect to irradiation conditions and endpoints under investigation. There were studies suggesting health effects of exposure, but these had not been replicated. Some theoretical mechanisms had also been proposed, but there was no experimental evidence for them.

4.2.1.2 Cancer

The SCENIHR concluded that, overall, the epidemiological studies on mobile phone RF EMF exposure showed neither an increased risk of brain tumours, nor an increased risk for other cancers of the head and neck region. Some studies, however, had raised questions regarding an increased risk of glioma and acoustic neuroma in heavy users of mobile phones. The results of cohort and incidence time trend studies did not support an increased risk for glioma at that time (2015), while the possibility of an association with acoustic neuroma remained open. Epidemiological studies did not indicate increased risk for other malignant diseases, either, including childhood cancer.

4.2.1.3 Brain physiology and function

The SCENIHR found good evidence that mobile phone RF EMF exposure might affect brain activities as reflected by EEG studies during wake and sleep. However, given the variety of applied fields, duration of exposure, number of considered leads, and statistical methods, it was not possible at that time to derive firm conclusions. For event-related potentials and slow brain oscillations, results were inconsistent, as well. The relevance of the small physiological changes reflected on the EEG remains unclear and mechanistic explanation is still lacking. Moreover, at that time (2015), there was a lack of evidence that mobile phone RF EMF affected cognitive functions in humans, because effects had been found in individual studies (typically observed only in a small number of endpoints) but with little consistency between studies.

According to the SCENIHR, symptoms attributed to RF EMF exposure could sometimes cause serious impairments to a person's quality of life. However, the SCENIHR concluded that RF EMF exposure was not causally linked to these symptoms, and this applied to the general public, to children and adolescents, as well as to people with idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF).

Human studies on neurological diseases and symptoms showed no clear effect, but the evidence was limited.

4.2.1.4 Fertility, Reproduction, and Childhood Development

The SCENIHR Opinion concluded that there were no adverse effects on reproduction and development from RF fields at non-thermal exposure levels. Human studies on child development and behavioural problems presented conflicting results and methodological limitations. Therefore, the evidence of an effect is weak. Effects of exposure on foetuses from mother's mobile phone use during pregnancy were not plausible owing to extremely low foetal exposure. Studies on male fertility were of poor quality and provided little evidence.

4.2.2 ICNIRP (2020) Guidelines - Summary on biological and health effects

4.2.2.1 Introduction

The ICNIRP bases its guidelines on substantiated adverse health effects, which are different from biological effects. The ICNIRP considers that reported adverse effects of RF EMF health need to be independently verified, be of sufficient scientific quality and be consistent with current scientific understanding in order to be used for setting exposure restrictions. However, these requirements may be relaxed if there is sufficient additional knowledge (such as understanding of the relevant biological interaction mechanism) to confirm that adverse health effects are reasonably expected to occur. The ICNIRP considers the potential for different types of RF EMF exposure to adversely affect health, including sinusoidal (e.g., continuous wave) and non-sinusoidal (e.g., pulsed) signals, and both acute and chronic exposures.

4.2.2.2 Brain physiology and function

Most double-blind human experimental studies on cognitive performance, cerebral blood flow or event-related potential measures of cognitive function did not report an association with RF EMF exposure. A number of sporadic findings have been reported, which may be a result of the large number of statistical comparisons and occasional chance findings. However, studies analysing frequency components of the EEG have reliably shown that the 8–13 Hz alpha band in waking EEG and the 10–14 Hz "sleep spindle" frequency range in sleep EEG are affected by RF EMF exposure with specific energy absorption rates (SAR) <2 W/kg, but there is no evidence that these relate to adverse health effects. There is limited epidemiological research on higher cognitive function. There have been reports of subtle changes to performance measures with RF EMF, but findings have been contradictory and alternative explanations for observed effects are plausible.

A small portion of the population attributes non-specific symptoms to RF EMF exposure (IEI-EMF). Double-blind experimental studies have provided evidence that "belief about exposure" (e.g., the so-called "nocebo" effect), and not exposure itself, is the relevant symptom determinant. Epidemiological research has addressed potential long-term effects of radiofrequency EMF exposure from fixed site transmitters and devices used close to the body on both symptoms and well-being. Methodological concerns for such studies include selection bias, reporting bias, poor exposure assessment, and nocebo effects. In studies on mobile phone use, for example, it is difficult to differentiate between potential effects from RF EMF exposure and other consequences of mobile phone use, such as sleep deprivation when using the mobile phone at night. In summary, no reports of adverse effects of RF EMF exposures on symptoms and wellbeing have been substantiated, except for pain, which is related to elevated temperature at high exposure levels (from both direct and indirect exposure).

Several studies have included multiple cell lines and assessed functions such as intra- and intercellular signalling, membrane ion channel currents and input resistance, Ca^{2+} dynamics, signal transduction pathways, cytokine expression, biomarkers of neurodegeneration, heat shock proteins, and oxidative stress-related processes. However, most of these studies have focused on *in vitro* experiments. There is no evidence of effects of RF EMF on physiological processes that impair human health.

4.2.2.3 Auditory, Vestibular, and Ocular function

A change in the ICNIRP (2020) Guidelines compared to the ICNIRP (1998) Guidelines is that the latest Guidelines do not provide a restriction to specifically account for "microwave hearing", a biological phenomenon, which can result from brief (35 - 100 µs) RF pulses exposing the head and causing thermoelastic expansion that is detected by sensory cells in the cochlea via the same processes involved in normal hearing. The decision of the ICNIRP not to provide an exposure restriction is based on the lack of evidence that microwave hearing in any realistic exposure scenarios can affect health.

Epidemiological research addressing sensory effects has concentrated on mobile phones. The research does not provide evidence that this exposure is associated with increased risk of tinnitus, hearing impairment, or other adverse effects on vestibular or ocular function of humans. Some evidence of superficial eye damage has been shown in rabbits at exposures of at least 1.4 kW/m^2.

4.2.2.4 Neuroendocrine System

The effect of RF EMF exposure on several hormones (including melatonin, growth hormone, luteinizing hormone, cortisol, epinephrine, and norepinephrine) has been assessed in a small number of studies, and no consistent evidence of effects has been observed. The lowest exposure level at which an effect of RF EMF on the neuroendocrine system has been observed is 4 W/kg (in rodents and primates), accompanied by a core temperature increase of 1°C or more. There is no evidence that this experimental finding translates to humans or that it is relevant to human health.

4.2.2.5 Neurodegenerative diseases

Due to ethical considerations, no human experimental studies exist for adverse effects on neurodegenerative diseases. It has been reported that exposure to pulsed RF EMF increased neuronal death in rats, which could potentially contribute to an increased risk of neurodegenerative disease. However, other studies have failed to confirm these results.

A cohort study has investigated potential effects of mobile phone use on neurodegenerative disorders. It reported reduced risk estimates for Alzheimer disease, vascular and other dementia, and Parkinson disease, which could be the result of reverse causation: Prodromal symptoms of the disease may prevent persons with early symptoms to start using a mobile phone. Results from studies on multiple sclerosis are inconsistent, with no effect observed among men, and a borderline increased risk in women, but with no consistent exposure-response pattern.

4.2.2.6 Cardiovascular system, Autonomic Nervous System, and Thermoregulation

Body heating from the absorption of RF energy can put the cardiovascular system under stress and may lead to adverse health effects. Numerous human studies have investigated indices of cardiovascular, autonomic nervous system, and thermoregulatory function, including measures of heart rate and heart rate variability, blood pressure, body, skin and finger temperatures, and skin conductance. Most studies indicate that there are no effects on endpoints regulated by the autonomic nervous system. Few epidemiological studies on cardiovascular, autonomic nervous system, or thermoregulation outcomes are available, and they have not demonstrated a link between RF EMF exposure and measures of cardiovascular health. Human health and the cardiovascular system are not compromised when the whole-body average SAR is below approximately 4 W/kg, with harm only found in animals exposed to whole-body average SAR substantially higher than 4 W/kg.

4.2.2.7 Immune System and Haematology

According to the ICNIRP, the few human studies that have been conducted have not provided any evidence that RF EMF affect health in humans via the immune system or haematology.

4.2.2.8 Fertility, Reproduction, and Childhood Development

Several animal studies have shown that exposure to RF EMF leading to a significant temperature increase can cause effects on reproduction and development, which include increased embryo and foetal losses, increased foetal malformations and anomalies, and reduced foetal weight at term. Such exposures can also cause a reduction in male fertility. Some studies have reported effects on male fertility at exposure levels below a whole-body average SAR of 4 W/kg, but these studies have had methodological limitations.

The ICNIRP mentions that some epidemiological studies have reported associations between RF EMF and sperm quality or male infertility, but these studies suffer from limitations in study design or exposure assessment. The few epidemiological studies performed about maternal mobile phone use during pregnancy have not shown any substantiated evidence that RF EMF exposure from maternal mobile phone use affects child cognitive or psychomotor development or causes developmental milestone delays.

4.2.2.9 Cancer

ICNIRP concludes that, despite the reports of effects of RF EMF exposure on several cellular and molecular processes (including cell proliferation, differentiation and apoptosis-related processes, proto-oncogene expression, genotoxicity, increased oxidative stress, and DNA strand breaks), there is no substantiated evidence of health-relevant effects.

Concerning animal studies on the effect of RF EMF exposure on carcinogenesis there have been reports of positive effects, but, in general, these studies either have shortcomings in methodology (e.g., untested animal models) or dosimetry, or the results have not been verified in independent studies.

The ICNIRP makes special note of the two recent animal studies investigating the carcinogenic potential of long-term exposure to RF EMF associated with mobile phones and mobile phone base stations: four by the U.S. National Toxicology Program and the other from the Ramazzini Institute in Italy. According to ICNIRP, although both studies used large numbers of animals, best laboratory practice, and exposed animals for the whole of their lives, they also have inconsistencies and important limitations that affect the usefulness of their results for setting exposure guidelines. Of particular importance is that the statistical methods employed were not sufficient to differentiate between radiofrequency-related and chance differences between treatment conditions; interpretation of the data is difficult due to the high body core temperature changes that resulted from the very high exposure levels used; and no consistency was seen across these two studies.

A large number of epidemiological studies of mobile phone use and cancer risk have been performed. Most have focused on brain tumours, acoustic neuroma and parotid gland tumours, although some studies have also been conducted on other types of tumours (leukaemia, lymphoma, uveal melanoma, pituitary gland tumours, testicular cancer, and malignant melanoma). With a few exceptions, the studies have used a case-control design and have relied on retrospectively collected self-reported information about mobile phone use history. Only two cohort studies with prospective exposure information are available. No cohort studies (which unlike case control studies are not affected by recall or selection bias) report a higher risk of glioma, meningioma, or acoustic neuroma among mobile phone subscribers or when estimating mobile phone use through prospectively collected questionnaires. The only study available on mobile phone use in children and brain tumour risk showed no increased risk of brain tumours.

Studies of exposure to environmental RF EMF, for example from radio and television transmitters, have not provided evidence of an increased cancer risk either in children or in adults. The ICNIRP concludes that no effects of RF EMF on the induction or development of cancer have been substantiated.

4.2.3 WHO Survey on Priority Outcomes

Given the large number of health endpoints that have been studied, WHO wanted to prioritise those that would merit systematic reviews (Verbeek *et al.*, 2021). They developed a survey listing of 34 health endpoints reported in the literature organised in eight broad categories:

- Health effects due to temperature increase
- Cancer
- Fertility and birth outcomes

- Symptoms affecting health
- Neurological impairments and disorders
- Neuroendocrine effects
- Immunological effects
- Haematological effects

They asked 300 RF EMF experts and researchers to prioritise these health effects for systematic review following the GRADE approach. They asked the respondents to use a scale from 1 to 9, where 1–3 meant unimportant, 4–6 meant important but not critical for decision-making and 7–9 meant critical for decision-making. For ratings above 3, the respondents were asked to provide a rationale for their rating based on one or more of the following five categories: (1) evidence from human studies, (2) evidence from animal studies, (3) evidence from *in vitro* studies, (4) possible public health impact, (5) public concern. An open-ended answer was also provided, where the respondent could list other outcomes not included the list. To include an outcome in a systematic review, the WHO team used a cut-off at around 30% of the participants answering that this outcome was critical for decision making.

Of the 300 RF EMF experts queried, 164 (54%) responded to the online questionnaire in the period between 29 May 2018 and 24 June 2018. They rated cancer, heat-related effects, adverse birth outcomes, electromagnetic hypersensitivity, cognitive impairment, adverse pregnancy outcomes and oxidative stress as the most critical outcomes regarding RF EMF exposure. WHO has recently commissioned systematic reviews on ten of these outcomes through an open call for expression of interest. A selection committee convened by WHO ranked the teams based on the criteria related to qualifications and skills mentioned in the calls, including expertise in systematic review methodology, RF EMF expertise and expertise in the outcome of interest. All team members were assessed for conflicts of interest, as per WHO's requirements. Some protocols for the systematic reviews have already been published in Elsevier's *Environment International*, and more are expected to follow:

- The protocol to conduct the systematic review of *in vivo* and *in vitro* experimental studies to analyse and synthesize the available evidence on oxidative stress induced by RF exposure has been already published (Henschenmacher *et al.*, 2021), while the systematic review is in progress.
- A protocol for a systematic review on the effects of exposure to radiofrequency electromagnetic fields on cognitive performance in human experimental studies was published (Pophof *et al.*, 2021). If the data basis permits, evidence will be reviewed separately for seven domains of cognitive performance: (1) Orientation and attention, (2) Perception, (3) Memory, (4) Verbal functions and language skills, (5) Construction and motor performance, (6) Concept formation and reasoning, and (7) Executive functions.
- The protocol for the systematic review of human observational studies on the effects of RF EMF exposure on tinnitus, migraine, and non-specific symptoms in the general and working population has been published by Röösli *et al.* (2021).
- The effects of RF EMF exposure on human self-reported symptoms studied in human experimental studies will be systematically reviewed with a protocol published by Bosch-Capblanch *et al.* (2022).
- The protocol for the systematic review of effects on male fertility and pregnancy and birth outcomes has been published by Pacchierotti *et al.* (2021).

4.2.4 Differences in methodology from SCENIHR (2015)

In the six-year period between the 2009 and 2015 SCENIHR Opinions, about 2700 articles on RF and health effects were published, according to a search in the EMF-PORTAL (https://www.emf-portal.org/en), which is the internet information platform of the RWTH Aachen University summarising systematically scientific research data on the effects of

EMF. (All information is made available in both English and German.) In the six-year period between 2015 and 2020, a further 3270 articles were published. Due to the increased number of meta-analyses and systematic reviews, it was decided to address the Terms of Reference of the current Opinion using mainly meta-analyses and systematic reviews, since they can efficiently handle the heterogeneity of individual studies resulting in an improved reliability of the level of evidence. When there was a lack of meta-analyses and/or systematic reviews on a biological/health effect, other reviews or research papers that fulfilled the required quality criteria were used for risk assessment (SCHEER, 2018).

5 ASSESSMENT

5.1 Exposure to RF EMF

5.1.1 Wireless communication technologies

5.1.1.1 Typical exposure of population

In a systematic literature review, Sagar *et al.* (2017) assessed RF EMF exposure in everyday microenvironments in Europe. The authors systematically searched the ISI Web of Science for relevant literature published between 30 April 2015 and 1 January 2000. Twenty-one published studies met their eligibility criteria, of which 10 were spot measurements studies, five were personal measurement studies with trained researchers (microenvironmental), five were personal measurement studies with volunteers and one was a mixed methods study combining data collected by volunteers and trained researchers. The mean total RF EMF exposure for spot measurements in European "Homes" and "Outdoor" microenvironments was 0.29 and 0.54 V/m, respectively. In the studies of personal measurements by trained researchers, the mean total RF EMF exposure was 0.24 V/m in "Home" and 0.76 V/m in "Outdoor". In the personal measurement studies with volunteers, the population-weighted mean total RF EMF exposure was 0.16 V/m in "Homes" and 0.20 V/m in "Outdoor". Among all European microenvironments in "Transportation", the highest mean total RF EMF of 1.96 V/m was found in trains in Belgium during 2007 (more than 95% of exposure was contributed by uplink). There were considerable differences between studies according to the type of measurements procedures, which prevented cross-country comparison or evaluating temporal trends.

Jalilian *et al.* (2019) updated the systematic review mentioned above. They reported that mean RF EMF values in homes, schools and offices were between 0.04 and 0.76 V/m. Mean outdoor exposure values ranged from 0.07 to 1.27 V/m, with downlink signals from mobile phone base stations being the most relevant contributor to environmental EMF. Exposure tended to increase with increasing urbanity. The values of EMF exposure in public transport (bus, train and tram) and cars were between 0.14 and 0.69 V/m. The highest levels, up to 1.97 V/m, were measured in public transport stations with downlink as the most relevant contributor. In line with previous studies, RF EMF exposure levels were highest in the transportation systems, followed by outdoor and private indoor environments. According to the authors, there has been no noticeable increase in everyday RF EMF exposure since 2012, despite increasing use of wireless communication devices.

