

**Draft****ICNIRP Guidelines****GUIDELINES FOR LIMITING EXPOSURE TO TIME-VARYING ELECTRIC,  
MAGNETIC AND ELECTROMAGNETIC FIELDS****(100 kHz TO 300 GHz)****Appendix B: Health Risk Assessment Literature****International Commission on Non-Ionizing Radiation Protection****1. INTRODUCTION**

The World Health Organization (WHO) has recently undertaken an in-depth review of the literature on radiofrequency electromagnetic fields (EMF) and health, which will be released as a Technical Document in the near future. This independent review is the most up-to-date, comprehensive and thorough appraisal of the effects of radiofrequency EMFs. Further, the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), a European Commission initiative, also recently produced a report on potential health effects of exposure to electromagnetic fields (SCENIHR, 2015). Accordingly, the present guidelines have used the literature review from the WHO (World Health Organization, 2014) and SCENIHR report as the scientific health literature bases for determining hazards and/or risks associated with radiofrequency EMF, rather than providing a review of the individual studies in the literature. To complement the WHO and SCENIHR reviews, ICNIRP also considered research published subsequent to that included in the WHO and SCENIHR reviews in the development of the current guidelines. In order to provide an indication of ICNIRP's evaluation process, overviews of the literature and conclusions that ICNIRP reached, as well as a limited number of examples, are provided.

The summary of the research on biological and health effects of radiofrequency EMF presented below considers effects on body systems, processes or specific diseases. This research feeds into the determination of thresholds for adverse human health effects. Research domains considered range from experimental tests of the effect of radiofrequency EMF on cells, animals and humans, to observational studies assessing relationships between radiofrequency EMF and a range of potentially health-related outcomes. The former has the advantages of being able to control a large number of potential confounders and to manipulate radiofrequency EMF exposure. However, it can also be limited in terms of generalizability to realistic exposure environments, as well as exposure durations sufficient to assess many disease processes, and in the case of in vitro and animal research, generalization to humans can also be difficult. Epidemiological research is mostly observational and thus, depending on the type of studies, various types of bias are of concern. These include confounding, selection bias, information bias, reverse causality and exposure misclassification; in general, prospective cohort studies are least affected by bias but large sample sizes are needed for rare diseases. Therefore, it is important to consider research across a range of study types in order to arrive at useful

45 conclusions concerning the relation between radiofrequency EMF exposure and adverse health  
46 effects.

47 It is important to note that ICNIRP bases its guidelines on substantiated<sup>1</sup> adverse health effects.  
48 This makes the difference between a biological and an adverse health effect an important  
49 distinction, where only adverse health effects require limits for the protection of humans.  
50 Research on the health effects of radiofrequency EMF has tended to concentrate on a few areas  
51 of particular interest and concern, whereas information on a number of other systems of the  
52 body is inadequate to contribute to the guidelines. Specifically, there is insufficient information  
53 about the effects of radiofrequency EMF on the skeletal, muscular, respiratory, digestive, and  
54 excretory systems. Therefore, these systems are not considered further.

## 55 **2. BRAIN PHYSIOLOGY AND FUNCTION**

### 56 **2.1 Brain electrical activity and cognitive performance**

57 Human research addressing higher cognitive function has primarily been conducted within the  
58 ICNIRP (1998) basic restriction values, with very limited research at levels high-enough to  
59 provide health-effect threshold information. This has primarily been assessed via performance  
60 measures, and derivations of the electroencephalogram (EEG) and cerebral blood flow (CBF)  
61 measures (sensitive measures of brain electrical activity and blood flow/metabolism,  
62 respectively). Most double-blind human experimental studies on cognitive performance, CBF  
63 or event-related potential (a derivative of the EEG) measures of cognitive function did not  
64 report an association with radiofrequency EMF. A number of sporadic findings have been  
65 reported, but these do not show a consistent or meaningful pattern. This may be a result of the  
66 large number of (uncontrolled-for) statistical comparisons, a possibility consistent with the lack  
67 of replication of such reports. Of particular importance is that the larger, more  
68 methodologically rigorous studies have failed to identify effects of radiofrequency EMF  
69 exposure on these cognitive domains. There are therefore no substantiated reports of  
70 radiofrequency EMF negatively affecting performance, CBF or event-related potential  
71 measures of cognitive function. Studies analyzing frequency components of the EEG have  
72 reliably shown that the 8–13 Hz alpha band in waking EEG and the 10–14 Hz ‘sleep spindle’  
73 frequency range in sleep EEG, are affected by radiofrequency EMF exposure with SARs <2 W  
74 kg<sup>-1</sup>, but there is no evidence that these relate to adverse health effects.

