Submission to Honourable Rona Ambrose
Minster of Health

Re: Health Canada consultation on proposed revisions to Safety Code 6.

Title: Relevant Scientific Studies (140) Omitted by Health Canada in its Scientific Review of Draft Safety Code 6 (2014), Canada's Safety Guidelines for Safe Exposure to Radiofrequency/Microwave Radiation

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on behalf of Canadians for Safe Technology (C4ST)

July 15, 2014

We would appreciate a response to this submission that includes the evidence reviewed, what was included and excluded and why, and where it can be found in Safety Code 6. Please reply to scienceteam@C4ST.org

Summary

Health Canada currently determines the guidelines for safe levels of radiofrequency/microwave radiation each Canadian is exposed to from all sources, including cell towers, cell phones, Wi-Fi, smart metres, baby monitors, cordless phones, and other wireless devices.

On May 15th 2014, Health Canada announced a 60 day window for public input into proposed revisions to Safety Code 6. It is the first time in history that Health Canada has asked for scientific input from the public regarding wireless radiation. Officially, Safety Code 6 only covers federal workplaces, but in the absence of any other guideline in Canada, it has become the fall back for all levels of government, school boards, utility companies, hospitals, offices and microwave exposure from smart metres or nearby cell towers.

In our analysis of the scientific aspects of Health Canada's latest update, C4ST discovered that at least 140 relevant scientific studies, that show harm from wireless radiation, were omitted.

Health concerns range from immediate health effects to long term consequences of cancer and impairment of young and old. Canadian doctors are reporting an increasing number of patients across the country with symptoms of electrohypersensitivity related to radiofrequency/microwave radiation from wireless devices. There are untold numbers of people suffering, and taxing our healthcare system.

The omitted studies (some studies cover multiple topics) have been grouped into the following topics:

- Cancer and Genetic Damage - 25
- Male and Female Infertility - 14
- Impairment to Development, Learning and Behaviour from Conception to Old Age - 31
- Harmful Effects on the Brain and Central Nervous System - 44
- Effects on the Eyes - 6
- Cardiovascular Effects - 4
- Electrohypersensitivity (EHS) - 9
- Biochemical Changes - 65

At least 140 studies are missing from Health Canada's rationale document and literature review, as well as the report from the Royal Society of Canada and the largest, most recent European review. Of these 140 studies, 103 studies (74%) were submitted by C4ST to Health Canada in 2013, yet were still omitted.

The scientific basis of Safety Code 6 is clearly in disarray. Meanwhile, C4ST regularly hears from Canadians who report being sickened and disabled by exposures to radiofrequency/microwave radiation. The immediate response should be to take measures to ensure that exposures are recognized, and *As Low As Reasonably Achievable* (ALARA). This involves public education, training of medical personnel, minimization of use of wireless technologies in schools and workplaces, safe areas for those with EHS (and to prevent development of EHS), safer technological advancements and more. We present some preliminary recommendations to accomplish this.

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Background

Canada's guidelines for maximum exposure to radiofrequency/microwave radiation are established by Health Canada in Safety Code 6 (SC6). Today, as wireless communications devices and associated infrastructure increase exponentially, exposures are increasing too. Situations will increasingly occur when the sum of exposures from devices plus supporting infrastructure will approach the SC6 limits. It is more important than ever that these limits be based on the best available science, to protect all Canadians and their environment, especially the most vulnerable. The only way to ensure that SC6 is based on today's scientific knowledge regarding health effects of RF energy is to examine the scientific literature thoroughly and systematically, in an objective, unbiased manner.

In 2013, Health Canada retained the Royal Society of Canada (RSC) to review SC6. The RSC panel also conducted a day of public hearings in October 2013, and accepted submissions. Among these submissions was an extensive list of potentially relevant literature, the "Friesen Update." A proper systematic review would capture these records, and with the services of a specialist librarian even more relevant literature. Health Canada did not review this science nor conduct a full literature review.

Health Canada and the RSC also relied upon other "authoritative reviews," so this exploration of the rigour of Canada's review was extended to the rigour of reviews upon which they were building. The present SC6 review process follows a 2009 review; albeit of unknown quality. For this reason, examination of citations was limited to scientific articles published in 2009 and later. The exception is for cancer and related Genetic Damage, which was reviewed from 2011 on, because the World Health Organization's International Agency for Research on Cancer published a monograph reviewing studies up to 2011.

Objective

High quality scientific review is comprehensive, transparent and unbiased. The present project explores the thoroughness of the Health Canada and RSC reviews of the scientific literature, as well as the previous "authoritative reviews" to which they refer.

Methods and Results

The comprehensiveness of Health Canada's review of health effects of radiofrequency/microwave radiation was examined by comparing reference lists in key documents with recent (2009-on) scientific references available through publicly available scientific searches (e.g. US Library of Medicine).

References were managed using Zotero open source software.

Summaries are presented of scientific publications describing biological and possibly harmful health effects omitted from reference lists of all of:

1. Health Canada Safety Code 6 (2014) Draft - posted on the Health Canada website 16 May 2014. An earlier version had been reviewed by the RSC Expert Panel, that recommended no substantial changes;
2. Health Canada's Safety Code 6 (2014) - Rationale;
3. Chapter 7 "Reported Adverse Health Effects" in The Royal Society of Canada Expert Panel: A Review of Safety Code 6 (2013): Health Canada's Safety Limits for Exposure to Radiofrequency Fields. Spring 2014 (RSC SC6 (2014)); and
4. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR): Preliminary Opinion on Potential Health Effects of Exposure to Electromagnetic Fields (EMF) December 2013 (cited in Safety Code 6 (2014) Draft).