In an attempt to assess RF EMF exposure in the general population, van Wel *et al.* (2021) took an integrative approach (distinguishing the contribution of various sources) for individual exposure assessment at the organ scale. They developed the Integrated Exposure Model (IEM), which combines energy absorbed due to use of and exposure to RF EMF sources and applied it to a sample of the general population to derive population RF EMF estimates. The IEM used SAR transfer algorithms to provide RF EMF daily dose estimates (mJ/kg/day) using source-specific attributes (e.g., output power, distance), personal characteristics and usage patterns. Information was obtained from an international survey performed in four European countries with 1755 participants. The model-obtained median whole-body and whole-brain doses were 183.7 and 204.4

mJ/kg/day, respectively. Main contributors to whole-brain dose were mobile phone near the head for calling (2G networks) and far-field sources, whereas the latter together with multiple other RF EMF sources were main contributors for whole-body dose. For other anatomical sites, 2G phone calls, mobile data and far-field exposure were important contributors.

Using an integrated exposure model, Birks *et al.* (2021) estimated the daily RF dose in the brain (whole-brain, cerebellum, frontal lobe, midbrain, occipital lobe, parietal lobe, temporal lobes) and the whole body in 8358 children (ages 8–12) and adolescents (ages 14–18) from the Netherlands, Spain, and Switzerland during 2012–2016. The integrated model estimated RF dose from near-field sources (digital enhanced communication technology (DECT) phone, mobile phone, tablet, and laptop) and far-field sources (mobile phone base stations via 3D modelling or RF measurements). The results of the study show that adolescents were more frequent mobile phone users and experienced higher modelled RF doses in the whole-brain (median 330.4 mJ/kg/day) compared to children (median 81.8 mJ/kg/day). Children spent more time using tablets or laptops compared to adolescents, resulting in higher RF doses in the whole-body (median whole-body dose of 81.8 mJ/kg/day) compared to adolescents (41.9 mJ/kg/day). Among brain regions, temporal lobes received the highest RF dose (medians of 274.9 and 1786.5 mJ/kg/day in children and adolescents, respectively) followed by the frontal lobe. In most children and adolescents, calling on 2G networks was the main contributor to RF dose in the whole-brain (medians of 31.1 and 273.7 mJ/kg/day, respectively). This study of RF dose to the brain and body of children and adolescents shows that mobile phone calls on 2G networks are the main determinants of brain dose, especially in temporal and frontal lobes, whereas whole-body doses are mostly determined by tablet and laptop use.

Since pattern of use is the main determinant for the dose produced by mobile phone devices, recent studies have also focused on the exposure assessment of specific groups by examining use patterns within these groups. Langer *et al.* (2017) reported the pattern of cellular phone use among young people in 12 countries during the Mobi-Expo study. Participants in the study were 534 young people (10–24 years) who installed a specifically designed software application on their smartphones to collect data on the use of wireless telecommunications devices (Table 1). The role of gender, age, maternal education, calendar period, and country was evaluated through multivariate models mutually adjusting for all variables. Call number and duration were higher among females compared to males (geometric mean (GM) ratio 1.17 and 1.42, respectively), among 20–24 year olds compared to 10–14 year olds (GM ratio 2.09 and 4.40, respectively), and among lowest compared to highest social classes (GM ratio 1.52 and 1.58, respectively). The number of SMS was higher in females (GM ratio 1.46) and the middle-age group (15–19 year olds: GM ratio 2.21 compared to 10–14 year olds) and decreased over time. Mobile data use was highest in the oldest age group, whereas Wi-Fi use was highest in the middle-age group. Both data and Wi-Fi use increased over time. Large differences in the number and duration of calls, SMS, and data/Wi-Fi use were seen by country, with country and age accounting for up to 50% of the variance. Hands-free and laterality of use did not show significant differences by sex, age, education, study period, or country.

Table 1. Data on the use of wireless telecommunication devices (adapted from Langer *et al.*, 2017)

Variable	Mean (SD)	Median (IQR)
Number of calls per week	30.6 (32.0)	20.9 (29.0)
Total duration in minutes per week	60.8 (80.1)	34.3 (65.3)
Number of SMS sent and received per week	106.3 (251.7)	26.6 (80.5)
Data use per week (Mb)	121.4 (246.8)	36.1 (116.4)
Wi-Fi use per week (Mb)	768.1 (1352.4)	249.2 (733.5)
% hands-free of total call time	18.8 (20.3)	10.6 (18.1)

% right-handed laterality of call time near head	63.8 (25.3)	70.8 (37.2)

5.1.1.2 Dosimetry in epidemiological studies

The problem of dosimetry in epidemiological studies was also highlighted in the SCENIHR Opinion of 2015. Here we summarize the studies that have since been published.

It is difficult to interpret the epidemiological studies on health effects from mobile phone use because of uncertainties in the exposure assessment. A newly developed smart phone application (XMobiSense) is used to validate self-reported mobile phone use and behaviour among adults in (Goedhart *et al.*, 2015). XMobiSense was used by 107 adults recruited in the Netherlands. Participants with no (n=5) or less than 3 weeks (n=6) of data recorded by the app were excluded from the analyses, leaving a final sample of 96 participants for the analyses. For participants with a long period of data recording (n=5), data were truncated at 6 weeks. Recorded outgoing calls included both successful and unsuccessful (ie, no connection) calls, while the self-reported information most likely only included the successful calls. Sensitivity analyses were performed to explore the impact of excluding recorded outgoing calls of 10 s or less (potentially unsuccessful). Recorded data transfer was calculated in megabytes (MB) per week, while self-reported total time spent using the Internet was calculated in minutes per week. The recorded variables laterality (right/left side), hands-free device usage and 'other hands-free usage' were recalculated from seconds per call to percentage over the total call time, thereby accounting for call duration.

An important finding was the significant impact of the level of phone use on the recall, that is, participants with a higher level of reported phone use were more likely to overestimate their number and duration of calls, while underestimation was more likely among participants who reported lower levels of use. The same trend was observed in the INTERPHONE study.

This has important implications for epidemiological studies on mobile phone use, as it will most likely lead to an underestimation of the risk, if any, for adverse health outcomes. RF dose models based on the recalled number and duration of calls should therefore account for differential recall errors by level of phone use.

Although the location of RF exposure from data transfer (frontal lobe of the brain and/or other parts of the body) and the distance to the body is different from voice calls, the enormous increase in data transfer due to the arrival of smart phones makes it an important source to consider in defining RF dose from mobile phones. People are often unaware of the data transfer on their mobile phone, possibly by applications that run in the background (push messages).

A study was devoted to recall of mobile phone usage (Goedhart *et al.*, 2018). The authors observed differences in recall by country, age, maternal educational, and amount of reported phone use. Differences by country were not observed in the CEFALO validation study (2 countries) (Aydin *et al.*, 2011a), but were seen in the Interphone validation study among adults (11 countries; (Vrijheid *et al.*, 2006a, Vrijheid *et al.*, 2006b)). In the Goedhart *et al.* study, where, as in the Interphone one, the same protocol and software app were applied in each country, the authors cannot easily explain the different ratios between self-reported and recorded use (ranging from 0.31 to 0.96 for number of calls and from 0.56 to 3.61 for duration of calls) found between the countries, other than cultural differences in the way people recall their use. It might be important to take these differences into account in future studies and in exposure studies.

Toledano *et al.* (2018) investigated the validity of self-reported mobile phone use in a subset of 75 993 adults from the international prospective cohort study of mobile phone users and health (COSMOS). Agreement between self-reported and operator-derived mobile call frequency and duration for a 3-month period was assessed using Cohen's weighted Kappa (κ). Sensitivity and specificity of both self-reported high (≥10 calls/day or ≥4 h/week) and low (≤6 calls/week or<30 min/week) mobile phone use were

calculated, as compared to operator data. For users of one mobile phone, agreement was fair for call frequency (κ=0.35, 95% CI: 0.35, 0.36) and moderate for call duration (κ=0.50, 95% CI: 0.49, 0.50). Self-reported low call frequency and duration demonstrated high sensitivity (87% and 76% respectively), but for high-call frequency and duration sensitivity was lower (38% and 56% respectively), reflecting a tendency for greater underestimation than overestimation. Validity of self-reported mobile phone use was lower in women, younger age groups and those reporting symptoms during/shortly after using a mobile phone. This study highlights the ongoing value of using self-report data to measure mobile phone use. Furthermore, compared to continuous scale estimates used by previous studies, categorical response options used in COSMOS appear to improve validity considerably, most likely by preventing unrealistically high estimates from being reported.

The issue of epistemic uncertainty is reviewed and interpreted in the context of the MoRPhEUS, ExPOSURE and HERMES cohort studies which investigate the effect of radiofrequency electromagnetic radiation from mobile phones on memory (Brzozek *et al.*, 2018). These uncertainties are derived from a wide range of sources including human error, such as data transcription, model structure, measurement and linguistic errors in communication. Research into this field has found inconsistent results due to limitations from a range of epistemic sources. Potential analytic approaches are suggested based on quantification of epistemic error using Monte Carlo simulation. It is recommended that future studies investigating the relationship between radiofrequency electromagnetic radiation and memory performance pay more attention to the treatment of epistemic uncertainties as well as further research into improving exposure assessment. Use of directed acyclic graphs is also encouraged to display the assumed covariate relationship.

On the issue of dosimetry for epidemiological studies on potential health effects of mobile phones, the SCHEER can conclude that

- the assessment of the exposure should be based on objective measurements, not on the personal recalls or provider's information originating mainly from the bills paid (unsuccessful calls are not paid but the EMF emission is there while the customer waits);
- estimation of the EMF dose received should reflect the differences observed (both self-reporting and the app usage – the solid angle of the EMF flux depends on the device location with respect to human body/head);
- validity can be improved considerably by preventing unrealistically high estimates from being considered from self-reports;
- epistemic or reducible uncertainties can also affect the total error in results in addition to statistical variability usually considered as the main source of errors; these uncertainties must be derived from a wide range of sources including human error, such as data transcription, model structure, measurement and linguistic errors in communication.

5.1.2 Exposure from emerging technologies

Smart meters and sensor networks (the Internet of Things, IoT) are becoming increasingly popular in all environments. Measurements of the RF EMF emitted from such devices in the residential environment have shown that residential levels of RF EMF exposure are low. Some residential devices can significantly increase the exposure if their duty cycles are high enough (>10%), especially when held or used close to the body. Individual smart meters, on the other hand, contribute little in general, despite emissions of up to 20 V/m at 50 cm, due to their low duty cycles (maximum 1%) and locations (Aerts *et al.*, 2019). So, in addition to the continuous exposure to environmental EMF, wireless access points (due to frequent use) and especially mobile phones and other personal communication devices (due to their use close to the body) continue to represent the bulk of the RF EMF exposure in the smart home.

The fifth generation (5G) of broadband cellular networks technology is a key enabling technology for the proliferation of the IoT (Dangi *et al.*, 2022). It uses devices within frequency range 1 (FR1) (< 6 GHz) and frequency range 2 (FR2) (24 – 54 GHz), that is a range of higher frequencies than those used in 4G (fourth generation) networks. The result is that some 5G signals do not travel large distances (over a few hundred meters), unlike 4G or lower frequency 5G signals (sub 6 GHz). The use of the higher frequency band (FR2) requires positioning 5G base stations every few hundred meters.

Millimetre waves are very weak in their ability to connect two devices, which is why 5G needs something called 'small cells' to give full, uninterrupted coverage. Small cells are essentially miniature cell towers that would be placed 250 meters apart throughout cities and other areas needing coverage. The small cells are necessary as emissions (or signals) at this higher frequency/shorter wavelength have more difficulty passing through solid objects and are even easily intercepted by rain. The small cells could be placed on anything from trees to streetlights to the sides of businesses and homes to maximise connection and limit 'dead zones' (areas where connections are lost) (Al-Falahy & Alani, 2017).

The fastest 5G speeds would be in the millimetre wave band and can reach 4 Gbit/s with carrier aggregation and MIMO (multiple-input multiple-output) technology.

Another novel feature in 5G that triggers health concerns among the public is MIMO adopted in 5G Base Stations (BS). In fact, MIMO and beamforming techniques have also been considered in 4G networks. However, there are two substantial differences compared to previous networks, *i.e.*, higher maximum output power and dynamic pencil beam forming with a larger number of antenna elements. The maximum transmitted power by a 5G BS can reach up to 200 W, almost double the corresponding value for a 4G BS. This increase in power can trigger the population's concern about potential health risks (Ericsson, 2018). Since the radiation pattern with massive MIMO varies over time and space, traditional assessment of compliance procedures to quantify the exposure can be misleading. These classical methods rely on conservative assumptions, e.g., all the users are in the same location that coincides with the testing point. These assumptions over-estimate the exposure from 5G BSs, leading to a lower maximum allowable power and a larger exclusion zone (Baracca *et al.*, 2018; Chiaraviglio *et al.*, 2021). However, stochastic dosimetry approaches offer a solution to exposure characterisation in 5G MIMO networks (Al Hajj *et al.*, 2020; Bonato *et al.*, 2021).

5.1.3 Factors affecting exposure to RF EMF

The factors that determine exposure to RF EMF (mainly from cellular networks) have been detailed with the introduction of the Exposure Index (EI) concept, which looks at the exposure of a population during a given time frame in a given area incurred by a wireless cellular network as a whole, aggregating downlink (DL) exposure induced by base stations and access points and the uplink (UL) exposure incurred by all individual wireless communication devices, including devices operated by other users nearby. To assess the realistic exposure of a population, many factors need to be considered: age (adult and child exposure are different), posture, usage, technology, environment, and more (Varsier *et al.*, 2015).

The EI is given by the formula:

$$EI^{\mathrm{SAR}} = \frac{1}{\mathrm{T}} \sum_{t}^{N_T} \sum_{p}^{N_P} \sum_{e}^{N_E} \sum_{r}^{N_R} \sum_{c}^{N_C} \sum_{l}^{N_L} \sum_{\mathrm{pos}}^{N_{\mathrm{pos}}} f_{\mathrm{t,p,e,r,l,c,pos}} \left[\sum_{u}^{N_{\mathrm{U}}} \left(d^{\mathrm{UL}} \bar{P}_{TX} \right) + d^{\mathrm{DL}} \bar{S}_{\mathrm{inc}} + d^{\mathrm{DL,closeddevices}} S_{\mathrm{inc}}^{\mathrm{DLclosed\ devices}} \right] \left[\frac{W}{kg} \right]$$

where:

N_T is the number of Time periods within the time frame T, e.g., a single day;

N_P is the number of Population categories;

N_E is the number of Environments;

N_R is the number of Radio access technologies (RAT);

N_C is the number of Cell types;

N_U is the number of Usages with devices;

N_L is the number of user Load profiles;

N_{pos} is the number of considered Postures;

$\overline{P}_{TX}$ (W) is the mean transmission (TX) power by the users' devices during period *t*, in usage mode *u*, connected to RAT *r*, in environment *e*. A TX power values map is given for the whole considered geographical area and the average value is taken into account for EI evaluation;

$\overline{S}_{inc}$ (W/m^2) is the mean incident power density on the human body during period *t*, induced by RAT *r*, in environment *e*. A distribution of the incident power density for the whole considered geographical area is considered and the average value over this area is taken into account for EI evaluation;

$S_{inc}^{DL,closeddevices}$ (W/m^2) is incident power density on the human body during period *t*, induced by a wireless device connected to RAT *r* of a user in proximity to environment *e*. This term will be significant for people in proximity of users of a wireless device; for instance, in a crowded meeting room, in public transportation, etc.;

d^{UL}(J/kg/W), $d^{DL,closeddevices}$ (J/kg/(W/m^2)) and d^{DL} (J/kg/(W/m^2)) are normalised raw dose values for UL, DL from the user in the proximity, and DL from base stations and access points, respectively, all multiplied by time spent in configuration; and $f_{t,p,e,r,l,c,pos}$ is the fraction of the total population that corresponds to population category *p*, user load profile *l*, in posture *pos*, connected to RAT *r*, for cell type *c*, in environment e, during time period *t*.

In more detail, for a given geographical area, EI takes the following into account: time period: configurations of the network and of usages depend on time of day (power density will be higher during rush hours); population: segmented in different categories, as different population categories will have different life segmentations and different usages of wireless devices, e.g., children (less than 15 years old), young people (15–29), adults (30–59), and seniors (60 and older); different user load profiles: wireless device usages will be dramatically different depending on the profile, and as repartitions of user profiles will also differ depending on the population category (e.g., heavy, medium, light, or non-users); environment: indoor (office, home), outdoor, and in transportation (bus, car, subway etc.); different available Radio Access Technologies (RATs): e.g., 2G (900 and 1800 MHz), 3G, 4G, WiFi; the number of considered RATs depends on the scenario; different cell types: macro, micro, pico, and femto cells; the accessibility to different cell types depends on scenario; posture: sitting, standing; different body postures will lead to different absorption rates in the human body; and usage: a device (e.g., mobile, PC, laptop) and its usage (e.g., voice call, data) (Varsier *et al.*, 2015).

As technology progresses, the spectrum of wireless devices broadens (e.g., wireless virtual reality devices) (Liorni *et al.*, 2020), more information is collected on 'life segmentation' (*i.e.*, people's activities and the way they spend their time) and other factors (e.g., sex/gender) that define the usage of these wireless devices (van Wel *et al.*, 2021). It is clear by now that near-field exposure is related not only to the RAT but also to the mobile application (*i.e.*, the software) running on the wireless terminal (Paljanos *et al.*, 2016). At the same time the computational and experimental techniques for assessing exposure to EMF are advancing, allowing for increasingly accurate exposure characterisation and dosimetry (Hirata *et al.*, 2021).