75 Both rodents and non-human primates have shown a decrease in food-reinforced memory  
76 performance with exposures to radiofrequency EMF at a whole body average SAR >5 W kg<sup>-1</sup>  
77 for rats, and a whole body average SAR >4 W kg<sup>-1</sup> for non-human primates, exposures which  
78 correspond to increases in body core temperatures of approximately 1 °C. However, there is no  
79 indication that these changes were due to reduced cognitive ability, rather than the normal  
80 temperature-induced reduction of motivation (hunger). Such changes in motivation are  
81 considered normal and reversible thermoregulatory responses, and do not in themselves  
82 represent an adverse health effect. Similarly, although not considered an adverse health effect,  
83 behavioral changes to reduce body temperature have also been observed in non-human  
84 primates at a whole body average SARs of 1 W kg<sup>-1</sup>, with the threshold the same for acute,  
85 repeated exposures and for long-term exposures.

86 There is limited epidemiological research on higher cognitive function. There have been  
87 reports of subtle changes to performance measures with radiofrequency EMF, but findings  
88 have been contradictory and alternative explanations for observed effects are plausible.

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<sup>1</sup> Further details concerning the term ‘substantiated’ can be found in the main guidelines document.

89 In summary, there is no substantiated experimental or epidemiological evidence that exposure  
90 to radiofrequency EMF affects higher cognitive functions relevant to health.

## 91 **2.2. Symptoms and wellbeing**

92 There is research addressing the potential for radiofrequency EMF to influence mood, behavior  
93 characteristics and symptoms.

94 A number of human experimental studies testing for acute changes to wellbeing or symptoms  
95 are available, and these have failed to identify any substantiated effects of exposure. A small  
96 portion of the population attributes non-specific symptoms to various types of radiofrequency  
97 EMF exposure; this is referred to as Idiopathic Environmental Intolerance attributed to EMF  
98 (IEI-EMF). Double-blind experimental studies have consistently failed to identify a relation  
99 between radiofrequency EMF exposure and such symptoms in the IEI-EMF population, as well  
100 as in healthy population samples. These human experimental studies provided evidence that  
101 'belief about exposure' (e.g. the so-called 'nocebo' effect), and not exposure itself, is the  
102 relevant symptom determinant.

103 Epidemiological research has addressed potential long-term effects of radiofrequency EMF  
104 exposure from fixed site transmitters and devices used close to the body on both symptoms and  
105 well-being, but with a few exceptions these are cross-sectional studies with self-reported  
106 information about symptoms and exposure. Selection bias, reporting bias, and nocebo effects  
107 are of concern in these studies. In studies on transmitters, no consistent associations between  
108 exposure and symptoms or well-being were observed when objective measurements of  
109 exposure were made, or when exposure information was collected prospectively. In studies on  
110 mobile phone use, associations with symptoms and problematic behavior have been observed.  
111 However, these studies can generally not differentiate between potential effects from  
112 radiofrequency EMF exposure and other consequences of mobile phone use, such as sleep  
113 deprivation in adolescents using the mobile phone at night. Overall, the epidemiological  
114 research does not provide evidence of a causal effect of radiofrequency EMF exposure on  
115 symptoms or well-being.