Full abstracts are presented with underlined highlights indicating significant, potentially harmful effects. Availability at the time of publication, and whether the study is among the references in the above four reports is summarized. Publications are listed by year (starting in 2014), and then alphabetically by first author. The numbers of publications relevant to each topic, as well as the number of these that were provided to the Royal Society of Canada in 2013 are summarized in Table 1 (primarily 2014 publications were not provided).

Limitations

Limitations of this work include that the literature search was not conducted by an information specialist. This undoubtedly under-estimates the volume of relevant scientific information that is not being considered in setting Canadian guidelines for exposure to radiofrequency/microwave radiation. As well, the analysis is based upon the contents of the abstracts, not the full text publications.

Table 1. Publications (2009 to 2014) indicating significant effects of radiofrequency/microwave radiation that were not reviewed by Health Canada, the Royal Society of Canada, nor the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks

Topic	Total number of studies not reviewed in Safety Code 6 2014 update	The number of these studies that were provided to Health Canada by C4ST in 2013
A1. Cancer (2011-2014)	11	7
A2. Genetic Damage (2011-2014)	14	10
B. Male and Female Infertility	14	10
C. Impairment to Development, Learning and Behaviour from Conception to Old Age	31	25
D. Effects on the Brain and Nervous System	44	31
E. Effects on the Eye	6	5
F. Cardiovascular Effects	4	2
G. Electrohypersensitivity (EHS)	9	8
H. Biochemical Effects	65	47
TOTAL UNIQUE PUBLICATIONS[1]	140[2]	103[3]

[1] Some publications cover more than one topic area

[2] Virtually all publications were available to Health Canada when the Safety Code 6 (2014) Draft was posted online May 16, 2014.

[3] 103 of 140 (74%) of the publications were submitted to Health Canada in 2013.

Topic Overviews

A 1. Cancer

Eleven omitted studies include:

- a 2014 case series of multifocal invasive breast cancer cases in four young women, where they customarily tucked their cell phones into their bras;
- a May 2014 case-control study of 253 gliomas, 194 meningiomas and 892 matched controls in France, demonstrating double to triple the risk of brain tumours for highest users of cell phones, measured as numbers of calls, and cumulative hours of use;
- a 2014 study of vestibular schwannoma (acoustic neuroma) indicating increasing tumour volume with use of mobile phones;
- two studies from Lennart Hardell's group in Sweden. This is the only group to assess exposures to radiation from both cell phone and cordless phones, along with habitual side of phone use. This group has found higher risks of brain tumours than other researchers. Risk increases with time of use, and is higher for individuals who started using phones at younger ages;
- re-analyses of a study of brain tumours in adolescents, highlighting that the data supported elevated risks, the opposite of the authors' conclusion;
- a critique of the Danish Cohort Study. This was fundamentally flawed research wherein "exposed" individuals had a private cell phone subscription in the mid-nineties. The supposedly "unexposed" individuals either had a corporate cell phone subscription or started using a cell phone after enrollment. This study is among the most highly criticized studies on the British Medical Journal website and is not credible; and
- publications addressing brain tumour incidence and cell phones.

The Rationale for the present draft of Safety Code 6 includes references to one report of the Interphone study (that interprets findings as "no increased risk"), as well as three analyses of cancer rates. The premise that increased brain tumours would be an early indicator that cell phones cause cancer is a highly criticized approach, because: 1) many factors may contribute to risks for brain tumours so a large surge in cell phone related cancers must occur before a significant increase would be detected; and 2) if other contributors (e.g. chemical exposures) were decreasing at the same time, an increase from cell phones would be masked by a decrease from other causes.

A 2. Genetic Damage

Fourteen studies reported damage to genetic material.

In people exposed to cell phones genetic damage was reported in:

- hair root cells where a phone is placed; and
- cells from inside the cheek (oral epithelium) of cell phone users;

At a somewhat higher exposure, DNA was damaged in the blood of marine workers.

In animals, evidence of genetic damage with exposure to microwave radiation was seen in:

- male rats in 2 studies (DNA damage in brain cells and liver cells; excretion of a DNA building block)
- rats of various ages. DNA damage increased with dose, and was greater in younger rats compared with mature ones;
- embryonal cells in quail eggs; and
- eggs (oocytes) in female fruit flies.

In the laboratory DNA damage from low level microwave exposure was seen in:

- human sperm exposed to mobile phones;
- a mouse sperm cell line; and
- calf thymus tissue.

B. Male and Female Infertility

Fourteen studies that were not examined during Canada's review of Safety Code 6 show strengthening evidence that phones in pockets bode poorly for future parenthood.

In 2014 a large, high-quality systematic review and meta-analysis found that cell phone radiation reduced human sperm motility and viability by a factor of 4, while effects were 2 to 4 times worse in animal studies. Another research study of human sperm then found more DNA fragmentation and less motility with exposure to a mobile phone. Early human embryonic development was also reduced with exposure to cell phone radiation.

In animals:

- mobile phone radiation reduced sperm viability and motility, with increased oxidative stress in two studies in rats;
- cell phone radiation induced testicular damage in rats;
- rats exposed in utero had fewer eggs in the ovaries; and
- fruit flies developed damaged eggs when exposed to GSM radiation.

C. Impairment to Development, Learning and Behaviour from Conception to Old Age

A multitude of events orchestrate the progression from a fertilized egg to a newborn infant, through childhood and adolescence, and stages of adulthood. If radiation changes embryonic development, the trajectory of a life is altered.

This collection of 31 publications includes research that reports behaviour or cognition, and/or that involved chronic or pre-natal exposure. Cancer as a result of long term exposure is reported in Section A1 but a discussion of children's risk of brain tumours (not in Section A1) is included here. This section also includes two discussions of exposure assessment of particular relevance for children, as well as Harvard paediatrician Dr. Herbert's extensive review of EMFs and autism, that she submitted to the RSC.