5.2 Interaction mechanisms

5.2.1 Thermal effects

Tissue heating is an important effect of RF EMF exposure of biological organisms that has been unequivocally demonstrated. The amount and distribution of the energy absorbed in a biological object exposed to RF energy is related to the internal electric and magnetic fields. As the incident wave penetrates a biological object, the fields interact at the various tissue interfaces resulting in a complex distribution of the local fields. These internal fields are related to a number of parameters including frequency, dielectric properties of the tissues, geometry and orientation of the object with respect to the incident field vectors, and whether the exposure is in the near or far field of the source. The resulting distribution of energy can be described in terms of the specific absorption rate (SAR), *i.e.*, the time derivative of the incremental energy absorbed by (dissipated in) an incremental mass contained in a volume element of a given density (Adair and Petersen, 2002).

As frequency increases, the penetration depth of the field decreases[15]. For muscle (tissues with high water content) it reduces from about 3.5 cm at 1 GHz to about 0.3 mm at 100 GHz (millimetre waves). As a result, energy absorption becomes superficial and can lead to surface heating. Heat transport near the skin surface is dominated by thermal conduction into the tissue due to the high temperature gradients at the skin, and only a small fraction of the absorbed energy is lost back into the surrounding environment. The increase in surface temperature is determined by the rate of heat generation in the layer near the surface where most of the RF radiation is absorbed, the rate of diffusion of heat out of the region of high SAR (a relatively fast process due to the small thickness of this layer), and the rate of removal of heat to the body core by blood perfusion (a much slower process). Heat rapidly diffuses from the thin layer where most RF energy at millimetre wave frequencies is absorbed, but if energy is pushed into it sufficiently rapidly (*i.e.*, if the incident power density is high), significant temperatures increases can develop (Hirata *et al.*, 2021). Short pulses of millimetre waves at high fluence can induce large transient increases in surface temperature (Foster *et al.*, 2018; Neufeld and Kuster, 2018) as can pulsed narrow beams (Neufeld *et al.*, 2020).

It has been shown that the surface temperature elevation strongly correlates the transmitted or absorbed power density (APD) across the millimetre wave range (30–300 GHz), whereas the SAR remains a good metric for skin temperature rise for exposure at frequencies lower than 3 GHz (Li *et al.*, 2019).

5.2.2 Cellular interaction mechanisms

The preamble to the IARC Monographs on the Identification of Carcinogenic Hazards to Humans, has given new emphasis and highlighted the importance of mechanistic studies in corroborating evidence and providing biological plausibility to other types of studies, and the possibility that they could provide strong evidence in case of consistent findings demonstrated across a number of different systems and in different species. Given the increasing emphasis on mechanistic data, the IARC Preamble also recognises the importance of evaluating the quality of the study design, exposure assessment methods and biological assay validity (IARC 2019).

Several studies have investigated potential cellular mechanisms that can operate at RF exposure levels found in the everyday environment. Here we focus on *in vitro* studies that can provide essential information on specific cell properties, and allow a more rapid, cost-effective and well-controlled approach to molecular and mechanistic studies than conventional laboratory animal models. Several cellular endpoints have been analysed as presented in a recent metanalysis by Halgamuge *et al.* (2020) which included data from *in vitro* studies published between 1990 and 2015 and investigating effects of weak RF EMF from mobile phones.

[15] Penetration depth in a medium is the distance from the boundary of a medium to the point at which the field strengths have been reduced to *1/e* of their initial boundary value in the medium.

To date the most investigated critical conditions that could provide evidence of a mechanism by which RF exposure might affect human health are oxidative stress, genotoxicity, epigenetics effects, effects on calcium signalling pathways and on apoptosis. It is worth mentioning that for these studies to be effective in providing mechanistic understanding, methodological quality is mandatory but it still is a critical issue since the majority of studies do not comply with quality criteria which include adequate attention to dosimetry, inclusion of sham control, positive control, blind evaluation and temperature control (Zeni and Scarfì, 2012; Simko *et al.*, 2016; Vijayalaxmi and Foster, 2021) Moreover, in the majority of review papers, the study inclusion criteria did not take into account the aspects of quality of experimental methods, which have been widely demonstrated to affect the results (Simko *et al.*, 2016; Vijayalaxmi and Foster, 2021).

5.2.2.1 Oxidative stress

Oxidative stress is a critical condition that could provide evidence of a mechanism by which RF exposure might affect human health. It occurs when the production of oxidants overrides the antioxidant capability of the cells. As a result, the oxidants react with macromolecules like proteins, lipids and nucleic acids giving raise to alteration in cellular functions related to several diseases like cancer and neurodegenerative diseases.

In many studies, experimental evidence has been accumulated that RF exposure may affect biomarkers of oxidative stress at exposure level close to or above the ICNIRP guidelines but there are no systematic reviews or meta-analysis available. In 2020, the WHO commissioned a systematic review of *in vivo* and *in vitro* experimental studies to analyse and synthesise the available evidence on oxidative stress induced by RF exposure (see 4.2.3 above). For this reason, we focus here on narrative reviews. Most of the identified narrative reviews do not apply a systematic literature search and include studies that do not adhere to basic quality criteria defined a priori and have a high risk of bias. Therefore, these reviews are not informative enough to conclude on oxidative stress mechanisms induced by RF exposure, and thus are not useful for the purpose of this Opinion.

The most comprehensive and informative narrative review is the one co-authored by Schuermann and Mevissen (2021). It includes information sources and, although the authors did not set quality criteria for the inclusion of studies, they discussed the importance of sham control and temperature control together with the quality of the dosimetry analysis to determine the actual SAR level experienced by the animals and the cultured cells. This review reports on key experimental findings on oxidative stress deriving from *in vivo* (animals, 70 studies) and *in vitro* (cells, 56 studies) studies published in the last decade. The results are discussed in the context of molecular mechanisms that can be relevant for human health. The authors grouped the studies for the impact on nervous system, on reproduction, and on blood and immune system. Also, a correlation with functional analysis is included to look for temporary or persistent effects. They concluded on the increased oxidative stress due to RF EMF as from the majority of animal studies and from half of the cellular studies, but they pointed out that some studies were subjected to methodological uncertainties or weakness or were not very comprehensive regarding exposure time, SAR level, number and quantitative analysis of the endpoints analysed. The trend the authors evidenced is that, even at low dose exposure, RF can affect cellular oxidative balance that can also lead to an adaptation mechanism after a recovery phase, thus not leading to health effects. Authors evidenced that standardised conditions are mandatory to better understand and confirm their conclusions.

5.2.2.2 Genetic and epigenetic effects

The DNA integrity and epigenetic mechanisms (the regulation of genes by environmental influence) are crucial for human health. Genotoxicity is one of the key biological indicators of carcinogenicity and the most common characteristics of established carcinogens (Smith and Guyton, 2020), while the epigenome is well known to be susceptible to every kind of environmental influence including the exposure to non-mutagenic carcinogens (Feil and

Fraga, 2012). The biological effects of RF EMF on epigenetic factors are less investigated with respect to the genotoxic effects and, in both cases, there are no systematic reviews available in the period of interest of this Opinion.

Genotoxicity is mainly evaluated by analysing the effects on primary (chromosomal aberrations, micronuclei, sister chromatid exchanges, aneuploidy, or mutation) and secondary (single and double strand breaks, chromatin condensations) endpoints, which are biomarkers of irreversible and repairable damage, respectively.

From recent narrative review papers, it appears that results are mainly inconsistent, with many experimental (*in vitro* and *in vivo*) studies showing significant genotoxicity and others reporting absence of an effect from RF exposure at intensities similar to those in the public environment. The effects, when present, are a function of frequency, amplitude, and modulation, and in most cases are not replicated in follow-up studies. (Lai, 2021; Karidipis *et al.*, 2021; Kocaman *et al.*, 2018; Jagetia, 2022). One of the most important agents explaining the genotoxic effects of RF are the reactive oxygen species (ROS), since the energy level of RF EMF is not sufficient to break the intermolecular chemical bonds, and the intracellular effects of RF appear indirectly, the effect of free radicals being the most relevant (Kocaman *et al.*, 2018).

Most of these review papers also highlight the importance of the methodological quality of the experimental studies. Thus, in order to consider the available genotoxicity results concerning exposure to RF EMF, it is important to check if quality control measures were included in the experiments, as the absence of the latter introduce a methodological bias. The SCHEER noted that based on the review by Vijayalaxmi and Prihoda (2019), the percentages of publications reporting no significant difference (NSD) in genetic damage between RF-exposed and control cells were positively correlated with the increase in the number of quality control measures/score adopted in the investigations. On the other hand, the number of publications reporting increased genetic damage (INC) in RF-exposed animal and human cells was negatively correlated with the number of quality control measures/score used in the investigation. The meta-analysis data also highlighted the existence of publication bias. Moreover, the comprehensive review of quality assessment made in this study also revealed that when exposure to RF energy was at a high SAR level, there was increased damage due to a thermal phenomenon or due to the presence of highly localised hot spots.

The same authors, in a previously carried out meta-analysis, showed that the mean indices for chromosome aberration, micronuclei, and sister-chromatid exchanges in RF-exposed and sham-exposed/unexposed controls were within the spontaneous levels reported in a large database. Studies, published from 1990 to 2011, addressing genetic damage in animal and human cells exposed *in vitro* to RF EMF were included in that meta-analysis (Vijayalxmi and Prihoda, 2012).

The SCHEER noted that in 2021 a protocol for a quality-based systematic review of experimental studies investigating genotoxic effects induced by RF EMF in *in vitro* cell models was published. It is worth noting that WHO did not commission this protocol, but the systematic review that will follow will surely contribute to providing a mechanistic understanding with respect to the genotoxic potential of RF EMF. The importance of conducting genetic damage investigations is supported by the fact that most genotoxic agents are carcinogens. Since no single genetic damage test is capable of detecting all genotoxic agents, the recommendation is to conduct a battery of *in vitro* and *in vivo* tests for genetic damage assessment (Sasaki *et al.*, 2000).

5.2.2.3 Calcium signalling

A role for calcium as a molecular mechanism underlying the non-thermal interaction of RF EMF has been hypothesised due to the involvement of calcium signalling pathways in the regulation of many essential cellular processes.

A well-conducted narrative review has been co-authored by Wood and Karidipis (2021). As a result of a transparent bibliographic search, 30 *in vitro* and *in vivo* papers dealing with the effect of RF exposure on Ca^{2+} levels have been analysed to see whether a consistent picture can be drawn. To analyse effects in the single papers, the authors computed the effect size (ES) defined as the difference between the means of the exposed and sham groups divided by the standard deviation of the sham group. Moreover, they assigned a quality score to each paper based on the attention given to aspects like dosimetry, sham control, positive controls and blinding. In 60% of the analysed papers, a change in intracellular calcium was reported with the number of papers reporting an increase approximately equal to the papers reporting decrease. The greatest proportion (40%) reported no changes. Analysis of effects size (ES) vs. carrier frequency and modulation type did not evidence any significant relationship. The majority of the studies with a higher quality score did not report an effect. There was no consistent evidence of PD or SAR windows although the authors pointed out that estimation of exposure is to be used with caution since in some cases the procedure for exposure levels is not clearly described. Moreover, they evidenced that the direction of the effect moved from cytoplasmic loss to cytoplasmic gain as methods for estimating calcium levels have become more sophisticated. The papers in which the voltage-gated calcium channels (VGCCs) were investigated by direct measurement of cell Ca^{2+} current are particularly interesting since such channels have been suspected to be susceptible to RF fields due to the coupling of RF to cells and the demodulation of extremely low frequency modulations from the RF carrier (Pall M., 2013; Pall M., 2014). These papers did not show significant effect due to RF exposure and thus do not support the claim that VGCCs are particularly sensitive to environmental RF exposure. Based on the overall results of these reviews, the authors concluded that future good quality experiments are needed to support the claim that calcium levels are affected by RF exposure.

5.2.2.4 Apoptosis

Apoptosis is an important cell death programme, highly conserved within multicellular organisms and genetically controlled, which is responsible for the removal of damaged, dysfunctional or no longer necessary cells to promote homeostasis and the survival of organisms.

A scoping review (Romeo *et al.*, 2022) has been recently published that systematically maps the research regarding the effects of RF EMF on apoptosis in mammalian cells. A systematic literature search was performed, and the review was restricted to studies that adhere to basic quality criteria defined a priori (sham control, at least three independent experiments, appropriate dosimetry analysis and temperature monitoring). The authors concluded that most retrieved papers failed in complying with the presence of sham controls and dosimetry analysis, or of appropriate methods for dosimetry analysis. Moreover, most of the included studies did not find significant alterations of the apoptotic process due to RF EMF exposure. The authors pointed out that the scoping review laid the ground for a quantitative analysis of the papers included and addressing mainly questions on the direction of the effect (induction or suppression of apoptosis), effect size, possible dose-response relationship, possible major capability of certain exposure parameters to exert an effect.

5.2.3 Conclusions on interaction mechanisms

Thermal effects of RF EMF are well established and have been extensively studied. Computational and experimental studies have shown that by limiting recently introduced dosimetric quantities, like absorbed power density (APD), it is possible to control the superficial and fast tissue heating that might result from emerging applications using millimetre waves.

Reviews dealing with the effects of RF exposure on oxidative stress, genetic and epigenetic effects, and calcium signalling have been considered here to provide evidence of a cellular mechanism operating at RF exposure levels found in the everyday environment.

There are no systematic reviews and meta-analyses available for oxidative stress, epigenetic effects and calcium signalling.

The current scientific evidence, based on the narrative reviews, suggests that the cellular oxidative balance may likely be affected, although its correlation with possible adverse effects is not clear.

The interaction mechanisms causing genotoxicity and epigenetic effects are not fully understood. The induction of increased levels of ROS (reactive oxygen species) measured in cells and tissues has been used as a marker of DNA impairment. In this sense, it is anticipated that exposure over time to RF EMF might result in building up ROS and disruption of homeostasis with epigenetic effects.

There are no consistent effects on calcium signalling or on apoptosis.

In all cases, methodological quality arises as a critical issue that needs to be taken into account both in the case of individual studies and for the inclusion of studies in review papers.

In conclusion, there is no consistent evidence of biological effects involving oxidative balance, genetic and epigenetic effects, and calcium signalling that can support and strengthen the evidence from epidemiological and *in vivo* studies on RF exposure, following the WoE assessment of health risks.

5.3 Health effects

5.3.1 Neoplastic diseases

5.3.1.1 Epidemiological studies

Results from several epidemiological studies on the association between use of mobile phones and the development of brain cancer are ambiguous. In the following paragraphs, a presentation and discussion of findings from systematic reviews and meta-analysis are presented.

In one of the first meta-analyses in the field conducted in 2016, Prasad *et al.* (2017) analysed information from 14 case control studies (that were conducted from 1996-2016); This showed no significant increase in the risk of brain tumours due to mobile phone use [OR 1.03 (95% CI 0.92–1.14)]. However, for mobile phone use of 10 years or longer (or >1640 h), the authors concluded that the overall result of the meta-analysis showed a significant 1.33-times increased risk. Meta-regression analysis indicated that the observed effect was significantly associated with methodological study quality, but no relationship between source of funding and the pooled effect was evident.

In 2016, Wang and Guo published a meta-analysis that aimed to evaluate the association between mobile phone use and glioma risk through pooling the published data from 2001 to 2008. They screened the open access published case–control or cohort studies about mobile phone use and glioma risk. After searching the relevant databases, they included 11 studies. The combined data showed that there was no association between mobile phone use and glioma odds (OR = 1.08, 95% confidence interval 0.91–1.25); but a significant association was found between mobile phone use of more than 5 years and glioma risk (OR = 1.35, 95% CI: 1.09–1.62). Thus, the authors concluded that long-term mobile phone use may increase the risk of developing glioma. Another, more recent meta-analysis (Wang *et al.*, 2018) also evaluated wireless phone use risk of glioma. Ten studies on the association of wireless phone use and risk of glioma were included. The combined odds ratio of adult gliomas associated with "ever use of wireless phones", as reported by the participants, was 1.03 (95% confidence interval 0.92, 1.16), with high heterogeneity (I2 54.2%). In subgroup analyses, no significant association was found between tumour location in the temporal lobe and adult glioma risk. A significant association with risk of glioma was more prominent in long-term users (>10 years) with odds ratio of 1.33 (95% CI 1.05-1.67). The authors concluded that "ever use of wireless phones" was not

significantly associated with risk of adult glioma, but there could be increased risk in long-term users.