116 However, there is evidence that radiofrequency EMF, at sufficiently high levels, can cause  
117 pain. Walters et al. (2000) reported a pain threshold of  $12.5 \text{ kW m}^{-2}$  for 94 GHz, 3-second  
118 exposure to the back, which raised temperature at a rate of  $3.3 \text{ }^\circ\text{C}$  per second (from  $34 \text{ }^\circ\text{C}$  to  
119  $43.9 \text{ }^\circ\text{C}$ ). This is similar to that found for heating due to sources other than EMF, where 'weak  
120 to moderate' pain was reported for smaller temperature elevations ( $+4 \text{ }^\circ\text{C}$ ) but with a similar  
121 rate of temperature elevation ( $4 \text{ }^\circ\text{C}$  per second; Green & Akirav, 2010). However, as Walters et  
122 al. used an exposure scenario more relevant to radiofrequency EMF, and as Green and Akirav  
123 (2010) has not been replicated (which is particularly important here due to the methodological  
124 difficulties associated with self-report measures), it is difficult to determine the relevance of  
125 'rate of temperature elevation' to human health at present.

126 Another instance of pain induced by radiofrequency EMF is due to 'indirect' exposure via  
127 contact currents, where radiofrequency EMF in the environment is redirected via a conducting  
128 object to a person, and the resultant current flow, dependent on frequency, can stimulate  
129 nerves, cause pain and/or damage tissue. Thresholds are very difficult to determine, with the  
130 best estimates of thresholds for health effects being for pain, which is approximately 10 and 20  
131 mA for children and adults respectively (extrapolated from Chatterjee et al., 1986). There is  
132 thus no evidence that high frequency EMF exposure affects symptoms, except for pain (and  
133 potentially tissue damage) at high exposure levels.

134 In summary, no reports of adverse effects on symptoms and wellbeing have been substantiated,  
135 except for pain, which is related to elevated temperature at high exposure levels. Thresholds for

136 these have not been clearly identified, but the best estimate is within the vicinity of 10 and 20  
137 mA for indirect contact currents, for children and adults respectively, and 12.5 kW m<sup>-2</sup> for  
138 direct millimeter-wave exposure.

### 139 2.3. Other brain physiology and related functions

140 A number of studies of physiological functions that could in principle lead to adverse health  
141 effects have been conducted, primarily using *in vitro* techniques. These have included multiple  
142 cell lines and assessed such functions as intra- and intercellular signaling, membrane ion  
143 channel currents and input resistance, Ca<sup>2+</sup> dynamics, signal transduction pathways, cytokine  
144 expression, biomarkers of neurodegeneration, heat shock proteins, and oxidative stress-related  
145 processes. Some of these studies also tested for effects of co-exposure of radiofrequency EMF  
146 with known toxins. Although some effects have been reported for some of these endpoints,  
147 there is currently no evidence of effects relevant to human health. There have been some  
148 reports of morphological changes to cells, but these have not been replicated, and their  
149 relevance to health has not been demonstrated. There have also been reports of radiofrequency  
150 fields inducing leakage of albumin across the blood-brain barrier, but due to methodological  
151 limitations of the studies and failed attempts to independently replicate the results, there  
152 remains no evidence of an effect.

153 Intense pulsed low frequency electric fields (with radiofrequency components) can cause cell  
154 membranes to become permeable, allowing exchange of intra- and extra-cellular materials  
155 (Joshi and Schoenbach, 2010); this is referred to as electroporation. 18 GHz continuous wave  
156 exposure can result in a similar effect (Nguyen et al., 2017). These require very high field  
157 strengths (e.g. 10 kV m<sup>-1</sup> (peak) in tissue in terms of the former, and 5 kW kg<sup>-1</sup> for the latter).  
158 These levels have not been shown to adversely affect health in realistic exposure scenarios in  
159 humans, and given their very high thresholds, are protected against by limits based on effects  
160 with lower thresholds and are not discussed further.