In humans:

- prenatal and postnatal exposure to cell phone exposure was associated with behavioural problems during childhood. This study replicates previous findings; and
- children with higher exposure to mobile phones exhibited more symptoms of Attention Deficit Hyperactivity Disorder (ADHD), only among those who also had higher levels of lead. It is thought that greater membrane permeability with radiofrequency exposures (see section H) increases access of many toxins to the cell, and so will magnify the toxicity of many toxins including metals such as lead, mercury, etc. Examination of toxic exposures in isolation, without consideration of co-exposures, leads to under-estimation of risks.

In animals:

- in numerous studies, rats exposed to *in utero* had higher oxidative stress in the brain and liver early in life, loss of brain cells [pyramidal cells in the hippocampus], poorer learning and working memory, and lower passive avoidance (potentially associated with anti-social behaviour);
- injection of serum from exposed rats, to pregnant rats, impaired development and led to higher foetal loss, presumed due to auto-antibodies;
- cell phone radiation damaged pregnant and foetal rat brains;
- across four studies radiofrequency/microwave exposure from a GSM phone affected grooming and rearing of adolescent rats, a month of exposure (1 h/day) altered passive avoidance behaviour and hippocampal morphology, as well as learning and memory, and also decreased locomotion;
- in two studies, long term exposure of rats to a cell phone impaired memory and increased error rates, with changes in the hippocampus. One study reported an age-dependent variation. A further study reported formation of auto-antibodies;
- exposure of rats reduced the efficacy of a pain-killer;
- in two studies, mice exposed *in utero* had impaired memory and were hyperactive because neuronal programming was altered. Exposed mice embryos had impaired bone and cartilage formation;
- the neuro-immune system of middle-aged rats was affected by GSM exposure, in a manner distinct from younger rats;
- formation of the retina of the eye was deranged in chicks;
- ants' memory was severely impaired by exposure to GSM 900 MHz radiation; and
- honeybees exposed to mobile phones gave signals of warning/distress that may trigger swarming.

D. Effects on the Brain and Nervous System

Forty-four studies address neurological effects. Many of the effects listed here were replicated in numerous studies.

Four studies of human volunteers found that:

- short term exposure to radiofrequency energy decreased spontaneous brain activity in multiple regions of the brain, measured with functional MRI;
- mobile phone exposure reduced cochlear nerve compound action potential (CNAP) during surgery;
- GSM mobile phone (cell phone) exposure caused lower amplitude of P300 waves; and
- alterations in brain wave activity with exposure were different according to gender.

Dozens of studies in rodents found that:

- exposure *in utero* led to lower levels of a range of antioxidants, smaller numbers of pyramidal cells in the hippocampus in month-old pups, inflammation, degenerative nuclear and cellular changes and edema in the brain, electrophysiological impairment of Purkinje cells (the largest neurons in the brain), impaired transmission across synapses, DNA damage, neuronal loss, changed calcium efflux (an indication of breakdown of cellular membranes), and altered electroencephalyogram (EEG) readings;
- in rats, daily exposure caused lower levels of neurotransmitters, DNA damage, degenerative changes, oxidative stress, higher beta-amaloid, extensive changes in various protein levels, altered firing of neurons, changed calcium binding and immunoreactivity along with cell loss;
- shorter term exposure caused cell death in the brain;
- a single exposure affected neuro-immunity, stress and behaviour differently in young versus middle-aged rats, and led to impaired integrity of the blood brain barrier a week later;
- sleep cycles were altered in rats exposed to a modulated radiofrequency signal; and
- in mice, chronic radiofrequency energy reduced neurotropins (chemicals for maintenance of neurons), and caused loss of pyramidal brain cells and alteration of calcium movement across cell membranes.

In two studies of insects, short term exposure affected behaviour, memory and physiology.

Laboratory studies of cell cultures revealed:

- 3 minute exposures to GHz range radiation caused a reversible 30% decrease in firing rate and bursting rate in a synthetic neural network; and
- modulation of heat shock proteins in differentiated neuroblastoma cells (neuron-like cells).

In summary, regular cell phone exposure can lead to altered structure, biochemistry and function of the brain. Function is impaired, with cell death and increased levels of compounds associated with chronic degenerative disease.

E. Effects on the Eye

Six scientific publications highlight effects of low level radiofrequency energy on the eye. Cataract formation with higher levels of a broad range of electromagnetic radiation is well known, and eyes are at risk of thermal effects because they lack blood flow for cooling. Research now points to other effects at lower exposure levels that do not induce heating.

In animals it was found that:

- rat corneal epithelium (the growing layer on the cornea) was thicker in animals exposed to low intensity microwave radiation for two hours daily over three weeks;
- radiation from computer monitors caused changes in rat corneas and lenses, including oxidative stress and indications of genetic damage; and
- development of the retina in chick embryos was disrupted with radiation from a cell phone.

In two laboratory cell culture studies, lens epithelial cells exhibited oxidative stress, altered protein and decreased cell viability following short term (0.5 to 2 hours) exposure to low levels of 1.8 GHz RF radiation.

This research replicates the findings of a 2010 review, that summarized that radiofrequency exposure affects lens transparency, cell growth and cell death, inhibits intercellular communication, and induces stress responses and genetic damage.

F. Cardiovascular Effects

Four research publications identify effects on the cardiovascular system:

- consistent with earlier findings regarding EHS (below) a 2013 study found a “non-thermal” (low exposure) vasodilator effect of cell phone radiation exposure to the jaw and cheek;
- rats exposed to 900 MHz pulse-modulated radiofrequency radiation (similar to phone “talk mode”) daily 20 minutes/day for three weeks experienced oxidative damage to the heart (as well as the lungs, testis and liver);
- a very large study of rats, with a range of exposure durations, found heart damage that increased with dose, as well as higher blood pressure and lower blood calcium levels; and
- in the laboratory, radiofrequency exposure altered the structure of hemoglobin and lowered its capacity to carry oxygen in the blood.