In line with the aims of the previous meta-analysis, the objective of Yang *et al.*, (2017) study was to investigate the potential association between mobile phone use and subsequent glioma risk using meta-analysis. They performed a systematic search for studies reporting relevant data on mobile phone use and glioma in the period 1980 to 2016. This meta-analysis included 11 studies comprising a total of 6,028 cases and 11,488 controls. There was a significant positive association between long-term mobile phone use (> 10 years) and glioma incidence (OR = 1.44, 95% CI 1.08-1.91), and a significant positive association between long-term ipsilateral mobile phone use and the risk of glioma (OR = 1.46, 95% CI 1.12-1.92). Moreover, long-term mobile phone use was associated with 2.22 times greater odds of low-grade glioma incidence (OR = 2.22, 95% CI 1.69-2.92). It is notable that mobile phone use of any duration was not associated with the odds of high-grade glioma. Contralateral mobile phone use was not associated with glioma regardless of the duration of use. Similarly, this association was not observed when the analysis was limited to high-grade glioma. In another meta-analysis by Bortkiewicz *et al.* (2017), which included 24 case-control studies (26,846 cases, 50,013 controls) that were published before the end of March 2014, a significantly higher risk of an intracranial tumour (all types) was noted for the period of mobile phone use over 10 years (odds ratio (OR) = 1.324, 95% CI: 1.028–1.704), and for the ipsilateral location (OR = 1.249, 95% CI: 1.022–1.526). The authors concluded that findings support the hypothesis that long-term use of mobile phone increases the risk of intracranial tumours, especially in the case of ipsilateral exposure.

In a more recent meta-analysis of 46 case-control studies, Choi *et al.* (2020) investigated whether cellular phone use was associated with increased risk of tumours. Compared with never or rarely having used a cellular phone, regular use was not associated with tumour risk in the random-effects models. However, in the subgroup meta-analysis by research group, there was a statistically significant positive association (harmful effect) in the Hardell *et al.* studies (OR, 1.15, 95% CI: 1.00-1.33, n = 10), a statistically significant negative association (beneficial effect) in the INTERPHONE-related studies (case-control studies from 13 countries coordinated by the International Agency for Research on Cancer (IARC); (OR, 0.81, 95% CI: 0.75-0.89, n = 9), and no significant association in other research groups' studies. The authors concluded that cellular phone use with cumulative call time more than 1000 h significantly increased the risk of tumours; however, the heterogeneity on the findings should be further explored. In addition, the later meta-analysis triggered significant criticism. Brzozek *et al.* (2021) underlined important methodological issues and incorrect interpretations in their commentary. In particular, Brzozek *et al.* noted that the authors of the meta-analysis mentioned that the INTERPHONE group was unfairly and repeatedly criticised for being funded by the cellular phone industry, even whilst acknowledging agreements that guaranteed the study's complete scientific independence. Secondly, the authors of the meta-analysis argued that the Hardell subset of studies were of higher quality compared to the INTERPHONE studies. Although the Hardell studies were like the INTERPHONE studies, there were subtle methodological differences in recruitment, subject age and status, exclusion criteria, data collection, definition of regular phone use etc., which could account for the different results. According to Brzozek *et al.*, a closer look at the methodological differences does not show the Hardell studies to be of higher quality than the INTERPHONE studies. Moreover, the Hardell studies included a wider age range (20–80 years) compared to the INTERPHONE studies (generally 20–69 years); it could be hypothesised that a greater age-range although increasing the sample size of the study, it did not add to statistical power and may lead to the inclusion of tumours with recognizably different aetiology. Moreover, exposure misclassification remains a prominent issue in both groups of studies with Hardell defining "any use" as regular phone use. This is questionable because it includes casual phone users. If mobile phones truly cause cancer, but only at higher exposures, employing such a definition of regular use means that the effect might be weakened. Finally, Brzozek *et al.* noted that the meta-analysis which pooled different types of case-control studies

and tumour types together was limited, as these tumours may have different aetiologies and no viable biological mechanism to how a cellular phone use exposure could cause these various tumours. Moreover, de Vocht and Röösli (2021) also made significant criticism of the meta-analysis by Choi *et al.*; they underlined that the observational epidemiological studies used were susceptible to various biases that can result in under- or over-reporting of the true effects. De Vocht and Röösli suggest that in-depth evaluation is needed to understand why the studies by the Hardell group provide different results than most other case-control studies. In the absence of direct evidence for any causes of these differences, triangulation of epidemiological studies susceptible to different types of biases, as well as with evidence from animal and laboratory studies is warranted. Although some uncertainties remain, de Vocht and Röösli concluded, most notably for highest exposed users, that we can be reasonably sure that the current evidence has converged to somewhere in the range of an absence of excess risk to a moderate excess risk for a subgroup of people with highest exposure.

Intracranial tumours are rare diseases, with their incidence rates varying between 7 to 10 per 100,000. Current epidemiologic evidence suggest that the most frequently reported histology is meningioma, followed by gliomas, pituitary gland tumours, and nerve sheath tumours. In a meta-analysis published in 2019 by Röösli *et al.*, mobile phone use and risk of intracranial and salivary gland tumours was evaluated. The meta-analysis included both case-control and cohort studies published up to the end of 2017. Glioma was the most frequently studied type of tumour in relation to mobile phone use; results of the meta-analysis showed no indication for an increased risk of glioma (pooled RR 1.11, 95%CI 0.85 to 1.46, n =7), acoustic neuroma (pooled RR 1.19, 95%CI 0.80 to 1.79, n =6), meningioma (pooled RR 1.03, 95%CI 0.90 to 1.17, n =6), pituitary (pooled RR 1.07, 95%CI 0.64 to 1.77, n =4) and salivary gland tumours (pooled OR 0.74, 95%CI 0.48 to 1.15, n =6). Authors of the meta-analysis also underlined that the inconsistencies in their findings with some other meta-analyses might be due to methodological reasons, such as multiple counting of the same individual data or combined different disease entities and recall bias, particularly in case-control studies. Especially for glioma and acoustic neuroma, the pooled effect estimates of the meta-analysis were mainly driven by the pooled Orebro studies (Hardell and Carlberg, 2015; Hardell *et al.*, 2013), which produced excess pooled estimates of risk that are hardly ever observed in clinical setting.

In another meta-analysis of three case-control studies that evaluated the association between mobile phone use and parotid gland tumours, authors reported that cell phone use was associated with greater odds (OR = 1.28, 95%CI: 1.09-1.51) to develop salivary gland tumours. It is noted that an ecological study by Karipidis *et al.* (2021) exists, in which the investigators performed analyses of incidence time trends to estimate the annual percentage change of salivary gland cancers of all available national registration data from 1982 to 2016, in Australia. Their results did not indicate that mobile phone use was correlated with the incidence of parotid or other salivary gland cancers across time. However, these findings should be interpreted in light of several methodological issues that such designs carry, like ecological bias, residual confounding, and effect modification of exposure-related factors.

Finally, in a recently published large-scale observational prospective study that was conducted during 1996-2001 with follow up in 2011, among 1.3 million women born between 1935-1950, and followed up via record linkage to National Health Services databases, no significant associations were observed of "ever mobile phone use" with incident brain tumours, meningioma, pituitary tumours, and acoustic neuroma, as compared to "never users" (Schüz *et al.*, 2022). Specifically, compared with never-users, no significant associations were found, overall or by tumour subtype, for daily cellular telephone use or for having used cellular telephones for at least 10 years. However, the authors acknowledged a number of limitations which the SCHEER also considered, namely, that the exposure to mobile phones assessment was very simple, there was a lack of detailed cellular telephone use history and lack of information on the type of cellular

telephone technology used. Moreover, misclassification may have also occurred in the first years of follow-up, especially due to the rapid grow of mobile phones use observed in the later years. Although this was an observational study with known limitations, the SCHEER has presented its results here because of its methodological merits in the recruitment of participants.

5.3.1.2 *In vivo* studies

Between 2015 and 2021, in total five carcinogenicity studies published in three papers (NTP, 2018a; NTP, 2018b; Falcioni *et al.*, 2018), one pilot study (de Seze *et al.*, 2020) and one co-carcinogenicity study were identified (Lerchl *et al.*, 2015).

Several aspects of the NTP and Falcioni *et al.* studies were already commented on elsewhere (e.g., ARPANSA 2018; Belpoggi *et al.*, 2021; BERENIS, 2018; Elwood & Wood, 2019; FDA, 2020; Garofalo *et al.*, 2020; ICNIRP, 2020; Kuhne *et al.*, 2020; Lin, 2019; Melnick, 2020; SSM, 2019).

Results from four extensive carcinogenesis studies conducted by the National Toxicology Program (NTP), USA, were published in two reports (NTP, 2018a; NTP, 2018b). Hsd: Sprague Dawley SD rats were exposed to 900 MHz GSM- or CDMA-modulated signals at whole-body specific absorption rates (wbSAR) of 1.5, 3 or 6 W/kg (NTP, 2018a), and B6C3F1/N mice to 1900 MHz GSM- or CDMA-modulated signals at wbSARs of 2.5, 5 or 10 W/kg (NTP, 2018b). Each sham and exposure group consisted of 90 males and 90 females. The animals were exposed daily in an intermittent 10-min field on, 10 min-field off scheme. Exposures were interrupted from 7 to 11 a.m. and from 2 to 3:40 p.m. which led to a cumulative exposure of 9 h 10 min per day. Average wbSARs were kept constant during animals' entire life. Rats' exposure began in utero (on gestation day 5) and continued for 107 weeks after birth. In mice, it started at 5-6 weeks of age and continued for 106 and 108 weeks in males and females respectively.

The prominent finding was an increased incidence of malignant schwannomas in the heart of male rats. It occurred with a statistically positive trend (GSM, p=0.041; CDMA, p=0.011) with increasing wbSAR. In 1.5, 3, and 6 W/kg exposed males the malignant heart schwannomas (GSM 2/90 [p=0.297], 1/90 [p=0.540], and 5/90 [p=0.080], respectively; CDMA 2/90 [p=0.273], 3/90 [p=0.175], and 6/90 [p=0.030], respectively) were increased compared to sham exposed rats (0/90). Thus, it may be concluded that the observation of malignant heart schwannomas in male rats is considered to be significant at the highest dose level (6 W/kg wbSAR) tested in CDMA.

Overall, NTP's summarising conclusions were: In male SD rats "for both GSM- and CDMA-modulated RFR, we conclude that exposures increased the number of animals with tumours in the heart. Tumours of the brain were also considered to be related to exposure; and increased numbers of male rats with tumours of the adrenal gland were also related to exposure. We are uncertain whether occurrences of prostate gland, pituitary gland, and pancreatic islet tumours in male rats exposed to GSM-modulated RFR and pituitary gland and liver tumours in male rats exposed to CDMA-modulated RFR were related to RFR exposures. This was also the case with female rats, where we conclude that exposure to GSM- or CDMA-modulated RFR may have been related to tumours in the heart. For females exposed to CDMA-modulated RFR, occurrences of brain and adrenal gland tumours may have been related to exposure" (NTP, 2018a).

"For GSM-modulated RFR, we conclude that exposure to RFR may have caused tumours in the skin and lungs of male B6C3F1/N mice and malignant lymphomas in female mice. For CDMA-modulated RFR, we conclude that exposure to RFR may have caused tumours in the liver of male mice and malignant lymphomas in female mice" (NTP, 2018b).

The strengths of the NTP studies are:

- study reports with all study details are publicly available (NTP, 2018a,b),
- detailed dosimetry (Capstick *et al.*, 2017; Gong *et al.*, 2017),

- testing two species as it is usual practice when interpreting cancer results for application to humans (Elwood & Wood, 2019),
- three exposure levels used in each study,
- GLP, animal facility accredited by AAALAC International,
- sentinel animal programme,
- single cage housing (one animal per cage), *i.e.*, no shielding by other animals in the cage
- complete histopathology including peer review and standardized pathology nomenclature,
- availability of published historical control data (NTP 2020),
- group size above average.

Limitations are:

- no temperature measurements but strong evidence on thermoregulatory stress in the "high dose" groups (wbSAR of 6 W/kg) of male rats (Kuhne *et al.*, 2020),
- differences in body weight development and survival between sham and exposed males,
- only one concurrent sham control group per species,
- no cage control group.

The controversial discussion about the results of the rat studies is mainly based on

- the lack of tumours in the sham controls, while there were tumours in the historical controls (NTP, 2020), and
- the strong evidence on significant temperature fluctuations in exposed aged male rats, likely causing lower body weights and probably effecting survival and tumour incidences.

This results in a considerable uncertainty about how to interpret the results of the NTP rat studies (SSM, 2019) whereas the mouse studies showed equivocal results describing background fluctuations of the observed tumours "and not an increase caused by exposure to RF radiation" (FDA, 2020).

A fifth large rat carcinogenicity study reporting heart schwannomas was conducted by Falcioni *et al.* (2018). Already in 2005 starting the experiment, they exposed 2,448 male and female of the Institute's own Sprague-Dawley rats prenatally from the 12th day of gestation until their natural death for 19 h/day to a 1800 MHz GSM far field signal which was reported to be 0.001, 0.03 or 0.1 W/kg wbSAR. After weaning, five rats per cage (1025 cm² floor area) were irradiated. Histopathology data were reported for brain and heart only.

In-life data of mean water and food consumption, body weight development or survival did not differ between sham and exposed groups, either in male or female rats. Compared to sham controls the incidence of heart schwannomas in male rats exposed at the highest wbSAR (0.1 W/kg) increased significantly (0/412 vs. 3/207). In addition, increased incidences of heart Schwann cell hyperplasia in males (3/412 vs. 5/207) and females (2/405 vs. 2/202) and malignant glial tumours in females only (2/405 vs. 3/202) were reported, but these were not statistically significant.

Strengths of the study are

- the group sizes (n >>200 per group and sex),
- three exposure levels,
- survival time of animals, and
- standardised pathology nomenclature.

Limitations are

- the lack of dosimetry,
- crowded cages resulting in rats' shielding each other and potentially stressed animals (hierarchy conflicts and fights, particularly in males),

- missing data on potential loss of animals due to group housing,
- no sentinel programme regarding animals' hygienic status (microbiology, parasitology) reported,
- very limited tumour data due to incomplete histopathology (two organs only were evaluated),
- no reference for historical control data given, and
- overall, a lot of study details according to OECD 451 and GLP guidelines are not publicly available.

By contrast to the authors' conclusion, the results are not consistent with those of the NTP study, where no increased tumour incidences were found with the exposure level of 1.5 W/kg (SSM, 2019). In addition, selective reporting of specific tumours is not state of the art. The authors may overcome this shortcoming with a further publication presenting all tumour data and adequate dosimetry data.

Finally, de Seze *et al.* (2020) tested in male Sprague Dawley rats the effects of nanosecond high power pulsed microwaves (ns HPM). In a complex experimental design, a pilot study addressing cancer was included. Twenty-four rats were sham-exposed, another 24 animals were exposed to 3.7 GHz ns HPM. HPM were produced by a superradiance generator in the S band at 3.7 GHz with pulses of 2.5 ns. The exposure lasted 26 min/day (2 x 8 min with 10 min interval), 5 days/week for 8 weeks. The peak E-field was 0.56 MV/m. Calculations of peak SAR revealed 3.33 MW/kg and an average SAR of 0.83 W/kg. Following the 8 weeks-exposure all 48 rats were observed up to two years of age. All (tumour) masses detected in-life and during necropsy were histopathologically examined. HPM exposure caused a 4-month decrease of lifespan compared to sham controls (median lifespan of 590 days compared to 722 days). The exposed group consisted of 17 tumour-bearing rats compared to 3 in the sham group. Most of the tumours were diagnosed as (subcutaneous) fibroma, fibroadenoma and fibrosarcoma. Unfortunately, the tumour reporting did not follow international standards, and tumour statistics were not presented. But the other study limitations were discussed by the authors:

- missing numerical and experimental dosimetry and thermometry, *i.e.* SAR values were calculated,
- 0.8 Gy residual X-rays (20 mGy/d) emitted from the exposure device.

Summarising, the obtained results need to be proven in further state-of-the-art cancer studies, using different species and both sexes, different exposure levels, and including a positive control exposed at 0.8 Gy.

Addressing co-carcinogenicity, Lerchl *et al.* (2015) performed a replication of the study by Tillmann *et al.* (2010) testing the same UMTS signal but at different exposure levels and using more animals per group. Tillmann *et al.* had found an increased incidence and multiplicity of lung carcinomas as well as more liver tumours in ENU-induced and up to 24 mo. (20 h/d) RF-exposed female mice compared with animals treated ENU alone. The effects on liver tumours were discounted due to possible confounding caused by bacterial (Helicobacter sp.) infection. UMTS exposure alone had no tumourigenic effect. Due to limitations in the design, Tillmann *et al.* rated their experiment as a pilot study which showed some co-carcinogenic effect of lifelong UMTS exposure (4.8 W/m²) in female B6C3F1 mice (SCENIHR, 2015).

In the study of Lerchl *et al.* (2015), ENU was administered to pregnant mice on day 16 post conception (pc), which remain, starting on day 6 pc, to be exposed to a UMTS signal for 19.5 h per day during the entire pregnancy, and the offspring continued to be exposed up to a total exposure period of 72 weeks. Nominal wbSAR were 0 (sham), 0.04, 0.4 and 2 W/kg and 96 females per group were used, added by a (non-ENU) cage control group. Increased incidences of bronchoalveolar and hepatic tumours and lymphomas were reported, but without an exposure-response pattern. Bronchoalveolar carcinomas and lymphomas were only increased with 0.4 W/kg, while bronchoalveolar adenomas were

more increased with 0.04 and 0.4 W/kg then with 2 W/kg. Hepatocellular carcinomas were increased in all exposure groups about 10 -16 % compared to sham controls.