161 Animal studies have also reported that the heating that results from radiofrequency EMF  
162 exposure may lead to formation of cataract in rabbits. In order for this to occur, very high local  
163 SAR levels (100 – 140 W kg<sup>-1</sup>) at low frequencies (< 6 GHz) are needed, with increases of  
164 several degrees centigrade maintained for several hours. However, the rabbit model is more  
165 susceptible to cataract formation than primates (with primates more relevant to human health),  
166 and cataracts have not been found in primates exposed to radiofrequency fields. No  
167 substantiated effects on other deep structures of the eye have been found (e.g. retina, lens or  
168 iris). However, rabbits can be a good model for damage to superficial structures of the eye at  
169 higher frequencies (30-300 GHz), because the shape of the facial structure is less relevant to  
170 exposure in the more superficial tissue that receives the highest exposure at higher frequencies.  
171 However, as the baseline temperature of the anterior portion of the eye (including the cornea) is  
172 relatively low (compared with the posterior portion of the eye that would be exposed at lower  
173 frequencies), very high exposure levels are required to cause harm superficially. For example,  
174 Kojima et al. (2018) reported that adverse health effects to the cornea can occur at > 1.4 kW m<sup>-2</sup>  
175 across frequencies from 40 to 95 GHz, and no effects were found below 500 W m<sup>-2</sup>; the  
176 authors concluded that the blink rates in humans would preclude such effects in humans.

177 In summary, there is no evidence of effects of radiofrequency EMF on physiological processes  
178 or eye pathology that impair health in humans. Some evidence of superficial eye damage has  
179 been shown in rabbits at exposures of at least 1.4 kW m<sup>-2</sup>, although the relevance of this to  
180 humans has not been demonstrated.

181 **3. AUDITORY, VESTIBULAR, AND OCULAR FUNCTION**

182 A number of animal and some human studies have tested for potential effects of  
183 radiofrequency EMF on function and pathology of these systems.

184 Sub-millisecond pulses of radiofrequency EMF can result in audible sound. Specifically,  
185 within the 200-3000 MHz range the *microwave hearing effect* can result from brief  
186 (approximately 100  $\mu$ s) radiofrequency pulses to the head, which cause thermoelastic  
187 expansion that is detected by sensory cells in the cochlea via the same processes involved in  
188 normal hearing. This effect is perceived as a brief low-level noise, often described as a ‘click’  
189 or ‘buzzing’. The most recent report has provided a specific absorption (SA) value of 4.5 mJ  
190  $\text{kg}^{-1}$  per pulse to reach the 20 mPa auditory sound pressure threshold at the cochlea for 10 and  
191 20  $\mu$ s pulses at 2.45 GHz, which by definition is barely audible (Roschmann, 1991). This  
192 equates to a temperature rise of approximately  $1 \times 10^{-6}$  °C per pulse. There is no evidence that  
193 the microwave hearing effect can affect health, and so the present Guidelines do not provide a  
194 restriction to specifically account for microwave hearing.

195 A few studies reported effects of mobile phone emissions on auditory function and cellular  
196 structure in animal models. However, results are inconsistent, and no association of  
197 radiofrequency EMF exposure with risk of tinnitus, hearing impairment or vestibular  
198 dysfunction has been substantiated in epidemiological studies. Human laboratory studies also  
199 failed to identify any adverse health effects of exposure.

200 A number of experimental human studies have tested for changes to normal sensory processing  
201 due to radiofrequency EMF exposure. These have largely been conducted at exposure levels  
202 within the ICNIRP (1998) basic restriction levels, and although there are some reports of  
203 effects in both categories of research, the results are highly variable, with the larger and more  
204 methodologically rigorous studies failing to find such effects.

205 There is very little epidemiological research addressing sensory effects of devices that emit  
206 radiofrequency EMF. The available research has focused on mobile phone use and does not  
207 provide substantiated evidence that this is associated with increased risk of tinnitus, hearing  
208 impairment, vestibular or ocular function.