In summary, research indicates that radiofrequency radiation may make the blood carry less oxygen, harm the heart, increase blood pressure and affect blood vessels. Effects identified in people with electromagnetic hypersensitivity (below) include heart rate variability.

G. Electrohypersensitivity (EHS)

We all have our strengths and vulnerabilities, and some people experience diverse symptoms that correlate reproducibly with exposure to electromagnetic energy. Research can tend to find no effect (be "biased to the null") with these individuals, due to delayed onset and resolution of symptoms, as well as other sensitivities that may be provoked in research settings.

Nine publications were identified, including:

- a study of more than 400 participants that identified a suite of biochemical markers for those with EHS;
- an overview of diagnosis of EHS by measuring heart rate variability, microcirculation and electric skin potentials;
- the Guideline of the Austrian Medical Association for the diagnosis and treatment of EMF- related health problems and illnesses (EMF syndrome), a consensus paper of the Austrian Medical Association's EMF Working Group (AG-EMF);
- research indicating that avoidance of radiation from video display terminals allowed affected individuals to return to productivity;
- research comparing individuals with symptoms associated specifically with cell phones, individuals with EHS and healthy controls found that those affected by a broader range of exposures were more likely also to suffer psychological distress than healthy controls or those with symptoms related to cell phones alone;
- an overview of the status of EHS, as a disability that is accommodated in Sweden. Differences in the skin may be markers of this disability; and
- research indicating a higher prevalence of thyroid and liver dysfunction, and chronic inflammation in patients presenting with EHS. It is recommended to check for treatable conditions in these patients.

Research is progressing on diagnosis (traits, symptoms and objective markers), treatment and accommodation of individuals with EHS, with clinical guidelines in place and under review.

H. Biochemical Effects

Research often includes biochemical measurements, so literature touching on biochemical effects is not surprisingly the largest collection of publications indicating significant and potentially harmful effects of radiofrequency radiation. Several themes run through the 65 publications examining laboratory research that were identified, some of which were touched upon above.

In animal studies, radiofrequency radiation affects biochemical parameters that correspond to:

- increased oxidative stress;
- damage to genetic material;
- damage to cellular membranes, with reduced fluidity and increased permeability;
- cellular damage and cellular death, in the brain, heart, liver, testis, blood and reproductive cells (sperm and eggs); and
- changes in neurotransmitters that govern operation of the nervous system.

These findings are replicated and explored further in diverse cell culture systems simulating the nervous system, white blood cells [lymphocytes], sperm cells and tissues.

Conclusions

This collection of 140 recent publications contains highly significant, relevant data related to health effects, ranging from biochemical to subcellular, animal models and human studies. Extensive evidence of harms was not considered in this revision of Safety Code 6. This includes cancer, reproductive, developmental, neurological and cardiac harms, electrohypersensitivity, and the biochemical underpinnings of these conditions.

Across the board, it is clear that the scientific literature has not been completely searched, collated nor assessed. C4ST is particularly concerned, because almost three quarters of these references were provided during consultations. The materials presented here may constitute the tip of the iceberg, because an information professional may well have uncovered considerably more research.

The current evidence base allegedly supporting draft Safety Code 6 is lacking a great deal of information demonstrating the potential for significant harm from low levels of radiofrequency/microwave radiation. It is necessary to follow modern, established international best practices for systematic review in environmental health, with knowledgeable interpretation of study strengths and limitations, with full transparency for Health Canada to bring together a more comprehensive, up to date evidence base.

In the absence of a complete evidence base, it is impossible that Health Canada has founded Safety Code 6 on a "weight of evidence" as claimed. Given the absence of studies showing harm, and suggestions of bias in selection of evidence, Safety Code 6 as it stands will not protect the health of Canadians.

As Low as Reasonably Achievable (ALARA)

C4ST regularly hears from Canadians who report being sickened and disabled by exposures to radiofrequency/microwave radiation. The immediate response to the current scientific shambles and clear public health issue should be to ensure that health effects are recognized and that exposures are *As Low As Reasonably Achievable* (ALARA).

Measures to do so should include, but not be limited to:

- provide guidelines and resources to assist Canadian physicians in becoming apprised of radiofrequency/microwave exposure and related health problems and clinical presentations that may be associated with over-exposure or sensitivity;
- advise Canadians to limit their exposure, especially the exposure of children;
- use of only wired computers in schools and workplaces. If that is impossible, provide individuals the right to turn off the router in the classroom or workplace, and provide "safe havens" for electrosensitive individuals;
- development and urgent deployment of technologies with lower and less frequent emissions:
    - e.g. "smart" devices should send signals rarely and be set up in point-to-point networks rather than multiple layers of a "meshed network";
    - challenge and/or encourage industry to develop safer solutions (Bell, Rogers and Telus have all either presented solutions or signed agreements for emission levels significantly below Safety Code 6 that provide full cell phone coverage);
    - devices with significantly lower emissions that are available in other countries should be approved expeditiously by the CSA. Examples include cordless phones and baby monitors that only transmit when necessary; not continuously.

Appendix 1. Thoroughness of "Authoritative Reviews"

In the Health Canada and RSC documents, reference is made to 16 "authoritative reviews." The numbers of citations published each year from 2009 to 2014, in each of these reviews as well as in the Friesen Update are summarized in Table 2.

While over a thousand relevant recent publications (2009 to 2013) were identified in the Friesen Update and provided to the RSC, the RSC cited less than 15% of the number of studies. Moreover, of the "authoritative reviews" the largest and most recent (SCENIHR Preliminary 2013) cited 34% of the studies. Even if there was no overlap between the Canadian and SCENIHR citations (which is not true), more than half of the easily identifiable relevant studies were not examined. See Table 2 below.