With three exposure levels, group sizes of n = 96 and an extensive statistical evaluation Lerchl's study offers some major advantages. On the other hand, there was no temperature monitoring, no RF only control, no data which was "either simulated or measured that correlated E-field with the desired treatment levels of whole-body SAR" (FDA, 2020), and no sentinel programme, except Helicobacter testing after one year only.

Nevertheless, Lerchl's experiment resulted in similar findings as described by Tillmann *et al.* (2010). But the results are inconsistent in that they did not demonstrate a clear dose response (SSM, 2019; FDA, 2020). Furthermore, the study was designed with very specific experimental conditions which cannot directly be extrapolated to human exposures (SSM, 2019). But such studies testing potential tumour promoters may be useful as long as humans are simultaneously exposed to several tumour promoting agents and tumour initiating carcinogens, e.g., cigarette smoke (BERENIS, 2018).

5.3.1.3 Conclusions on neoplastic diseases

There is a weak weight of evidence on the interaction mechanisms causing genotoxicity and epigenetic effects, due to the severe data gaps that do not allow these mechanisms to be fully understood.

Regarding carcinogenicity in animals, there is an overall uncertain weight of evidence due to

- the inconsistencies and partial inaccuracies in the rat studies,
- the different tumour responses in the (NTP) mouse studies compared to the rat studies (lack of species consistency in terms of observed effects), which increases uncertainty about the relevance of these effects to humans.

For the pilot study at present a weighing of evidence is not possible. But results should be confirmed or refuted, since the (pilot study) rats repeatedly exposed to extremely high intensity microwave pulses[16] with an average SAR level below the thermal threshold of 4 W/kg demonstrated a tumour response.

Regarding co-carcinogenicity, the studies so far do not provide any further insight towards a carcinogenic risk, because mouse-specific tumours may have been promoted, but without an exposure-response pattern. Therefore, there is weak weight of evidence for the co-carcinogenicity of exposure to RF EMF, due to data gaps.

Several methodological issues of the reviewed meta-analyses of epidemiological studies could be identified, such as the number of independent studies included in the meta-analyses which varies considerably from very few, *i.e.*, 3, to several, *i.e.*, 15 studies. In addition, the heterogeneity of some of the meta-analyses was high, suggesting diversity in the design of the enrolled studies. For example, the variety in the period covered (e.g., some historical studies might introduce issues concerning varying data quality), or the recruitment criteria of the participants in the individual studies and the challenges of quantification of exposure (e.g., never used, frequent user, long term user- potentially different definitions in different studies and dependent on personal recall) could be possible sources of bias and lead to additional uncertainty.

Regarding carcinogenicity in humans, based on the available information provided in meta-analyses, and individual studies, the weight of evidence for adverse health effects from exposure to RF EMF is uncertain.

In conclusion, there is overall uncertain to weak weight of evidence that exposure to RF EMF increases the risk of neoplastic diseases.

[16] around 1 MV/m, "comparable to those that have in part been used in the Gulf War" (de Seze *et al.*, 2020)

5.3.2 Neurological and neurobehavioural effects

5.3.2.1 Epidemiological studies

There are some studies that have also focused on the impact of radio frequency EMF exposure on neurological and neurobehavioral effects.

Neurodegenerative diseases

No systematic review papers or meta-analyses could be identified regarding neurodegenerative effects of RF EMF. The Health Council of the Netherlands report (2020a, 2020b) underlines the limited number of studies. Indeed, only one clinical study was used for neurodegenerative diseases (13 were rejected) and 13 animal studies were considered. According to the report it is "not possible to make a statement on a relation between exposure to radiofrequency electromagnetic fields and neurodegenerative diseases" based on human studies. However, in some of the animal studies "an increased level of neurodegeneration was found, but (that) the endpoints used are widely varying. The conclusion for the frequency range of 700-2200 MHz is that effects are possible."

Neuropsychiatric conditions

No systematic review papers or meta-analyses with robust design (*i.e.*, solid research hypothesis, transparent literature search, adequate number of studies included with specific inclusion and exclusion criteria), could be identified regarding the potential effects of mobile phone use on neuropsychiatric conditions.

Neurodevelopmental disorders (e.g., autism, attention deficit, etc.)

No systematic review papers or meta-analyses with robust design could be identified regarding the potential effects of mobile phone use on neurodevelopmental disorders, either.

As a result, there are no new reviews on neuropsychiatric conditions or neurodevelopmental disorders meeting SCHEER criteria of the level of evidence, in addition to the ones included in the SCENIHR report of 2015 (SCENIHR, 2015).

5.3.2.2 Neurophysiological and neuropsychological human studies

Introduction

Effects of RF EMF exposure can be considered/analysed at various levels. Effects on the brain, which is largely disconnected from the environment and unresponsive to exogenous stimulation, can be investigated during sleep. Three approaches can be used: 1) self-assessment of sleep quality (which belongs to the section 5.3.3), 2) objective parameters of sleep initiation, sleep maintenance, and sleep structure as derived from polysomnographic measures, and 3) quantitative measures of the sleep EEG like power spectral values. As stated earlier (see sections 4.2.1.3. and 4.2.2.2) effects have been shown repeatedly for the power spectra of the sleep and the waking EEG. The resting state waking EEG, which is usually dominated by waves in the alpha frequency range, is physiologically completely different from the sleep EEG, where slower waves prevail, *i.e.* waves in the theta and delta frequencies ranges. When the brain is challenged by external stimuli it responds with specific response patterns, *i.e.* with event-related potentials (e.g. slow cortical potentials, evoked potentials). If a reaction to the stimulus is required or a cognitive task has to be processed effects on behavioural measures like reaction times, number of correct responses etc. can also be assessed. Brain physiology and function thus encompass a large number of independent outcome parameters. Despite the importance of brain function as a target parameter in studies of effects of radiofrequency exposure, the number of systematic reviews and meta-analyses, respectively, is comparatively small.

Cognitive function

For cognitive functions there is one meta-analysis (Zubko *et al.*, 2017) that addresses the effects of EMF emitted by GSM phones on working memory, which is one of several cognitive domains that can be considered. Working memory is a domain that is of special interest in normal and pathological age-related cognitive decline. The meta-analysis included 10 studies in which working memory was assessed in one or more of three tasks; n-back (0-back – 3-back), subtraction, and digit span task. Based on three to five studies, meta-analyses were performed separately for accuracy and reaction times of the four n-back tasks as well as for accuracy of the digit span task, and the reaction time of the subtraction task. The authors concluded that there is no evidence that short-term exposure has an effect on working memory.

In a narrative review, Curcio (2018) summarised the results of 43 experimental studies in volunteers which investigated effects of mobile phone-like signals on attention. Attention is another cognitive domain and covers selective, sustained, and divided attention. The studies are quite heterogeneous with regard to methodology, dosimetry, and statistical analyses. Thirty one studies did not report a statistically significant difference in attention between the sham and the RF exposure, nine observed a partial improvement, *i.e.* in speed of performance and/or in accuracy, while three showed inconsistent results or a worsening in performance.

The lack of evidence for exposure effects on attention and working memory are in line with the last SCENIHR Opinion (SCENIHR 2015). Based on criteria for inclusion, which are the same than those used by the WHO (2014), the Health Council of the Netherlands (2020a, 2020b) identified 48 experimental human studies investigating RF EMF effects on cognitive functions in the frequency ranges 700 – 2200 MHz (46 studies), 2.2 to 5.0 GH (two studies), and 20-40 GHz (no study). Thirty-one of the 46 experimental studies identified for the frequency range 700-2200 MHz did not find an effect of exposure, seven studies reported an unfavourable effect of exposure on cognitive function while eight observed a favourable effect. One of the two studies for the frequency range 2.2 – 5.0 GHz showed no effect while the other observed an unfavourable effect. Without differentiation between cognitive domains, the Health Council of the Netherlands concluded that both frequency ranges, for which data are available, favourable and unfavourable effects of RF EMF exposure are possible.

Event-related potentials

SCENIHR (2015) concluded that for event-related potentials (including slow cortical potentials) results were inconsistent. Since there is no meta-analysis and no systematic review available for ERPs, the following assessment is based on the report of The Health Council of the Netherlands (2020b). The Health Council of the Netherlands (2020b) identified 27 studies, addressing effects of RF EMF exposure on event-related potentials in the frequency range 700 – 2200 MHz: For the other frequency ranges no studies were found. All studies are listed under brain electrical activity. Nineteen investigated healthy adults, three children and five patients with different neurological diseases. Approximately 50% (14 out of 27) observed an effect (two of the studies in children, 4 of the studies in patients and eight in healthy subjects). For all studies in which effects were observed, it is not clear whether these are favourable or unfavourable.

Resting-state waking EEG

SCENIHR (2015) concluded that mobile phone RF EMF exposure might affect brain activities as reflected by EEG studies during wake and sleep. Due to various methodological issues, it was, however, not possible to derive firm conclusions. The Health Council of the Netherlands summarised 20 studies investigating the waking EEG (700 – 2200 MHz: 19; 2.2 – 5.0 GHz: 1). Overall, four studies did not observe an effect while 16 did, including the one referring to exposure at the higher frequency range. The latter observed an unfavourable effect of exposure while for all others the effect could not clearly be classified as favourable or unfavourable. Furthermore, the assessment did not take into account whether RF EMF exposure led to an increase or a decrease of the EEG spectral power.

Additionally, two narrative reviews were published that looked at the resting state waking EEG studies in more detail. Based on the following four inclusion criteria. 1) blind condition (single or double blind) with a crossover design, 2) EEG technique as experimental approach, 3) investigation of the waking spontaneous EEG, and 4) radiofrequency range related to MP technologies Wallace and Selmaoui (2019) identified 30 studies. Most of the studies (80%) observed an effect of RF EMF exposure on the EEG, 47% found an effect exclusively in the alpha frequency band while 30% found an effect in the alpha frequency band and other frequency bands (delta, theta, beta and gamma) as well. However, not all studies considered all frequency ranges. Studies on adolescents did not indicate that this age group had any higher degree of sensitivity than adults. On the other hand, four studies in epileptic patients showed an effect of RF EMF exposure from 2G on the EEG. The authors conclude that a direct and clear comparison of the main findings obtained so far is not easy due to the considerable differences in the experimental protocols and methods, like the nature of the RF EMF signal, its modulation, exposure duration, position of the exposure device and characteristics of the participants. The authors emphasise that future studies should use a randomised and counterbalanced double-blind cross-over design. Furthermore, studies should be carried out with a detailed dosimetry and standardised protocol criteria controlling the variability of the physiological state of the brain between participants, e.g., by performing test sessions at the same time of the day.

Almost at the same time, Danker-Hopfe *et al.* (2019) published a paper deriving at very similar results and recommendations. Based on a continuous monitoring of the literature published between 1997 and 2016, 39 studies investigating RF EMF effects on the resting state waking EEG were identified. Excluded were studies that were not published in English language, not published in peer-reviewed journals, where EEG was recorded for an interval of milliseconds prior to event-related potentials that did not provide sufficient description of the sample and results, or that did not explicitly investigate EEG power.Applying these criteria, 22 studies remained in the analysis. All investigated the alpha frequency band, the number of studies considering other frequency bands was lower (theta and beta: 19, delta: 17 and gamma: 7). In 64% of these studies, variation of EEG power in the alpha frequency band was observed, while in 36% no effect was observed. However, of the 14 studies that showed an effect, 10 observed an increase in alpha power while four observed a decrease. All other frequency bands were also affected in at least in one (theta) up to seven (beta band) studies. As for the alpha frequency band, increases and decreases in the band specific power were observed (delta and beta). Danker-Hopfe *et al.* (2019) described in detail how various factors (e.g., age, sex, individual basic EEG rhythm, recording of the EEG in an eyes open or an eyes closed condition, topographic aspects, control of vigilance, control of consumption of stimulating substances) affect the EEG. Furthermore, technical aspects of EEG recording (e.g., control of EMF interferences between the recording device and the electromagnetic field, when EEG is measured during exposure) and evaluation might affect EEG parameters. Finally, Danker-Hopfe *et al.* (2019) described how these factors as well as methods of statistical evaluation differ between studies.

Similarly to Wallace and Selmaoui (2019), Danker-Hopfe *et al.* (2019) emphasised that heterogeneous study protocols and different methodologies prevent a scientifically sound statement on the impact of RF EMF on human brain activity in the resting-state EEG. As in SCENIHR (2015), both studies strongly recommended more standardised study protocols that follow basic quality criteria in further research.

Sleep

With regard to RF EMF exposure effects on sleep, SCENIHR (2015) concluded that half of the studies looking at the macrostructure of sleep (especially those with a longer duration of exposure) observed effects. However, the results were not consistent with regard to the affected sleep parameters. Studies investigating effects of RF EMF exposure on the power spectra of the sleep EEG are quite heterogeneous with regard to several factors, e.g. the applied field, the duration of exposure, the timing of exposure (prior to or during sleep), the number of considered EEG leads, control of electromagnetic interference, the affected

frequency band, the affected sleep stage, and time frames of investigation (e.g. whole night, first 20 or 30 min of NREM sleep or NREM stage 2 sleep, first or later sleep cycles, 4th NREM episode). Furthermore, studies vary with regard to statistical analysis. Effect sizes and/or a priori sample size calculations are usually not reported. Given all these heterogeneities, SCENIHR (2015) concluded that it was not possible to derive firm conclusions on RF EMF effects on sleep.

No meta-analysis or systematic literature review were published. The Health Council of the Netherlands (2020b) identified 18 human sleep studies (all refer to the 700 – 2200 MHz frequency range). Three investigated effects of a mobile phone base station signal, two of them observed an effect. Of 15 studies, that investigated effects of mobile phone exposure (healthy adults: 13, patients: two), nine found an effect, including one study in patients. This review does not differentiate between effects on the macro- and the microstructure of sleep. It was not possible to clearly classify any of the studies that observed a RF EMF exposure effect on sleep as either favourable or unfavourable. Animal studies

Similar to human studies, systematic reviews are very rare.

Sienkiewicz and van Rongen (2019) published a systematic review of 62 animal (rodent) studies related to spatial learning and place memory. A total of 17 papers were excluded, primarily due to improper description of exposure or missing dosimetry. Overall, the remaining 45 reviewed studies between 1993 and 2017 are highly heterogenous. Morris water maze test was mostly used (66 %), followed by radial arm maze (27%) and others. No consistent outcome was seen. Both impairments (21) and no effects (20) were demonstrated, and four studies reported behavioural improvements. The range of frequencies included 900, 1800 and 2450 MHz, continuous and pulsed fields, and the wbSARs were in the range of 0.1 mW/g up to >10W/kg.

The Health Council of the Netherlands (2020b) classified the outcome of experimental animal studies as those with *no effect*, *unfavourable effect,* and *favourable effect.* In addition, excluded studies were listed and the reason for exclusion given. The three frequency ranges 700-2200 MHz, 2.2-5.0 GHz, and 20-40 GHz were discriminated but papers for the 20-40 GHz were not found. Neurological and neurobehavioural effects were divided in six subcategories.

1) Behavioural studies tested explorative behaviour, recognition of objects, anxiety and effects on learned behaviour. The Health Council concluded that an effect is possible for both frequency ranges of 700-2200 MHz, 2.2-5.0 GHz.
2) Cognitive studies looked at effects on memory, reaction speed and responsiveness. It was concluded that both favourable or unfavourable effects are possible for 700-2200 MHz, 2.2-5.0 GHz.
3) Brain neurotransmission. An effect is possible for both frequency ranges.
4) Brain electrical activity. The Health Council concluded that for 700-2200 MHz a (favourable or unfavourable) effect is likely, and is possible for 2.2-5.0 GHz.
5) Blood brain barrier (BBB) is protecting the brain against harmful substances in the blood. For both frequency ranges an effect is possible.
6) Neurodegeneration. It was concluded that effects are possible for 700-2200 MHz.

Summarising, the Opinion of SCENIHR (2015) still holds true that the weight of evidence for neurobehavioural findings in animal studies is uncertain and replication studies should be performed under much more stringent conditions (exposure and dosimetry, blinding, controls).

5.3.2.3 Conclusions on neurological and neurobehavioural effects

There is only limited evidence from meta-analyses on human studies concerning cognitive function.

Electrophysiological effects on the EEG spectra repeatedly appear in studies but they show contradictory results (either increasing or reducing the EEG power). However, there are

methodological issues that need to be taken into consideration before reaching a conclusion about potential health effects. Such issues include (a) the effect of multiple testing, which is or can be particularly high in EEG studies depending on the number of electrodes considered and whether the analysis is based on EEG frequency bands or bins; (b) the high physiological variability of EEG power spectra, e.g., within a day or with intake of activating substance like caffeinated beverages; and (c) the lack of strictly standardised protocols. Therefore, it is suggested to include a negative control, e.g., analysis of differences between two sham conditions. So far, the physiological variations observed under RF EMF exposure for some of the outcome parameters (which may constitute a potential biological effect) do not indicate any adverse health effect.