209 In summary, no effects on auditory, vestibular, or ocular function relevant to human health  
210 have been substantiated.

211 **4. NEUROENDOCRINE SYSTEM**

212 A small number of human studies have tested whether indices of endocrine system function are  
213 affected by radiofrequency EMF exposure. Several hormones, including melatonin, growth  
214 hormone, luteinising hormone, cortisol, epinephrine and norepinephrine have been assessed,  
215 but no consistent evidence of effects of exposure has been observed.

216 In animal studies, robust changes have only been reported from acute exposures with whole  
217 body SARs in the order of  $4 \text{ W kg}^{-1}$ , which result in core temperature rises of 1 °C or more.  
218 However, there is no evidence that this corresponds to an impact on health. Although there  
219 have been a few studies reporting field-dependent changes in some neuroendocrine measures,  
220 these have also not been substantiated. The literature as a whole reports that repeated, daily  
221 exposure to mobile phone signals does not impact on plasma levels of melatonin or on  
222 melatonin metabolism, oestrogen or testosterone, or on corticosterone or adrenocorticotropin in  
223 rodents under a variety of conditions.

224 The two epidemiological studies on potential effects of exposure to radiofrequency EMF on  
225 melatonin levels had conflicting results, and both had methodological limitations, including

226 possible placebo effects. For other hormonal endpoints no epidemiological studies of sufficient  
227 scientific quality have been identified.

228 In summary, the lowest level at which an effect of radiofrequency EMF on the neuroendocrine  
229 system has been observed is  $4 \text{ W kg}^{-1}$  (in rodents and primates), but there is no evidence that  
230 this translates to humans or is relevant to human health. No other effects have been  
231 substantiated.

## 232 **5. NEURODEGENERATIVE DISEASES**

233 No human experimental studies exist for neurodegenerative diseases.

234 Although one group has reported that exposure to pulsed radiofrequency EMF fields increased  
235 neuronal death in rats, which might contribute to an increased risk of neurodegenerative  
236 disease, two studies have failed to confirm these results. Some other effects have been reported  
237 (e.g. changes to neurotransmitter release in the cortex of the brain, protein expression in the  
238 hippocampus, and autophagy in neurons which was not accompanied by apoptosis), but such  
239 changes have not been shown to lead to neurodegenerative disease. Other studies investigating  
240 effects on neurodegeneration are not informative due to methodological or other shortcomings.

241 A Danish epidemiological cohort study has investigated potential effects of mobile phone use  
242 on neurodegenerative disorders, and reported reduced risk estimates for Alzheimer disease,  
243 vascular and other dementia, and Parkinson disease. These findings are likely to be the result of  
244 reverse causation, as prodromal symptoms of the disease may prevent persons with early  
245 symptoms to start using a mobile phone. Results for multiple sclerosis are inconsistent, with no  
246 effect observed among men, and a borderline increased risk in women, but with no consistent  
247 exposure-response pattern.

248 In summary, no adverse effects on neurodegenerative diseases have been substantiated.

## 249 **6. CARDIOVASCULAR SYSTEM, AUTONOMIC NERVOUS SYSTEM, AND** 250 **THERMOREGULATION**

251 As described above, radiofrequency EMF can induce heating in the body. Although humans  
252 have a very efficient thermoregulatory system, too much heat puts the cardiovascular system  
253 under stress and may lead to adverse health effects.