Table 2. Tally of numbers of references 2009 to 2014 cited in the Health Canada Safety Code 6 documents, the Royal Society of Canada report, the Friesen Update submission and various "Authoritative Reviews". Abbreviations are defined on the following page.

	Report	2009	2010	2011	2012	2013	2014	Total cited
Health Canada	SC 6 2013 Draft for RSC review	7	5	2	2			16
	SC 6 2014 Draft posted on HC website 16May 2014	9	6	2	3	3		23
	Health Canada SC6 2013 Rationale	7	3	4	3			17
	RSC SC6 Report 1 April 2014	21	40	36	39	29	3	168
	RSC SC6 Report 1 April 2014 Chapter 7 (Health Effects)	14	26	26	32	22	4	124
	FriesenM UPDATE provided to RSC (2013)	226	257	233	246	205	3 EAP	1170
"Authoritative Reviews" identified by Health Canada	SCENIHR Preliminary 2013	83	94	99	96	28		400
	ANSES 2013 France	84	102	104	64	15		369
	AGNIR 2012 United Kingdom (UK)	116	101	41	3			261
	SSM 2013 Sweden	11	31	113	98	4		257
	NIPH 2012 Norway	51	77	63	8			199
	IARC 2011 WHO Monograph 102	78	69	40				187
	EFHRAN 2012 European Commission	38	29	66	3			136
	The Hague 2013 The Netherlands	16	14	26	5			61
	SSK 2011 Germany	13	20	18				51
	CCARS 2011 Spain	29	14					43
	Latin America Experts Committee 2010	26	7					33
	Mugdal et al 2013 European Commission*	24	3					27*
	Reuben 2010	13						13
	ICNIRP 2009	10						10
	Victoria Dept Health 2012 Australia			5	2			7
	SCENIHR 2009	5						5
	Part&Jarasinski 2013 European Commission	1	1			2		4

EAP = e-publication ahead of print

* includes mis-entries and duplicates.

Report Title Abbreviations

AGNIR (2012) = Advisory Group on Non-ionising Radiation. “Health Effects from Radiofrequency Electromagnetic Fields”. Health Protection Agency. UK. http://www.ices-emfsafety.org/documents/publications/AGNIR_report_2012.pdf. 2012.

ANSES (2011) = Agence nationale de securite sanitaire de l’alimentation, de l’environnment et du travail. Radiofrequences et sante. Mis a jour de l’expertise. Maisons-Alfort, France;

CCARS (2011) = Scientific Advisory Committee on Radio Frequencies and Health. Report on Radiofrequencies and Health (2009-2010). Madrid, Spain. 2011;

EFHRAN (2012) = European Health Risk Assessment Network on Electromagnetic Fields Exposure. Risk analysis of human exposure to electromagnetic fields (revised). European Commission [Internet]. 2012;

Friesen M. UPDATE 2013 = Selected list of scientific and other literature on wireless radiation including radiofrequency and microwave radiation, for a full evaluation of biological effects by the Royal Society of Canada’s Expert Panel reviewing draft of Safety Code 6 (2013): Update, December 2013. Submitted to the RSC - public consultation process. 2013:108 pp.

Health Canada SC 6 (2013) Draft = Limits of Human Exposure to Radiofrequency Electromagnetic Energy in the Frequency Range from 3 kHz to 300 GHz: Safety Code 6: 2013 DRAFT. Health Canada; 2013.

Health Canada SC6 (2013) - Rationale . Safety Code 6 (2013) -Rationale. Health Canada. 2013;44.

Health Canada SC 6 (2014) Draft = Health Canada. Limits of Human Exposure to Radiofrequency Electromagnetic Energy in the Frequency Range from 3 kHz to 300 GHz: Safety Code 6: 2014 DRAFT. Health Canada; 2014.

IARC (2013) = International Agency for Research on Cancer (World Health Organization). Non-ionizing radiation, Part II: radiofrequency electromagnetic fields. IARC Working group on the evaluation of carcinogenic risks to humans. IARC Monographs on the evaluation of carcinogenic risks to humans 102. 2013;

ICNIRP (2009) = International Commission on Non-Ionizing Radiation Protection (ICNIRP). Exposure to high frequency electromagnetic fields, biological effects and health consequences (100 kHz-300 GHz). 2009 May 1]; Available from: http://www.icnirp.de/documents/RFReview.pdf

Latin American (2010) = Latin American Experts Committee on High Frequency Electromagnetic Fields and Human Health Latin American Experts Committee. Non-Ionizing Electromagnetic Radiation in the Radiofrequency Spectrum and its Effects on Human Health with a Review on the Standards and Policies of Radiofrequency Radiation Protection in Latin America. 2010. Available from: http://www.wireless-health.org.br/downloads/originals/LatinAmericanScienceReviewreportFinal-2MR.doc

Mugdal et al. 2013 = Mudgal S, Sonigo P, Toni de A, Johansson L, Rualt C, Schütz J, et al. Promoting healthy environments with a focus on the impact of actions on electromagnetic fields. European Commission.

NIPH (2012) = Norwegian Institute of Public Health. Low-level radiofrequency electromagnetic fields - an assessment of health risks and evaluation of regulatory practice (English Summary). Oslo, Norway [Internet]. 2012;

Part P, Jarosinska D 2013 = same authors as in: Electromagnetic fields. In: Environment and human health — Joint EEA-JRC report (EEA Report No 5/2013). European Commission. 2013;Chapter 8:58–9.

Reuben SH (2010) = President’s Cancer Panel (PCP). Reducing environmental cancer risk: what we can do now. DIANE Publishing. 2010;240.

RSC SC6 (2014) = The Royal Society of Canada Expert Panel: A Review of Safety Code 6 (2013): Health Canada’s Safety Limits for Exposure to Radiofrequency Fields. Spring 2014:164. Released to the public 1 April 2014.