Recent studies emphasise that heterogeneous study protocols and different methodologies prevent a scientifically sound statement on the impact of RF-EMF on human brain activity, in the resting-state EEG as one example. SCHEER conclusions are based on a small number of reviews, one of which is the review by the Health Council of the Netherlands (2020a, 2020b). As in SCENIHR (2015), recommendations of more standardised study protocols that follow basic quality criteria are needed in further research.

Across the various studies (and meta reviews considered), it is clear that there is a wide heterogeneity in findings both within and across studies, including differences in the protocols, sample size, etc. A systematic review on effects of exposure to radiofrequency electromagnetic fields on cognitive performance in human experimental studies was one of the systematic reviews commissioned recently by WHO (see section 4.2.3).

For animal studies the Opinion of SCENIHR (2015) still holds true that the weight of evidence for neurobehavioural findings is uncertain and replication studies should be performed under much more stringent conditions (exposure and dosimetry, blinding, controls).

Thus, in the interim, the SCHEER cannot update the original SCENIHR (2015) conclusions but looks forward to the new systematic WHO review.

5.3.3 Symptoms

Schmiedchen *et al.* (2019) published a systematic review to evaluate methodological limitations in experimental studies on symptom development in IEI-EMF individuals. They included blinded experimental studies that exposed individuals with IEI-EMF to different EMF exposure levels and queried the development of symptoms during or after each exposure trial. The exposure in the studies surveyed was not limited to RF EMF but included ELF electric and/or magnetic fields. The most common limitations were related to the selection of study participants, the counterbalancing of the exposure sequence and the effectiveness of blinding. Many studies further lacked statistical power estimates. The authors noted that methodically sound studies indicated that an effect of exposure was unlikely, and that, overall, the evidence pointed towards no effect of exposure.

A study in Taiwan performed by Huang *et al.* (2018), which also includes a survey of the international literature, has reported that on the basis of a sample of 3303 participants, the prevalence rate of IEI-EMF in Taiwan declined from 13.3% to 4.6% over a period of 5 years. The literature review also found the prevalence rates in other countries to be decreasing instead of increasing as had been predicted previously. The meta-analysis of the data from the literature showed that women were more likely to have IEI-EMF than men, with an odds ratio of 1.19 (95% CI: 1.01-1.40).

Leszczynski (2021) published a review of the scientific evidence on the individual sensitivity to EMF, in which he included both provocation and observational (survey) studies, although cross-sectional observational studies cannot provide evidence for causality between subjective or objective symptoms and exposure to EMF. Moreover, the review does not provide the criteria use for literature selection or a description of the methodological approach for reviewing the studies that were eventually selected. Leszczynski (2021) concludes that most of the studies did not find any causal link between

EMF and electromagnetic hypersensitivity (EHS), at least as far as acute effects were concerned, since the studies "did not have capability to examine delayed EMF responses". The author identifies several methodological shortcomings of the hitherto studies and proposes the use of both subjective symptoms and objective biomarkers to research for causality "because the scientific research data is of insufficient quality to be used as a proof of the lack of causality" (between EMF exposure and EHS).

5.3.3.1 Conclusions on symptoms

SCENIHR (2015) concluded that the results from multiple double-blind provocation studies gave a strong overall weight of evidence that such effects are not caused by RF exposure, and that the evidence from observational studies weighed against a causal effect between EMF exposure and non-specific symptoms (IEI-EMF). The SCHEER finds that this conclusion is still valid. Given the methodological limitations of the research in this area so far, the SCHEER is of the opinion that future research should always include objective measures (physical/biochemical/biological markers) of the response to EMF exposure together with other types of psychological measures or subjective reports.

5.3.4 Other health effects

5.3.4.1 Cardiovascular diseases

A meta-analysis that investigated the effects of using a GSM900 mobile phone on heart rate variability (HRV) has concluded that the minutes of exposure (minutes of speaking on the mobile phone) do not affect the autonomic nervous system of the heart or its sympathovagal balance (Geronikolou *et al.*, 2018). This result is in agreement with the conclusion of the review conducted by the Health Council of the Netherlands (2020a, 2020b) that no effects of exposure to radiofrequency electromagnetic fields on the cardiovascular system and the autonomic nervous system have been found in the frequency range of 700-2200 MHz.

The SCHEER is of the opinion that there is strong evidence for the lack of effects on the cardiovascular system in the above frequency range (700-2200 MHz), but weighing of evidence is not possible for other frequencies of RF EMF.

5.3.4.2 Immune System

The immune system is a complex network of special cells, tissues, organs, and the substances they produce that, through a series of steps called the immune response, work together in fighting infections and other diseases. This network allows the immune system to keep its dynamic equilibrium through activating and inhibitory signals and, at the same time, to adapt the response to environmental hints. A healthy immune system permits the organism to interact with the environment in a safe way, keeping invading agents under control.

There are no systematic reviews or meta-analysis available in the literature to determine whether RF EMF exposure may affect immune system. Narrative reviews with robust methodological design are also lacking.

In 2013, a review paper was published by Szmigielski in which the effects of *in vitro* and *in vivo* exposure to RF fields on several immune functions such as phagocytosis, lymphocyte proliferation and antibodies production were discussed. The general conclusion of the author was that in both *in vitro* and *in vivo* studies RF exposure may induce measurable weak effects in the number and/or activity of immune-competent cells. However, the results were incoherent (for instance, a number of lymphocyte functions resulted in being both enhanced and weakened under similar RF exposure conditions within single studies) and difficult to replicate. The author also pointed out the existence of certain indications of a temporary immunological stimulation after short term RF exposure, while prolonged exposure inhibited the same functions, although not substantiated by threshold effects (Szmigielski, 2013).

A review paper (Piszczek *et al.*, 2021) was recently published which reports on immunity and electromagnetic fields including RF. The authors focused on both *in vivo* and *in vitro* studies reporting on the effects on immune cell types involved in the innate and adaptive immunity. The general conclusion of the authors was that RF seems to be a promising tool for modulation of immune cell signaling pathways, although it is not possible to indentify an intracellular mechanism.

Both of the above review papers, however, lack the criteria for literature selection and characterisation of methodological quality of the individual included studies.

There are also several papers in the literature reporting the enhancement of immune system after millimetre-wave exposure. These papers are included in a couple of review articles in which the advantages of millimetre-waves therapy, which is widely used for the treatment of several diseases in many Eastern European countries, are highlighted. In these papers, the modulation of the immune system is mentioned as a plausible mechanism by which millimetre-waves can produce systemic whole-body effects after localized application. As a matter of fact, components of the immune system are present in the dermis portion of the skin and are, thus, accessible to millimetre-waves, at least at locations where the epidermis is thin and subcutaneous fat is sparse. Furthermore, millimetre-waves therapy, when used in combination with chemotherapy, is capable of protecting the immune system from the toxicity of chemotherapy without exerting toxicity of its own. Moreover, it has also been shown that the combination of millimetre-waves and chemotherapy is capable of reducing the tumour metastasis and tumour resistance to chemotherapeutic drugs (Logani *et al.*, 2011; Mattsson *et al.*, 2018).

Therefore, the SCHEER finds that the weight of evidence for any (beneficial and detrimental) effects of RF EMF on the immune system is uncertain due to the conflicting information from various studies.

5.3.4.3 Reproductive and Developmental effects

In accordance with the PRISMA guidelines, Kim *et al.* (2021) conducted a systematic review and a meta-analysis to determine whether the exposure to RF EMF affects human sperm quality. The outcome considered were motility, viability, and concentration, which are the most frequently used parameters in clinical settings to assess fertility. The authors evaluated 18 studies that included 4280 samples. They found that exposure to mobile phones was associated with reduced sperm motility, viability, and concentration, but the decrease in sperm quality after RF EMF exposure was not significant, even when the mobile phone usage increased. However, the SCHEER notes that many of the studies included in the meta-analysis did not provide adequate information on dosimetry. Moreover, at least one study was included in the meta-analysis that had been excluded from risk assessment in the SCENIHR (2015) Opinion due to methodological/quality issues. The same problem, of including in the analysis studies with insufficient dosimetry, uncontrolled exposure, and other methodological problems (some of these studies had been excluded from or criticised in the SCENIHR (2015) Opinion), exists for the other reviews scoping the impact of RF EMF exposure on the male reproductive system (Jaffar *et al.*, 2019; Maluin *et al.*, 2021; Sciorio *et al.*, 2022). Nevertheless, it should be noted that Sciorio *et al.* (2022) comprehensively present the limitations of the studies on RF EMF exposure and the reproductive system, like controlling confounders, assessing exposure, and using standardised methods for sperm analysis.

On the issue of male reproductive hormones, Maluin *et al.* (2021) concluded that existing animal and human data on the effect of RF EMF emitted from wireless devices on male reproductive hormones were inconsistent and difficult to evaluate due to the heterogeneity of study design. However, according to the authors, most studies were consistent with the assertion that long-term exposure to RF EMR from mobile phones and Wi-Fi devices could disrupt male reproductive hormones, particularly testosterone.

In these reviews (Jaffar *et al.*, 2019; Kim *et al.*, 2021) two potential mechanisms are mentioned for the effect of RF EMF on the reproductive system: tissue heating and

oxidative stress. However, Santini et al. (2018), in their scoping review about oxidative stress caused by EMF on both the female and the male reproductive systems, conclude that based on the current literature, the analysis of ELF-EMF and RF impact on the maintenance of male and female fertility potential reports contradictory results. The authors suggest that the main reason for these discrepancies may be the lack of uniformity in the experimental design, including the use of different models and the extremely variable exposure sources and protocols. Moreover, since ROS levels can be influenced by temperature, a possible criticism to many of these works is the lack of control of this parameter during EMF exposure. A further criticism emerging from the literature is the difficulty to understand whether EMF-induced fertility abnormalities are caused by direct gonadal damage or by disruption of the hypothalamic-pituitary-gonadal axis. On the other hand, the authors see growing evidence that damage induced by EMF to reproductive cells and organs is caused by deregulation of redox homeostasis due mitochondrial dysfunctions and ROS overproduction.

Mahaldashtian *et al.* (2022) reviewed the literature on the effect of cell phone radiation on mammalian embryos and foetuses and concluded that it is difficult from the available animal studies to confidently document the role of RF EMF exposure on human embryo development, both *in vivo* and *in vitro*. The SCHEER agrees with general methodological limitations of studies about developmental effects of RF EMF identified by the authors, but notes that they had included in their review studies with insufficient dosimetry, uncontrolled exposure, and other methodological problems.

The meta-analyses and reviews available since the SCENIHR (2015) Opinion show that the weight of evidence for reproduction and developmental effects is uncertain, due to conflicting information.

5.3.4.4 Auditory and thermoelastic effects

Electromagnetic waves can be seen in the frequency range of visible light, but they can also be heard, if they are pulsed. Initially, the auditory perception of microwave pulses was thought to be an interaction of pulsed radiation directly with the auditory nerves or neurons along the auditory neurophysiological pathways of the central nervous system. However, experimental and theoretical studies have shown that 'microwave hearing' (aka 'microwave auditory effect' or 'Frey effect') arises from the thermoelastic theory: Microwave pulses, upon absorption by soft tissues in the head, launch a thermoelastic wave of acoustic pressure that travels by bone conduction to the inner ear, where it activates the cochlear receptors via the same process involved in normal hearing (Lin and Wang, 2007; Lin, 2022).

Microwave hearing is an acute effect and occurs for as long as the head of a subject is exposed to pulsed RF EMF of specific frequency and pulse width. In the previous ICNIRP guidelines (ICNIRP, 1998) constraints had been imposed to the specific absorption from pulses to avoid microwave auditory effects, since "repeated or prolonged exposure to microwave auditory effects may be stressful and potentially harmful". In the latest ICNIRP guidelines (ICNIRP, 2020), a specific restriction to account for microwave hearing is not considered because "there is no evidence that microwave hearing in any realistic exposure scenarios can affect health". However, in a study about rigger safety in the telecommunications industry (Boulais, 2016), about 75% of the riggers who had experienced the microwave effect reported it as a distraction: as explained in the study, such a distraction poses an occupational risk that may result in indirect health damage.

Moreover, recently, there has been a discussion whether pulsed RF EMF can be weaponised (Lin, 2021; Dagro *et al.*, 2021; Foster *et al.*, 2021; Lin, 2022) to create a health syndrome with clinical symptoms resembling those of concussion. According to Foster *et al.* (2021), existing microwave systems can produce pulses with sufficient fluence to induce unexpected and perhaps frightening auditory sensations, but the equipment is large, e.g., the obsolete AN/FPS-67B radar system at 1.3 GHz. On the other hand, millimetre waves equipment is smaller and can be located close to a subject, allowing higher exposure levels

than those considered by Dagro *et al.* (2021), if the problem of shallower penetration can be overcome. Dagro *et al.* (2021) conclude that the required power densities to induce neuropathological effects to the brain are orders of magnitude larger than most real-world exposure conditions, but can be achieved with devices meant to emit high-power electromagnetic pulses in military and research applications.

The SCHEER is of the opinion that, although the power densities necessary to induce brain damage with pulsed RF EMF are feasible with current technology, they are unlikely to occur in a real-life exposure situation. However, pulsed RF EMF can induce microwave hearing, causing distraction in occupational settings that may jeopardize occupational safety. Therefore, occupational training of RF workers should include awareness about the microwave hearing effect and its management.

6 RECOMMENDATIONS FOR FUTURE WORK

The SCHEER welcomes the development of a number of WHO protocols for systematic reviews that will strengthen the level of evidence about health effects from RF EMF exposure. The SCHEER suggests that any future policy changes on the matter of EMF health effects should consider the conclusions of the systematic reviews that will result from these protocols.

There is a need for more research in the higher frequency bands of the RF spectrum (*i.e.*, millimetre waves) and their adverse, beneficial or lack of health effects.

Additional hypothesis-driven experiments on the interaction mechanisms of RF EMF (other than tissue heating) are necessary, but under strict methodological quality criteria about experimental design, exposure control and assessment, statistics and results analysis. The SCHEER notes that several experimental studies have been considered in meta-analyses and reviews, although they had not fulfilled these criteria.

The methodological limitations of the research performed in the area of symptoms call for the inclusion of objective measures (physical/biochemical/biological markers) of the response to EMF exposure, together with other types of psychological measures or subjective reports.

7 REFERENCES

Adair, E. R., & Petersen, R. C. (2002). Biological effects of radiofrequency/microwave radiation. IEEE Transactions on Microwave Theory and Techniques, 50(3), 953-962. https://doi.org/10.1109/22.989978

Aerts, S., Verloock, L., Van den Bossche, M., Martens, L., Vergara, X., & Joseph, W. (2019). Emissions From Smart Meters and Other Residential Radiofrequency Sources. Health physics, 116(6), 776–788. https://doi.org/10.1097/HP.0000000000001032

Al-Falahy, N. F. A., & Alani, O. Y. K. (2017). Potential technologies to 5G network: challenges and opportunities. IT Profesional, 19(1), 12-20. http://dx.doi.org/10.1109/MITP.2017.9

Al Hajj, M., Wang, S., Thanh Tu, L., Azzi, S., & Wiart, J. (2020). A Statistical Estimation of 5G Massive MIMO Networks' Exposure Using Stochastic Geometry in mmWave Bands. Applied Sciences, 10(23), 8753. https://doi.org/10.3390/app10238753

Aydin, D., Feychting, M., Schüz, J., Andersen, T. V., Poulsen, A. H., Prochazka, M., Klæboe, L., Kuehni, C. E., Tynes, T., & Röösli, M. (2011). Predictors and overestimation of recalled mobile phone use among children and adolescents. Progress in Biophysics and Molecular Biology, 107(3), 356-361. https://doi.org/10.1016/j.pbiomolbio.2011.08.013

Baracca, P., Weber, A., Wild, T., & Grangeat, C. (2018). A Statistical Approach for RF Exposure Compliance Boundary Assessment in Massive MIMO Systems. WSA 2018; 22nd International ITG Workshop on Smart Antennas, pp. 1-6.

Belpoggi, F., Falcioni, L., Panzacchi, S., Sgargi, D., & Mandrioli, D. (2021). Response to "Cancerogenic effects of radiofrequency radiation: A statistical reappraisal". Environmental research, 197, 111067. https://doi.org/10.1016/j.envres.2021.111067

Beratende Expertengruppe Nichtionisierende Strahlung (BERENIS) (2018). Newsletter BERENIS (Swiss expert group on electromagnetic fields and non-ionising radiation) - Special Issue November 2018. Evaluation of the NTP and Ramazzini studies. Available at: bafu.admin.ch/bafu/en/home/topics/electrosmog/newsletter-of-the-swiss-expert-group-on-electromagnetic-fields-a.html. Accessed on Jan. 7, 2022.