254 Numerous human studies have investigated indices of cardiovascular, autonomic nervous  
255 system, and thermoregulatory function, including measures of heart rate and heart rate  
256 variability, blood pressure, body, skin and finger temperatures, and skin conductance. Most  
257 studies indicate there are no effects on endpoints regulated by the autonomic nervous system.  
258 The relatively few reported effects of exposure were small and would not have an impact on  
259 health. The changes were also inconsistent and may be due to methodological limitations or  
260 chance. With exposures at higher intensities, up to a whole body SAR of about  $1 \text{ W/kg}$  (Adair,  
261 Mylacraine and Cobb, 2001b), sweating and cardiovascular responses occurred similar to that  
262 observed under increased heat load from other sources. The body core temperature increase  
263 was generally less than  $0.2 \text{ }^{\circ}\text{C}$ . The maximal increase in skin temperature of the exposed area  
264 observed with 2450 MHz was less than  $4 \text{ }^{\circ}\text{C}$  at a whole body SAR of approximately  $1 \text{ W kg}^{-1}$ ,  
265 which again does not represent an adverse health effect. With exposures to 100 and 250 MHz  
266 leading to a whole body average SAR of  $0.68 \text{ W kg}^{-1}$ , hot spots occurred in the skin of the  
267 ankles with an average temperature increase of up to  $4 \text{ }^{\circ}\text{C}$  (Adair et al., 2005). However,  
268 reports of effects that are sufficient to impact on health have not been substantiated.

269 The situation is different for animal research, in that far higher levels of exposure have been  
270 used, often to the point where thermoregulation is overwhelmed and temperature increases to

271 the point where death occurs. For example, Frei et al. (1995) exposed rats to 13 W kg<sup>-1</sup> 35 GHz  
272 fields, which raised body core temperature by 8 °C (to 45 °C), resulting in death. Similarly,  
273 Jauchem and Frei (1997) exposed rats to 13.2 W kg<sup>-1</sup> 350 MHz fields, and reported that  
274 thermal breakdown (i.e. where the thermoregulatory system cannot cope with the increased  
275 body core temperature) occurred at approximately 42 °C. These are serious adverse health  
276 effects that need to be avoided, however there is not sufficient research using lower exposures  
277 to evaluate the threshold for health effects in rodents. It is also difficult to relate these animal  
278 findings to humans, as humans are more-efficient thermoregulators than rodents, and thus their  
279 thermoregulatory systems can deal effectively with higher exposure levels than rodents.  
280 Taberski et al. (2014) reported that in hamsters, no body core temperature elevation is seen at 4  
281 W kg<sup>-1</sup>, with the only detectable effect a reduction on food intake (which is consistent with  
282 reduced eating in humans when warmer).

283 Few epidemiological studies on cardiovascular, autonomic nervous system, or  
284 thermoregulation outcomes are available. Those that are have not demonstrated a link between  
285 radiofrequency EMF exposure and measures of cardiovascular health.

286 In summary, no effects on the cardiovascular system, autonomic nervous system, or  
287 thermoregulation that compromise health have been substantiated for exposures with whole  
288 body average SARs below approximately 1 W kg<sup>-1</sup>, and there is some evidence that 4 W kg<sup>-1</sup> is  
289 not sufficient to alter body core temperature in hamsters. However, there is strong evidence  
290 that whole body exposures in rats that are sufficient to increase body core temperature by  
291 several degrees centigrade can cause serious adverse health effects in rats.

## 292 **7. IMMUNE SYSTEM AND HAEMATOLOGY**

293 There have been inconsistent reports of transient changes in immune function and haematology  
294 following radiofrequency EMF exposures. These have primarily been from *in vitro* studies,  
295 although some *in vivo* animal studies have also been conducted. There is currently no evidence  
296 that such reported effects, if real, are relevant to human health.

297 The few human studies have not indicated any evidence that radiofrequency EMF affects  
298 health in humans via the immune system or haematology.

## 299 **8. FERTILITY, REPRODUCTION, AND CHILDHOOD DEVELOPMENT**

300 There is very little human experimental research addressing possible effects of radiofrequency  
301 EMF exposure on reproduction and development. What is available has focused on hormones  
302 that are relevant to reproduction and development, and as described in the Neuroendocrine  
303 System section above, there is no evidence that they are affected by radiofrequency EMF  
304 exposure. Other research has addressed this issue by looking at different stages of development  
305 (on endpoints such as cognition and brain electrical activity), in order to determine whether  
306 there may be greater sensitivity to radiofrequency fields during these stages. There is currently  
307 no evidence that developmental phase is relevant to this issue.