SCENIHR (2009) = Health effects of exposure to EMF. Scientific Committee on Emerging and Newly Identified Health Risks Opinion, European Commission Directorate General for Health and Consumers, Luxembourg. 2009;

SCENIHR (2013) = Preliminary opinion on potential health effects of exposure to electromagnetic fields (EMF). Scientific Committee on Emerging and Newly Identified Health Risks Opinion, European Commission Directorate General for Health and Consumers, Luxembourg. 2013;219.

SSK (2011) = German Commission on Radiological Protection. Biological effects of mobile phone use: an overview. German Commission on Radiological Protection. 2011;64 pp.

SSM (2013) = Swedish Radiation Health Authority. Eighth report from SSM's Scientific Council on Electromagnetic Fields, 2013.

The Hague (2013) = The Health Council of The Netherlands. Mobile phones and cancer. Part 1. Epidemiology of tumours of the head. The Netherlands [Internet]. 2013;2013/11.

Victoria Depart. Health (2013) = Victoria Department of Health. Radiation Advisory Committee Annual Report 2012.pdf. Australia: 20 pp.

Appendix 2. Scientific Studies Omitted and Topic Overviews

A 1. Cancer

Eleven omitted studies include:

- a 2014 case series of multifocal invasive breast cancer cases in four young women, where they customarily tucked their cell phones into their bras;
- a May 2014 case-control study of 253 gliomas, 194 meningiomas and 892 matched controls in France, demonstrating double to triple the risk of brain tumours for highest users of cell phones, measured as numbers of calls, and cumulative hours of use;
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- re-analyses of a study of brain tumours in adolescents, highlighting that the data supported elevated risks, the opposite of the authors' conclusion;
- a critique of the Danish Cohort Study. This was fundamentally flawed research wherein "exposed" individuals had a private cell phone subscription in the mid-nineties. The supposedly "unexposed" individuals either had a corporate cell phone subscription or started using a cell phone after enrollment. This study is among the most highly criticized studies on the British Medical Journal website and is not credible; and
- publications addressing brain tumour incidence and cell phones.

The Rationale for the present draft of Safety Code 6 includes references to one report of the Interphone study (that interprets findings as "no increased risk"), as well as three analyses of cancer rates. The premise that increased brain tumours would be an early indicator that cell phones cause cancer is a highly criticized approach, because: 1) many factors may contribute to risks for brain tumours so a large surge in cell phone related cancers must occur before a significant increase would be detected; and 2) if other contributors (e.g. chemical exposures) were decreasing at the same time, an increase from cell phones would be masked by a decrease from other causes.

Year	References and extract	Reports	Cited?
2014	**Coureau G, Bouvier G, Lebailly P, Fabbro-Peray P, Gruber A, Leffondre K, et al. Mobile phone use and brain tumours in the CERENAT case-control study. Occup Environ Med. 2014 May 9;oemed–2013–101754.** The carcinogenic effect of radiofrequency electromagnetic fields in humans remains controversial. However, it has been suggested that they could be involved in the aetiology of some types of brain tumours. Objectives The objective was to analyse the association between mobile phone exposure and primary central nervous system tumours (gliomas and meningiomas) in adults. Methods CERENAT is a multicenter case-control study carried out in four areas in France in 2004–2006. Data about mobile phone use were collected through a detailed questionnaire delivered in a face-to-face manner. Conditional logistic regression for matched sets was used to estimate adjusted ORs and 95% CIs. Results A total of 253 gliomas, 194 meningiomas and 892 matched controls selected from the local electoral rolls were analysed. No association with brain tumours was observed when comparing regular mobile phone users with non-users (OR=1.24; 95% CI 0.86 to 1.77 for gliomas, OR=0.90; 95% CI 0.61 to 1.34 for meningiomas). However, the positive association was statistically significant in the heaviest users when considering life-long cumulative duration (≥896 h, OR=2.89; 95% CI 1.41 to 5.93 for gliomas; OR=2.57; 95% CI 1.02 to 6.44 for meningiomas) and number of calls for gliomas (≥18 360 calls, OR=2.10, 95% CI 1.03 to 4.31). Risks were higher for gliomas, temporal tumours, occupational and urban mobile phone use. Conclusions These additional data support previous findings concerning a possible association between heavy mobile phone use and brain tumours.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a n/a n/a

Year	References and extract	Reports	Cited?
2014	**MooIn Seok, Bo Gyung Kim, Jinna Kim, Jong Dae Lee, and Won-Sang Lee. "Association between Vestibular Schwannomas and Mobile Phone Use." Tumour Biology 35, no. 1 (January 2014): 581–87. doi:10.1007/s13277-013-1081-8.** Vestibular schwannomas (VSs) grow in the region where the energy from mobile phone use is absorbed. We examined the associations of VSs with mobile phone use. This study included 119 patients who had undergone surgical tumor removal. We used two approaches in this investigation. First, a case–control study for the association of mobile phone use and incidence of VSs was conducted. Both cases and controls were investigated with questions based on INTERPHONE guidelines. Amount of mobile phone use according to duration, daily amount, and cumulative hours were compared between two groups. We also conducted a case–case study. The location and volume of the tumors were investigated by MRI. Associations between the estimated amount of mobile phone use and tumor volume and between the laterality of phone use and tumor location were analyzed. In a case–control study, the odds ratio (OR) of tumor incidence according to mobile phone use was 0.956. In the case–case study, tumor volume and estimated cumulative hours showed a strong correlation ($r2 = 0.144$, $p = 0.002$), and regular mobile phone users showed tumors of a markedly larger volume than those of non-regular users ($p < 0.001$). When the analysis was limited to regular users who had serviceable hearing, laterality showed a strong correlation with tumor side ($OR = 4.5$). We found that tumors may coincide with the more frequently used ear of mobile phones and tumor volume that showed strong correlation with amount of mobile phone use, thus there is a possibility that mobile phone use may affect tumor growth.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No No No n/a