Birks, L. E., van Wel, L., Liorni, I., Pierotti, L., Guxens, M., Huss, A., Foerster, M., Capstick, M., Eeftens, M., el Marroun, H., Estarlich, M., Gallastegi, M., Safont, L. G., Joseph, W., Santa-Marina, L., Thielens, A., Torrent, M., Vrijkotte, T., Wiart, J., … Vrijheid, M. (2021). Radiofrequency electromagnetic fields from mobile communication: Description of modeled dose in brain regions and the body in European children and adolescents. Environmental Research, 193. https://doi.org/10.1016/j.envres.2020.110505

Bonato, M., Dossi, L., Chiaramello, E., Fiocchi, S., Tognola, G., & Parazzini, M. (2021). Stochastic Dosimetry Assessment of the Human RF EMF Exposure to 3D Beamforming Antennas in indoor 5G Networks. Applied Sciences, 11(4), 1751. https://doi.org/10.3390/app11041751

Bortkiewicz, A., Gadzicka, E., & Szymczak, W. (2017). Mobile phone use and risk for intracranial tumors and salivary gland tumors - A meta-analysis. International Journal of Occupational Medicine and Environmental Health, 30(1), 27–43. https://doi.org/10.13075/ijomeh.1896.00802

Bosch-Capblanch, X., Esu, E., Dongus, S., Oringanje, C. M., Jalilian, H., Eyers, J., Oftedal, G., Meremikwu, M., & Röösli, M. (2022). The effects of radiofrequency electromagnetic fields exposure on human self-reported symptoms: A protocol for a systematic review of human experimental studies. Environment international, 158, 106953. https://doi.org/10.1016/j.envint.2021.106953

Boulais, D. (2016). Microwave Hearing Effect: Rigger Safety in the Telecommunications Industry. Prof. Safety, 61(07): 26–30.

Brzozek, C., Abramson, M. J., Benke, G., & Karipidis, K. (2021). Comment on choi *et al.* Cellular phone use and risk of tumors: Systematic review and meta-analysis. int. j. environ. res. public health 2020, 17, 8079. International Journal of Environmental Research and Public Health, 18(10), 10–13. https://doi.org/10.3390/ijerph18105459

Brzozek, C., Benke, K. K., Zeleke, B. M., Abramson, M. J., & Benke, G. (2018). Radiofrequency Electromagnetic Radiation and Memory Performance: Sources of Uncertainty in Epidemiological Cohort Studies. International journal of environmental research and public health, 15(4), 592. https://doi.org/10.3390/ijerph15040592

Capstick, M., Kuster, N., Kuehn, S., Berdinas-Torres, V., Gong, Y., Wilson, P., Ladbury, J., Koepke, G., McCormick, D. L., Gauger, J., & Melnick, R. L. (2017). A Radio Frequency Radiation Exposure System for Rodents based on Reverberation Chambers. IEEE transactions on electromagnetic compatibility, 59(4), 1041–1052. https://doi.org/10.1109/TEMC.2017.2649885

Cassien, M., Tassistro, V., Culcasi, M., Ricquebourg, E., Thétiot-Laurent, S., Mercier, A., Orsière, T., & Pietri, S. (2015). Oxidative stress and DNA damages induced by 1-nitropyrene in human lung fibroblasts: New insights into the mechanisms of genotoxicity and EPR-spin trapping direct monitoring of free radicals at subcellular levels. Toxicology Letters, 238(2), S318.

Chiaraviglio, L., Di Paolo, C., & Blefari Melazzi, N. (2021). 5G Network Planning under Service and EMF Constraints: Formulation and Solutions. IEEE Transactions on Mobile Computing, early access. https://doi.org/10.1109/TMC.2021.3054482

Choi, Y. J., Moskowitz, J. M., Myung, S. K., Lee, Y. R., & Hong, Y. C. (2020). Cellular phone use and risk of tumors: Systematic review and meta-analysis. International Journal of Environmental Research and Public Health, 17(21), 1–21. https://doi.org/10.3390/ijerph17218079

Curcio G. (2018). Exposure to Mobile Phone-Emitted Electromagnetic Fields and Human Attention: No Evidence of a Causal Relationship. Frontiers in public health, 6, 42. https://doi.org/10.3389/fpubh.2018.00042

Dagro, A. M., Wilkerson, J. W., Thomas, T. P., Kalinosky, B. T., & Payne, J. A. (2021). Computational modeling investigation of pulsed high peak power microwaves and the potential for traumatic brain injury. Science advances, 7(44), eabd8405. https://doi.org/10.1126/sciadv.abd8405

Dangi, R., Lalwani, P., Choudhary, G., You, I., & Pau, G. (2022). Study and Investigation on 5G Technology: A Systematic Review. Sensors, 2(1):26. https://doi.org/10.3390/s22010026

Danker-Hopfe, H., Eggert, T., Dorn, H., & Sauter, C. (2019). Effects of RF-EMF on the Human Resting-State EEG-the Inconsistencies in the Consistency. Part 1: Non-Exposure-Related Limitations of Comparability Between Studies. Bioelectromagnetics, 40(5), 291–318. https://doi.org/10.1002/bem.22194

de Vocht, F., & Röösli, M. (2021). Comment on Choi, Y.-J., *et al.* cellular phone use and risk of tumors: Systematic review and meta-analysis. Int. J. Environ. Res. Public Health 2020, 17, 8079. In International Journal of Environmental Research and Public Health (Vol. 18, Issue 6, pp. 1–4). MDPI AG. https://doi.org/10.3390/ijerph18063125

de Seze, R., Poutriquet, C., Gamez, C., Maillot-Maréchal, E., Robidel, F., Lecomte, A., & Fonta, C. (2020). Repeated exposure to nanosecond high power pulsed microwaves increases cancer incidence in rat. *PloS one*, *15*(4), e0226858. https://doi.org/10.1371/journal.pone.0226858

de Siqueira, E. C., de Souza, F., Gomez, R. S., Gomes, C. C., & de Souza, R. P. (2017). Does cell phone use increase the chances of parotid gland tumor development? A systematic review and meta-analysis. Journal of oral pathology & medicine: official

publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology, 46(7), 480–483. https://doi.org/10.1111/jop.12531

Elwood, M., & Wood, A. W. (2019). Animal studies of exposures to radiofrequency fields. *The New Zealand medical journal*, *132*(1506), 98–100.

Ericsson (2018). EMF test report: Ericsson AIR 5121. Tech. Rep. Ericsson. Available at https://fccid.io/TA8AKRD901059-1/RF-Exposure-Info/RF-Exposure-information-3845517.pdf

Falcioni, L., Bua, L., Tibaldi, E., Lauriola, M., De Angelis, L., Gnudi, F., Mandrioli, D., Manservigi, M., Manservisi, F., Manzoli, I., Menghetti, I., Montella, R., Panzacchi, S., Sgargi, D., Strollo, V., Vornoli, A., & Belpoggi, F. (2018). Report of final results regarding brain and heart tumors in Sprague-Dawley rats exposed from prenatal life until natural death to mobile phone radiofrequency field representative of a 1.8 GHz GSM base station environmental emission. Environmental research, 165, 496–503. https://doi.org/10.1016/j.envres.2018.01.037

Feil, R., Fraga, M. (2021). Epigenetics and the environment: emerging patterns and implications. Nat Rev Genet 13, 97–109. https://doi.org/10.1038/nrg3142

Food and Drug Administration (FDA) (2020). Review of published literature between 2008 and 2018 of relevance to radiofrequency radiation and cancer. Available at: www.fda.gov/media/135043/download. Accessed on Jan. 7, 2022.

Foster, K. R., Ziskin, M. C., Balzano, Q., & Hirata A. (2018). Thermal analysis of averaging times in radio-frequency exposure limits above 1 GHz. IEEE Access, 6, 74536–74546. https://doi.org/10.1109/ACCESS.2018.2883175

Foster, K. R., Garrett, D. C., & Ziskin, M. C. (2021). Can the Microwave Auditory Effect Be "Weaponized"?. Frontiers in public health, 9, 788613. https://doi.org/10.3389/fpubh.2021.788613

Garofalo, S., Stefano, M., Mariagrazia, B., & Paola, T. (2020). Cancerogenic effects of radiofrequency radiation: A statistical reappraisal. Environmental research, 191, 110233. https://doi.org/10.1016/j.envres.2020.110233

Geronikolou, S.A., Johansson, Ö., Chrousos, G., Kanaka-Gantenbein, C., & Cokkinos, D. (2020). Cellular Phone User's Age or the Duration of Calls Moderate Autonomic Nervous System? A Meta-Analysis. In: Vlamos, P. (eds) GeNeDis 2018. Advances in Experimental Medicine and Biology, vol 1194. Springer, Cham. https://doi.org/10.1007/978-3-030-32622-7_46

Goedhart, G., Kromhout, H., Wiart, J., & Vermeulen, R. (2015). Validating self-reported mobile phone use in adults using a newly developed smartphone application. Occupational and Environmental Medicine, 72(11), 812–818. https://doi.org/10.1136/oemed-2015-102808

Goedhart, G., van Wel, L., Langer, C. E., de Llobet Viladoms, P., Wiart, J., Hours, M., Kromhout, H., Benke, G., Bouka, E., Bruchim, R., Choi, K. H., Eng, A., Ha, M., Huss, A., Kiyohara, K., Kojimahara, N., Krewski, D., Lacour, B., 't Mannetje, A., … Vermeulen, R. (2018). Recall of mobile phone usage and laterality in young people: The multinational Mobi-Expo study. Environmental Research, 165(April), 150–157. https://doi.org/10.1016/j.envres.2018.04.018

Gong, Y., Capstick, M., Kuehn, S., Wilson, P., Ladbury, J., Koepke, G., McCormick, D. L., Melnick, R. L., & Kuster, N. (2017). Life-Time Dosimetric Assessment for Mice and Rats Exposed in Reverberation Chambers of the 2-Year NTP Cancer Bioassay Study on Cell Phone Radiation. IEEE transactions on electromagnetic compatibility, 59(6), 1798–1808. https://doi.org/10.1109/TEMC.2017.2665039

Halgamuge, M. N., Skafidas, E., & Davis, D. (2020). A meta-analysis of *in vitro* exposures to weak radiofrequency radiation exposure from mobile phones (1990-2015). Environmental research, 184, 109227. https://doi.org/10.1016/j.envres.2020.109227

Hardell, L., Carlberg, M., Söderqvist, F., & Mild, K. H. (2013). Pooled analysis of case-control studies on acoustic neuroma diagnosed 1997-2003 and 2007-2009 and use of mobile and cordless phones. International journal of oncology, 43(4), 1036–1044. https://doi.org/10.3892/ijo.2013.2025

Hardell, L., & Carlberg, M. (2015). Mobile phone and cordless phone use and the risk for glioma - Analysis of pooled case-control studies in Sweden, 1997-2003 and 2007-2009. Pathophysiology : the official journal of the International Society for Pathophysiology, 22(1), 1–13. https://doi.org/10.1016/j.pathophys.2014.10.001

Health Council of the Netherlands. (2020a). 5G and health. The Hague: Health Council of the Netherlands, 2020; publication no. 2020/16e.

Health Council of the Netherlands. (2020b). Background document to the advisory report 5G and health. Background document to 5G and health. The Hague: Health Council of the Netherlands, 2020; publication no. 2020/16Ae

Henschenmacher, B., Bitsch, A., de las Heras Gala, T., Forman, H. J., Fragoulis, A., Ghezzi, P., Kellner, R., Koch, W., Kuhne, J., Sachno, D., Schmid, G., Tsaioun, K., Verbeek, J., & Wright, R. (2022). The effect of radiofrequency electromagnetic fields (RF EMF) on biomarkers of oxidative stress *in vivo* and *in vitro*: A protocol for a systematic review. Environment International, 158, 106932. https://doi.org/10.1016/J.ENVINT.2021.106932

Hirata, A., *et al.* (2021). Assessment of Human Exposure to Electromagnetic Fields: Review and Future Directions. IEEE Transactions on Electromagnetic Compatibility, 63(5), 1619-1630. https://doi.org/10.1109/TEMC.2021.3109249

Hirata, A., Kodera, S., Sasaki, K., Gomez-Tames, J., Laakso, I., Wood, A., Watanabe, S., & Foster, K. R. (2021). Human exposure to radiofrequency energy above 6 GHz: review of computational dosimetry studies. Physics in medicine and biology, 66(8). https://doi.org/10.1088/1361-6560/abf1b7

Huang, P. C., Cheng, M. T., & Guo, H. R. (2018). Representative survey on idiopathic environmental intolerance attributed to electromagnetic fields in Taiwan and comparison with the international literature. Environmental health: a global access science source, 17(1), 5. https://doi.org/10.1186/s12940-018-0351-8

International Agency for Research on Cancer (IARC) (2019) IARC Monographs on the Identification of Carginogenic Hazards to Humans - Preamble. In International Agency for Research on Cancer: Lyon, France. p 41. https://monographs.iarc.who.int/wp-content/uploads/2019/07/Preamble-2019.pdf

International Commission on Non-Ionizing Radiation Protection (ICNIRP) (1998) Guidelines for limiting exposure to time-varying electric, magnetic and electromagnetic fields (up to 300 GHz). Health Physics, 74(4), 494-522.

International Commission on Non-Ionizing Radiation Protection (ICNIRP) (2020a) Guidelines for limiting exposure to electromagnetic fields (100 kHz to 300 GHz). Health Physics 118(5):483–524. https://doi.org/10.1097/HP.0000000000001210

International Commission on Non-Ionizing Radiation Protection (ICNIRP) (2020b) ICNIRP Note: Critical Evaluation of Two Radiofrequency Electromagnetic Field Animal Carcinogenicity Studies Published in 2018. Health physics, 118(5), 525–532. https://doi.org/10.1097/HP.0000000000001137

Jaffar, F., Osman, K., Ismail, N. H., Chin, K. Y., & Ibrahim, S. F. (2019). Adverse Effects of Wi-Fi Radiation on Male Reproductive System: A Systematic Review. The Tohoku journal of experimental medicine, 248(3), 169–179. https://doi.org/10.1620/tjem.248.169

Jagetia G. C. (2022). Genotoxic effects of electromagnetic field radiations from mobile phones. Environmental research, 212(Pt D), 113321. https://doi.org/10.1016/j.envres.2022.113321

Jalilian, H., Eeftens, M., Ziaei, M., & Röösli, M. (2019). Public exposure to radiofrequency electromagnetic fields in everyday microenvironments: An updated systematic review for Europe. Environmental research, 176, 108517. https://doi.org/10.1016/j.envres.2019.05.048

Karipidis, K., Mate, R., Sanagou, M., Brzozek, C., Urban, D., & Elwood, M. (2021). Mobile phone use and trends in the incidence of cancers of the parotid and other salivary glands. Cancer epidemiology, 73, 101961. https://doi.org/10.1016/j.canep.2021.101961

Karipidis, K., Mate, R., Urban, D., Tinker, R., & Wood, A. (2021). 5G mobile networks and health-a state-of-the-science review of the research into low-level RF fields above 6 GHz. Journal of exposure science & environmental epidemiology, 31(4), 585–605. https://doi.org/10.1038/s41370-021-00297-6

Kim, S., Han, D., Ryu, J., Kim, K., & Kim, Y. H. (2021). Effects of mobile phone usage on sperm quality - No time-dependent relationship on usage: A systematic review and updated meta-analysis. Environmental research, 202, 111784. https://doi.org/10.1016/j.envres.2021.111784

Kocaman, A., Altun, G., Kaplan, A. A., Deniz, Ö. G., Yurt, K. K., & Kaplan, S. (2018). Genotoxic and carcinogenic effects of non-ionizing electromagnetic fields. Environmental research, 163, 71–79. https://doi.org/10.1016/j.envres.2018.01.034

Kuhne, J., Schmidt, J. A., Geschwentner, D., Pophof, B., & Ziegelberger, G. (2020). Thermoregulatory Stress as Potential Mediating Factor in the NTP Cell Phone Tumor Study. Bioelectromagnetics, 41(6), 471–479. https://doi.org/10.1002/bem.22284

Lai, H. (2021). Genetic effects of non-ionizing electromagnetic fields. Electromagnetic Biology and Medicine, 40(2), 264–273. https://doi.org/10.1080/15368378.2021.1881866

Langer, C. E., de Llobet, P., Dalmau, A., Wiart, J., Goedhart, G., Hours, M., Benke, G. P., Bouka, E., Bruchim, R., Choi, K. H., Eng, A., Ha, M., Karalexi, M., Kiyohara, K., Kojimahara, N., Krewski, D., Kromhout, H., Lacour, B., Mannetje, A., … Vrijheid, M. (2017). Patterns of cellular phone use among young people in 12 countries: Implications for RF exposure. Environment International, 107(May), 65–74. https://doi.org/10.1016/j.envint.2017.06.002

Lerchl, A., Klose, M., Grote, K., Wilhelm, A. F., Spathmann, O., Fiedler, T., Streckert, J., Hansen, V., & Clemens, M. (2015). Tumor promotion by exposure to radiofrequency electromagnetic fields below exposure limits for humans. Biochemical and biophysical research communications, 459(4), 585–590. https://doi.org/10.1016/j.bbrc.2015.02.151

Leszczynski D. (2021). Review of the scientific evidence on the individual sensitivity to electromagnetic fields (EHS). Reviews on environmental health, 10.1515/reveh-2021-0038. Advance online publication. https://doi.org/10.1515/reveh-2021-0038

Li, K., Sasaki, K., Watanabe, S., & Shirai, H. (2019). Relationship between power density and surface temperature elevation for human skin exposure to electromagnetic waves with oblique incidence angle from 6 GHz to 1 THz. Physics in medicine and biology, 64(6), 065016. https://doi.org/10.1088/1361-6560/ab057a

Lin, J. C. (2019). The Significance of Primary Tumors in the NTP Study of Chronic Rat Exposure to Cell Phone Radiation [Health Matters]. IEEE Microwave Mag, 20(11), 18-21. https://doi.org/10.1109/MMM.2019.2935361