308 Numerous animal studies have shown that exposure to radiofrequency EMF associated with a  
309 significant temperature increase can cause effects on reproduction and development. These  
310 include increased embryo and fetal losses, increased fetal malformations and anomalies, and  
311 reduced fetal weight at term. Such exposures can also cause a reduction in male fertility.  
312 However, extensive, well performed studies have failed to identify developmental effects at  
313 whole body average SAR levels up to 4 W kg<sup>-1</sup>. In particular, a large four-generation study on  
314 fertility and development using SAR levels up to 2.34 W kg<sup>-1</sup> found no evidence of adverse  
315 effects (Sommer et al., 2009). Some studies have reported effects on male fertility at exposure

316 levels below this value, but these studies have had methodological limitations, and reported  
317 effects have not been substantiated.

318 Epidemiological studies have investigated various aspects of male and female infertility and  
319 pregnancy outcomes in relation to radiofrequency EMF exposure. Some epidemiological  
320 studies found associations between radiofrequency EMF and sperm quality or male infertility,  
321 but taken together, the available studies do not provide strong evidence for an association with  
322 radiofrequency EMF exposure as they all suffer from limitations in study design or exposure  
323 assessment. A few epidemiological studies are available on maternal mobile phone use during  
324 pregnancy and potential effects on child neurodevelopment. There is no substantiated evidence  
325 that radiofrequency EMF exposure from maternal mobile phone use affects child cognitive and  
326 psychomotor development, or causes developmental milestone delays.

327 In summary, no adverse effects of radiofrequency EMF exposure on fertility, reproduction or  
328 development relevant to human health have been substantiated.

## 329 **9. CANCER**

330 There is a large body of literature concerning cellular and molecular processes that are of  
331 particular relevance to cancer. This includes studies of cell proliferation, differentiation and  
332 apoptosis-related processes, proto-oncogene expression, genotoxicity, increased oxidative  
333 stress, and DNA strand breaks. Although there are reports of effects of radiofrequency EMF on  
334 a number of these endpoints, there is no substantiated evidence of health-relevant effects.

335 A few animal studies on the effect of radiofrequency EMF exposure on carcinogenesis have  
336 reported positive effects, but in general, these studies either have shortcomings in methodology  
337 or dosimetry, or the results have not been replicated in independent studies. Indeed, the great  
338 majority of studies have reported a lack of carcinogenic effects in a variety of animal models.  
339 A replication of a study in which exposure to radiofrequency EMF increased the incidence of  
340 liver and lung tumors in an animal model with prenatal exposure to the carcinogen ENU  
341 (ethylnitrosourea) indicates a possible promoting effect (Lerchl et al., 2015; Tillmann et al.,  
342 2010). The lack of a dose-response relationship, as well as the use of an untested mouse model  
343 for liver and lung tumors whose relevance to humans is uncertain (Nesslany et al., 2015),  
344 makes interpretation of these results and their applicability to human health difficult, and  
345 therefore there is a need for further research to better understand these results.

346 A recent, large animal study, performed by the US National Toxicology Program (NTP)  
347 reported an increased rate of cardiac schwannoma in male rats exposed to radiofrequency  
348 EMF, but not in female rats or either male or female mice (NTP 2018). As the exposure was  
349 approximately 75 times higher than the ICNIRP (1998) whole body average general public  
350 limit, the results are not directly relevant to radiofrequency EMF levels that humans would  
351 typically be exposed to. Further, humans are far more efficient at diminishing the resultant  
352 body core temperature rise than rats. As noted by the internal NTP review (NTP 2018), there  
353 are also a number of methodological issues that limit the usefulness of the results for EMF  
354 health assessment. Of particular note is that the statistics were not able to determine whether  
355 the higher number of cardiac schwannomas that were reported was more than what would be  
356 expected by chance alone (given that no control for multiple comparisons was applied). This is  
357 particularly important given that a graded dose-response relation was not found, no consistency  
358 across rodent species or genders was found, and the results are not consistent with the  
359 radiofrequency EMF cancer literature more generally. A similar study that was conducted  
360 concurrently with the NTP study reported that they had replicated these NTP results on cardiac  
361 schwannoma (Falcioni et al., 2018). However, similar to the NTP study, the statistics were also  
362 not designed to determine whether the increase was higher than would be expected by chance  
363 alone (due to uncorrected multiple statistical comparisons). The schwannoma findings in these