Year	References and extract	Reports	Cited?
2013	**Hardell L, Carlberg M, Söderqvist F, Hansson Mild K. Pooled analysis of case-control studies on acoustic neuroma diagnosed 1997-2003 and 2007-2009 and use of mobile and cordless phones. Int J Oncol. 2013 Oct;43(4):1036–44.** We previously conducted a case-control study of acoustic neuroma. Subjects of both genders aged 20-80 years, diagnosed during 1997-2003 in parts of Sweden, were included, and the results were published. We have since made a further study for the time period 2007-2009 including both men and women aged 18-75 years selected from throughout the country. These new results for acoustic neuroma have not been published to date. Similar methods were used for both study periods. In each, one population-based control, matched on gender and age (within five years), was identified from the Swedish Population Registry. Exposures were assessed by a self-administered questionnaire supplemented by a phone interview. Since the number of acoustic neuroma cases in the new study was low we now present pooled results from both study periods based on 316 participating cases and 3,530 controls. Unconditional logistic regression analysis was performed, adjusting for age, gender, year of diagnosis and socio-economic index (SEI). Use of mobile phones of the analogue type gave odds ratio (OR) = 2.9, 95% confidence interval (CI) = 2.0-4.3, increasing with >20 years latency (time since first exposure) to OR = 7.7, 95% CI = 2.8-21. Digital 2G mobile phone use gave OR = 1.5, 95% CI = 1.1-2.1, increasing with latency >15 years to an OR = 1.8, 95% CI = 0.8-4.2. The results for cordless phone use were OR = 1.5, 95% CI = 1.1-2.1, and, for latency of >20 years, OR = 6.5, 95% CI = 1.7-26. Digital type wireless phones (2G and 3G mobile phones and cordless phones) gave OR = 1.5, 95% CI = 1.1-2.0 increasing to OR = 8.1, 95% CI = 2.0-32 with latency >20 years. For total wireless phone use, the highest risk was calculated for the longest latency time >20 years: OR = 4.4, 95% CI = 2.2-9.0. Several of the calculations in the long latency category were based on low numbers of exposed cases. Ipsilateral use resulted in a higher risk than contralateral for both mobile and cordless phones. OR increased per 100 h cumulative use and per year of latency for mobile phones and cordless phones, though the increase was not statistically significant for cordless phones. The percentage tumour volume increased per year of latency and per 100 h of cumulative use, statistically significant for analogue phones. This study confirmed previous results demonstrating an association between mobile and cordless phone use and acoustic neuroma.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** *** this publication was included as an attachment to the written (email) submission of Dr. Hardell to the RSC on 25 October 2013 as part of the RSC public consultation process.**	Yes* No No No* No

Year	References and extract	Reports	Cited?
2013	**Hardell L, Carlberg M. Using the Hill viewpoints from 1965 for evaluating strengths of evidence of the risk for brain tumors associated with use of mobile and cordless phones1). Rev Environ Health. 2013;28(2-3):97–106.** Background: Wireless phones, i.e., mobile phones and cordless phones, emit radiofrequency electromagnetic fields (RF-EMF) when used. An increased risk of brain tumors is a major concern. The International Agency for Research on Cancer (IARC) at the World Health Organization (WHO) evaluated the carcinogenic effect to humans from RF-EMF in May 2011. It was concluded that RF-EMF is a group 2B, i.e., a "possible", human carcinogen. Bradford Hill gave a presidential address at the British Royal Society of Medicine in 1965 on the association or causation that provides a helpful framework for evaluation of the brain tumor risk from RF-EMF. Methods: All nine issues on causation according to Hill were evaluated. Regarding wireless phones, only studies with long-term use were included. In addition, laboratory studies and data on the incidence of brain tumors were considered. Results: The criteria on strength, consistency, specificity, temporality, and biologic gradient for evidence of increased risk for glioma and acoustic neuroma were fulfilled. Additional evidence came from plausibility and analogy based on laboratory studies. Regarding coherence, several studies show increasing incidence of brain tumors, especially in the most exposed area. Support for the experiment came from antioxidants that can alleviate the generation of reactive oxygen species involved in biologic effects, although a direct mechanism for brain tumor carcinogenesis has not been shown. In addition, the finding of no increased risk for brain tumors in subjects using the mobile phone only in a car with an external antenna is supportive evidence. Hill did not consider all the needed nine viewpoints to be essential requirements. Conclusion**:** Based on the Hill criteria, glioma and acoustic neuroma should be considered to be caused by RF-EMF emissions from wireless phones and regarded as carcinogenic to humans, classifying it as group 1 according to the IARC classification. Current guidelines for exposure need to be urgently revised.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes* No No No No *** this publication was included as an attachment to the written (email) submission of Dr. Hardell to the RSC on 25 October 2013 as part of the RSC public consultation process.**