Lin, J. C. (2021). Sonic health attacks by pulsed microwaves in Havana revisited [Health Matters]. IEEE Microwave Mag, 22(3):71-73. https://doi.org/10.1109/MMM.2020.3044125

Lin, J. C. (2022). The Microwave Auditory Effect. IEEE Journal of Electromagnetics, RF and Microwaves in Medicine and Biology, 6(1), 16-28. https://doi.org/10.1109/JERM.2021.3062826

Lin, J. C., & Wang, Z. (2007). Hearing of microwave pulses by humans and animals: effects, mechanism, and thresholds. Health physics, 92(6), 621–628. https://doi.org/10.1097/01.HP.0000250644.84530.e2

Liorni, I., Capstick, M., van Wel, L., Wiart, J., Joseph, W., Cardis, E., Guxens, M., Vermeulen, R., & Thielens, A. (2020). Evaluation of Specific Absorption Rate in the Far-Field, Near-to-Far Field and Near-Field Regions for Integrative Radiofrequency Exposure Assessment. Radiation protection dosimetry, 190(4), 459–472. https://doi.org/10.1093/rpd/ncaa127

Logani, M. K., Bhopale, M. K., & Ziskin, M. C. (2011). Millimeter Wave and Drug Induced Modulation of the Immune System -Application in Cancer Immunotherapy. J Cell Sci Ther S5:002. https://doi.org/10.4172/2157-7013.S5-002

Maluin, S. M., Osman, K., Jaffar, F., & Ibrahim, S. F. (2021). Effect of Radiation Emitted by Wireless Devices on Male Reproductive Hormones: A Systematic Review. Frontiers in physiology, 12, 732420. https://doi.org/10.3389/fphys.2021.732420

Mattsson, M. O., Zeni, O. & Simkó, M. (2018). Is there a Biological Basis for Therapeutic Applications of Millimetre Waves and THz Waves?. J Infrared Milli Terahz Waves 39, 863–878. https://doi.org/10.1007/s10762-018-0483-5

Melnick R. (2020). Regarding ICNIRP'S Evaluation of the National Toxicology Program's Carcinogenicity Studies on Radiofrequency Electromagnetic Fields. Health physics, 118(6), 678–682. https://doi.org/10.1097/HP.0000000000001268

National Toxicology Program (NTP) (2018a). Toxicology and carcinogenesis studies in Sprague Dawley (Hsd:Sprague Dawley SD) rats exposed to whole-body radio frequency radiation at a frequency (900 MHz) and modulations (GSM and CDMA) used by cell phones. National Toxicology Program technical report series, (595), NTP-TR-595. https://doi.org/10.22427/NTP-TR-595

National Toxicology Program (NTP) (2018b). Toxicology and carcinogenesis studies in B6C3F1/N mice exposed to whole-body radio frequency radiation at a frequency (1,900 MHz) and modulations (GSM and CDMA) used by cell phones. National Toxicology Program technical report series, (596), NTP-TR-596. https://doi.org/10.22427/NTP-TR-596

National Toxicology Program (NTP) (2020). NTP Historical Controls Report, All Routes and Vehicles, Harlan Sprague-Dawley RATS. https://ntp.niehs.nih.gov/ntp/historical_controls/ntp2000_2019/r_hcrpt_allrte20191100.pdf

Neufeld, E., & Kuster, N. (2018). Systematic Derivation of Safety Limits for Time-Varying 5G Radiofrequency Exposure Based on Analytical Models and Thermal Dose. Health physics, 115(6), 705–711. https://doi.org/10.1097/HP.0000000000000930

Neufeld, E., Samaras, T., & Kuster, N. (2020). Discussion on Spatial and Time Averaging Restrictions Within the Electromagnetic Exposure Safety Framework in the Frequency Range Above 6 GHz for Pulsed and Localized Exposures. Bioelectromagnetics, 41(2), 164–168. https://doi.org/10.1002/bem.22244

Ostrom, Q. T., Gittleman, H., Stetson, L., Virk, S. M., & Barnholtz-Sloan, J. S. (2015). Epidemiology of gliomas. Cancer treatment and research, 163, 1–14. https://doi.org/10.1007/978-3-319-12048-5_1

Pacchierotti, F., Ardoino, L., Benassi, B., Consales, C., Cordelli, E., Eleuteri, P., Marino, C., Sciortino, M., Brinkworth, M. H., Chen, G., McNamee, J. P., Wood, A. W., Hooijmans, C. R., & de Vries, R. (2021). Effects of Radiofrequency Electromagnetic Field (RF-EMF) exposure on male fertility and pregnancy and birth outcomes: Protocols for a systematic

review of experimental studies in non-human mammals and in human sperm exposed *in vitro*. Environment international, 157, 106806. https://doi.org/10.1016/j.envint.2021.106806

Paljanos, A., Miclăuș, S., Bechet, P., & Munteanu, C. (2016). Assessment of mobile phone user exposure to UMTS and LTE signals: comparative near-field radiated power levels for various data and voice application services. Journal of Electromagnetic Waves and Applications, 30:9, 1101-1115. https://doi.org/10.1080/09205071.2016.1167634

Piszczek, P., Wójcik-Piotrowicz, K., Gil, K., & Kaszuba-Zwoińska, J. (2021). Immunity and electromagnetic fields. Environmental research, 200, 111505. https://doi.org/10.1016/j.envres.2021.111505

Pophof, B., Burns, J., Danker-Hopfe, H., Dorn, H., Egblomassé-Roidl, C., Eggert, T., Fuks, K., Henschenmacher, B., Kuhne, J., Sauter, C., & Schmid, G. (2021). The effect of exposure to radiofrequency electromagnetic fields on cognitive performance in human experimental studies: A protocol for a systematic review. Environment international, 157, 106783. https://doi.org/10.1016/j.envint.2021.106783

Prasad, M., Kathuria, P., Nair, P., Kumar, A., & Prasad, K. (2017). Mobile phone use and risk of brain tumours: a systematic review of association between study quality, source of funding, and research outcomes. Neurological Sciences, 38(5), 797–810. https://doi.org/10.1007/s10072-017-2850-8

Romeo, S., Zeni, O., Sannino, A., Lagorio, S., Biffoni, M., & Scarfì, M. R. (2021). Genotoxicity of radiofrequency electromagnetic fields: Protocol for a systematic review of *in vitro* studies. Environment international, 148, 106386. https://doi.org/10.1016/j.envint.2021.106386

Romeo, S., Zeni, O., Scarfì, M. R., Poeta, L., Lioi, M. B., & Sannino, A. (2022). Radiofrequency Electromagnetic Field Exposure and Apoptosis: A Scoping Review of *In Vitro* Studies on Mammalian Cells. International journal of molecular sciences, 23(4), 2322. https://doi.org/10.3390/ijms23042322

Röösli, M., Lagorio, S., Schoemaker, M. J., Schüz, J., & Feychting, M. (2019). Brain and Salivary Gland Tumors and Mobile Phone Use: Evaluating the Evidence from Various Epidemiological Study Designs. Annual review of public health, 40, 221–238. https://doi.org/10.1146/annurev-publhealth-040218-044037

Röösli, M., Dongus, S., Jalilian, H., Feychting, M., Eyers, J., Esu, E., Oringanje, C. M., Meremikwu, M., & Bosch-Capblanch, X. (2021). The effects of radiofrequency electromagnetic fields exposure on tinnitus, migraine and non-specific symptoms in the general and working population: A protocol for a systematic review on human observational studies. Environment international, 157, 106852. https://doi.org/10.1016/j.envint.2021.106852

Sagar, S., Dongus, S., Schoeni, A., Roser, K., Eeftens, M., Struchen, B., Foerster, M., Meier, N., Adem, S., & Röösli, M. (2018). Radiofrequency electromagnetic field exposure in everyday microenvironments in Europe: A systematic literature review. Journal of Exposure Science & Environmental Epidemiology, 28(2), 147–160. https://doi.org/10.1038/jes.2017.13

Santini, S. J., Cordone, V., Falone, S., Mijit, M., Tatone, C., Amicarelli, F., & Di Emidio, G. (2018). Role of Mitochondria in the Oxidative Stress Induced by Electromagnetic Fields: Focus on Reproductive Systems. Oxidative medicine and cellular longevity, 2018, 5076271. https://doi.org/10.1155/2018/5076271

Sasaki, Y.F., Sekihashi K., Izumiyama F., Nishidate E., Saga A., Ishida K., Tsuda, S. (2000). The comet assay with multiple mouse organs: comparison of comet assay results and carcinogenicity with 208 chemicals selected from the IRRC monographs and U.S. NTP carcinogenicity data base. Critical Reviews in Toxicology, 30(6), 629–799. https://doi.org/10.1080/10408440008951123

Schmiedchen, K., Driessen, S., & Oftedal, G. (2019). Methodological limitations in experimental studies on symptom development in individuals with idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF) - a systematic review. Environmental health: a global access science source, 18(1), 88. https://doi.org/10.1186/s12940-019-0519-x

Schuermann, D., & Mevissen, M. (2021). Manmade Electromagnetic Fields and Oxidative Stress - Biological Effects and Consequences for Health. International Journal of Molecular Sciences, 22(7), 3772. https://doi.org/10.3390/ijms22073772

Schüz, J., Pirie, K., Reeves, G. K., Floud, S., Beral, V., & Million Women Study Collaborators (2022). Cellular Telephone Use and the Risk of Brain Tumors: Update of the UK Million Women Study. Journal of the National Cancer Institute, 114(5), 704–711. https://doi.org/10.1093/jnci/djac042

Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) (2015) Potential health effects of exposure to electromagnetic fields (EMF). https://doi.org/10.2772/75635

Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) (2018) Memorandum on weight of evidence and uncertainties – Revision 2018. https://doi.org/10.2875/386011

Sciorio, R., Tramontano, L., & Esteves, S. C. (2022). Effects of mobile phone radiofrequency radiation on sperm quality. Zygote (Cambridge, England), 30(2), 159–168. https://doi.org/10.1017/S096719942100037X

Simkó, M., Remondini, D., Zeni, O., & Scarfi, M. R. (2016). Quality Matters: Systematic Analysis of Endpoints Related to "Cellular Life" *in Vitro* Data of Radiofrequency Electromagnetic Field Exposure. International journal of environmental research and public health, 13(7), 701. https://doi.org/10.3390/ijerph13070701

Smith, M. T., Guyton, K. Z. (2020). Identifying carcinogens from 10 key characteristics. A new approach based on mechanisms. in: Wild C. P., Weiderpass E., Stewart B. W., eds. World Cancer Report: Cancer Research for Cancer Prevention. Lyon: IARC Press

Swedish Radiation Safety Authority (SSM) (2019). Recent research on EMF and Health Risk. Thirteenth report from SSM's Scientific Council on Electromagnetic Fields, 2019. SSM Report, 08. Stockholm: Strålsäkerhetsmyndigheten.

Szmigielski S. (2013). Reaction of the immune system to low-level RF/MW exposures. The Science of the total environment, 454-455, 393–400. https://doi.org/10.1016/j.scitotenv.2013.03.034

Tillmann, T., Ernst, H., Streckert, J., Zhou, Y., Taugner, F., Hansen, V., & Dasenbrock, C. (2010). Indication of cocarcinogenic potential of chronic UMTS-modulated radiofrequency exposure in an ethylnitrosourea mouse model. International journal of radiation biology, 86(7), 529–541. https://doi.org/10.3109/09553001003734501

Toledano, M. B., Auvinen, A., Tettamanti, G., Cao, Y., Feychting, M., Ahlbom, A., Fremling, K., Heinävaara, S., Kojo, K., Knowles, G., Smith, R. B., Schüz, J., Johansen, C., Poulsen, A. H., Deltour, I., Vermeulen, R., Kromhout, H., Elliott, P., & Hillert, L. (2018). An international prospective cohort study of mobile phone users and health (COSMOS): Factors affecting validity of self-reported mobile phone use. International Journal of Hygiene and Environmental Health, 221(1), 1–8. https://doi.org/10.1016/j.ijheh.2017.09.008

van Wel, L., Liorni, I., Huss, A., Thielens, A., Wiart, J., Joseph, W., Röösli, M., Foerster, M., Massardier-Pilonchery, A., Capstick, M., Cardis, E., & Vermeulen, R. (2021). Radio-frequency electromagnetic field exposure and contribution of sources in the general population: an organ-specific integrative exposure assessment. Journal of Exposure Science and Environmental Epidemiology. https://doi.org/10.1038/s41370-021-00287-8

Varsier, N., Plets, D., Corre, Y., Vermeeren, G., Joseph, W., Aerts, S., Martens, L., & Wiart, J. (2015). A novel method to assess human population exposure induced by a wireless cellular network. Bioelectromagnetics, 36(6), 451–463. https://doi.org/10.1002/bem.21928

Vijayalaxmi, & Foster, K. R. (2021). Improving the Quality of Radiofrequency Bioeffects Research: The Need for a Carrot and a Stick. Radiation research, 196(4), 417–422. https://doi.org/10.1667/RADE-21-00079.1

Vijayalaxmi, & Prihoda, T. J. (2012). Genetic damage in human cells exposed to non-ionizing radiofrequency fields: a meta-analysis of the data from 88 publications (1990-2011). Mutation research, 749(1-2), 1–16. https://doi.org/10.1016/j.mrgentox.2012.09.007

Vijayalaxmi, & Prihoda, T.J. (2019). Comprehensive Review of Quality of Publications and Meta-analysis of Genetic Damage in Mammalian Cells Exposed to Non-Ionizing Radiofrequency Fields. Radiation Research, 191(1), 20-30. https://doi.org/10.1667/RR15117.1

Vrijheid, M., Cardis, E., Armstrong, B. K., Auvinen, A., Berg, G., Blaasaas, K. G., Brown, J., Carroll, M., Chetrit, A., Christensen, H. C., Deltour, I., Feychting, M., Giles, G. G., Hepworth, S. J., Hours, M., Iavarone, I., Johansen, C., Klæboe, L., Kurttio, P., … Woodward, A. (2006). Validation of short term recall of mobile phone use for the Interphone study. Occupational and Environmental Medicine, 63(4), 237–243. https://doi.org/10.1136/OEM.2004.019281

Vrijheid, M., Deltour, I., Krewski, D., Sanchez, M., & Cardis, E. (2006). The effects of recall errors and of selection bias in epidemiologic studies of mobile phone use and cancer risk. Journal of Exposure Science and Environmental Epidemiology, 16(4), 371–384. https://doi.org/10.1038/SJ.JES.7500509

Wallace, J., & Selmaoui, B. (2019). Effect of mobile phone radiofrequency signal on the alpha rhythm of human waking EEG: A review. Environmental research, 175, 274–286. https://doi.org/10.1016/j.envres.2019.05.016

Wang, Y., & Guo, X. (2016). Meta-Analysis of association between mobile phone use and glioma risk. Journal of Cancer Research and Therapeutics, 12(8), C298–C300. https://doi.org/10.4103/0973-1482.200759

Wang, P., Hou, C., Li, Y., & Zhou, D. (2018). Wireless phone use and risk of adult glioma: Evidence from a meta-Analysis. World Neurosurgery, 115, e629-e636. https://doi.org/10.1016/j.wneu.2018.04.122

Yang, M., Guo, W. W., Yang, C. S., Tang, J. Q., Huang, Q., Feng, S. X., Jiang, A. J., Xu, X. F., & Jiang, G. (2017). Mobile phone use and glioma risk: A systematic review and meta-analysis. PLoS ONE, 12(5), 1–13. https://doi.org/10.1371/journal.pone.0175136

Zeni, O., & Scarfi, M.R. (2012). Experimental requirements for *in vitro* studies aimed to evaluate the biological effects of radiofrequency radiation, microwave materials characterization; in: Costanzo S., ed., Microwave Materials Characterization. Rijeka, Croatia: InTech. https://doi.org/10.5772/51421

Zubko, O., Gould, R. L., Gay, H. C., Cox, H. J., Coulson, M. C., & Howard, R. J. (2017). Effects of electromagnetic fields emitted by GSM phones on working memory: a meta-analysis. International journal of geriatric psychiatry, 32(2), 125–135. https://doi.org/10.1002/gps.4581

8 GLOSSARY OF TERMS, UNITS

APD	Absorbed Power Density (W/m^2)
SAR	Specific Absorption Rate (W/kg)

9 LIST OF ABBREVIATIONS AND ACRONYMS

BS	Base Station
EEG	Electroencephalogram
EHS	Electromagnetic Hypersensitivity (IEI-EMF)
EI	Exposure Index
ELF	Extremely Low Frequency
EMF	Electromagnetic Field(s)
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
GSM	Global System for Mobile communications
ICNIRP	International Commission on Non-Ionizing radiation Protection
IEI-EMF	Idiopathic Environmental Intolerance attributed to EMF
IoT	Internet of Things
IQR	Interquartile Range
MIMO	Multiple-input multiple-output
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RAT	Radio Access Technology
RF	Radiofrequency
RFR	Radiofrequency radiation
ROS	Reactive Oxygen Species
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SD	Standard Deviation
UMTS	Universal Mobile Telecommunications System
WHO	World Health Organization