364 two studies are inconsistent in terms of the exposure-response association as the Italian study  
365 observed an ‘increased’ number of schwannomas at low exposure levels where no increase in  
366 schwannoma was observed in the NTP study. These studies therefore do not provide sufficient  
367 evidence to conclude that radiofrequency EMF can cause cancer.

368 A large number of epidemiological studies of mobile phone use and cancer risk have also been  
369 performed. Most have focused on brain tumors, acoustic neuroma and parotid gland tumors, as  
370 these occur in close proximity to the typical exposure source from mobile phones. However,  
371 some studies have also been conducted on other types of tumors, such as leukaemia,  
372 lymphoma, uveal melanoma, pituitary gland tumors, testicular cancer, and malignant  
373 melanoma. With a few exceptions, the studies have used a case-control design and have relied  
374 on retrospectively collected self-reported information about mobile phone use history. Only  
375 two cohort studies with prospective exposure information are available. Several studies have  
376 had follow-ups that were too short to allow assessment of a potential effect of long-term  
377 exposure, and results from case-control studies with longer follow-up are not consistent.

378 The large, IARC coordinated, Interphone study did not provide evidence of a raised risk of  
379 brain tumors, acoustic neuroma or parotid gland tumors among regular mobile phone users,  
380 and the risk estimates did not increase with longer time since first mobile phone use  
381 (Interphone, 2010; 2011). It should be noted that although somewhat elevated odds ratios were  
382 observed at the highest level of cumulative call time for acoustic neuroma and glioma, there  
383 were no trends observed for any of the lower cumulative call time groups, with among the  
384 lowest risk estimates in the penultimate exposure category. This, combined with the inherent  
385 recall bias of such studies, does not provide evidence of an increased risk. Similar results were  
386 observed in a Swedish case-control study of acoustic neuroma (Pettersson et al., 2014).  
387 Contrary to this, a set of case-control studies from the Hardell group in Sweden report  
388 significantly increased risks of both acoustic neuroma and malignant brain tumors already after  
389 less than five years since the start of mobile phone use, and at quite low levels of cumulative  
390 call time. However, they are not consistent with trends in brain cancer incidence rates from a  
391 large number of countries or regions, which have not found any increase in the incidence since  
392 mobile phones were introduced.

393 Furthermore, no cohort studies (which unlike case-control studies are not affected by recall or  
394 selection bias) report a higher risk of glioma, meningioma or acoustic neuroma among mobile  
395 phone subscribers, or when estimating mobile phone use through prospectively collected  
396 questionnaires. Studies of other types of tumors have also not provided evidence of an  
397 increased tumor risk in relation to mobile phone use. Only one study is available on mobile  
398 phone use in children and brain tumor risk. No increased risk of brain tumors was observed.

399 Studies of exposure to environmental radiofrequency EMF fields, for example from radio and  
400 television transmitters, have not provided evidence of an increased cancer risk either in  
401 children or in adults. Studies of cancer in relation to occupational radiofrequency EMF  
402 exposure have suffered substantial methodological limitations and do not provide sufficient  
403 information for the assessment of carcinogenicity of radiofrequency EMF fields. Taken  
404 together, the epidemiological studies do not provide evidence of a carcinogenic effect of  
405 radiofrequency EMF exposure at levels encountered in the general population.

406 In summary, no effects of radiofrequency EMF on cancer have been substantiated.

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