Year	References and extract	Reports	Cited?
2013	**Vocht F de, Hannam K, Buchan I. Environmental risk factors for cancers of the brain and nervous system: the use of ecological data to generate hypotheses. Occup Environ Med. 2013 May 1;70(5):349–56.** Background There is a public health need to balance timely generation of hypotheses with cautious causal inference. For rare cancers this is particularly challenging because standard epidemiological study designs may not be able to elucidate causal factors in an early period of newly emerging risks. Alternative methodologies need to be considered for generating and shaping hypotheses prior to definitive investigation. Objectives To evaluate whether open-access databases can be used to explore links between potential risk factors and cancers at an ecological level, using the case study of brain and nervous system cancers as an example. Methods National age-adjusted cancer incidence rates were obtained from the GLOBOCAN 2008 resource and combined with data from the United Nations Development Report and the World Bank list of development indicators. Data were analysed using multivariate regression models. Results Cancer rates, potential confounders and environmental risk factors were available for 165 of 208 countries. 2008 national incidences of brain and nervous system cancers were associated with continent, gross national income in 2008 and Human Development Index Score. The only exogenous risk factor consistently associated with higher incidence was the penetration rate of mobile/cellular telecommunications subscriptions, although other factors were highlighted. According to these ecological results the latency period is at least 11–12 years, but probably more than 20 years. Missing data on cancer incidence and for other potential risk factors prohibit more detailed investigation of exposure–response associations and/or explore other hypotheses. Conclusions Readily available ecological data may be underused, particularly for the study of risk factors for rare diseases and those with long latencies. The results of ecological analyses in general should not be overinterpreted in causal inference, but equally they should not be ignored where alternative signals of aetiology are lacking.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2013	**West JG, Kapoor NS, Liao S-Y, Chen JW, Bailey L, Nagourney RA. Multifocal Breast Cancer in Young Women with Prolonged Contact between Their Breasts and Their Cellular Phones. Case Reports in Medicine. 2013;2013:1–5.** Breast cancer occurring in women under the age of 40 is uncommon in the absence of family history or genetic predisposition, and prompts the exploration of other possible exposures or environmental risks. We report a case series of four young women-ages from 21 to 39-with multifocal invasive breast cancer that raises the concern of a possible association with nonionizing radiation of electromagnetic field exposures from cellular phones. All patients regularly carried their smartphones directly against their breasts in their brassieres for up to 10 hours a day, for several years, and developed tumors in areas of their breasts immediately underlying the phones. All patients had no family history of breast cancer, tested negative for BRCA1 and BRCA2, and had no other known breast cancer risks. Their breast imaging is reviewed, showing clustering of multiple tumor foci in the breast directly under the area of phone contact. Pathology of all four cases shows striking similarity; all tumors are hormone-positive, low-intermediate grade, having an extensive intraductal component, and all tumors have near identical morphology. These cases raise awareness to the lack of safety data of prolonged direct contact with cellular phones.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2012	**Carlberg M, Hardell L. On the association between glioma, wireless phones, heredity and ionising radiation. Pathophysiology. 2012 Sep;19(4):243–52.** We performed two case-control studies on brain tumours diagnosed during 1 January 1997 to 30 June 2000 and 1 July 2000 to 31 December 2003, respectively. Living cases and controls aged 20-80 years were included. An additional study was performed on deceased cases with a malignant brain tumour using deceased controls. Pooled results for glioma yielded for ipsilateral use of mobile phone odds ratio (OR)=2.9, 95% confidence interval (CI)=1.8-4.7 in the >10 years latency group. The corresponding result for cordless phone was OR=3.8, 95% CI=1.8-8.1. OR increased statistically significant for cumulative use of wireless phones per 100h and per year of latency. For high-grade glioma ipsilateral use of mobile phone gave OR=3.9, 95% CI=2.3-6.6 and cordless phone OR=5.5, 95% CI=2.3-13 in the >10 years latency group. Heredity for brain tumour gave OR=3.4, 95% CI=2.1-5.5 for glioma. There was no interaction with use of wireless phones. X-ray investigation of the head gave overall OR=1.3, 95% CI=1.1-1.7 for glioma without interaction with use of wireless phones or heredity. In conclusion use of mobile and cordless phone increased the risk for glioma with highest OR for ipsilateral use, latency >10 years and third tertile of cumulative use in hours. In total, the risk was highest in the age group <20 years for first use of a wireless phone.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2012	**Milham, S. 2012. Re: Mobile phone use and brain tumors in children and adolescents *** If, as the authors of this article* conclude, mobile phone use is not associated with brain cancer in children and adolescents, there should be as many odds ratios greater than 1 as the number of odds ratios less than 1 (1.0). In table 2, all of the 13 calculated odds ratios are greater than 1.0. A simple binomial probability for this result is $P = .0004$. In table 4, 33 of 36 odds ratios are greater than 1.0 and three are less than 1.0 ($P < .001$). In table 5, all of the 13 odds ratios for ipsilateral use are greater than 1.0, all of the 13 odds ratios for contralateral use are greater than 1.0, and, remarkably, all of the 13 odds ratios for central or unknown location are less than 1.0. The major media are already citing this article as a justification for cell phone use by children or adolescents. If anything, I think it may reflect a positive association between cell phone use and brain tumors. *** Aydin D., Feychting M., Schuz J. et al;. Mobile phone use and brain tumours in children and adolescents: a multi-center case-control study. J. Natl Cancer Inst. 2011; 103(16):1-13.** **Aydin (2011) was cited in AGNER (2012), ANSES (2013) and NIPH (2012).**	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extract	Reports	Cited?
2012	**Morgan LL, Herberman RB, Philips A, Lee Davis D. Re: Mobile phone use and brain tumors in children and adolescents: a multicenter case-control study. J Natl Cancer Inst. 2012 Apr 18;104(8):635–637; author reply 637–638.** Aydin et al.* contradict their widely publicized conclusion that there is no relationship between cell phone use and brain tumors. They conclude that there is "The absence of an exposure–response relationship… in terms of the amount of mobile phone use." Yet they also report an increased brain tumor risk, with their odds ratio (2.15, 95% confidence interval = 1.07 to 4.29, *P* = .001) indicating a clear exposure–response relationship 2.8 years after the first cell phone subscription. Their results suggest that brain cancer in children and adolescents may have a shorter latency than in adults—a finding that others have also indicated ... These numerous discrepancies suggest a poor peer-review process and/or a rush to publish. Overall, the findings of Aydin et al.* are supportive of a positive relationship between cell phone use in children and increased risk for brain tumors with shorter latency than those that have generally been found for adults. In that regard, it is noteworthy that Cardis et al. ... recently reported that heaviest cell phone users had a statistically significantly (*P* = .01) "increasing trend in gliomas with increasing radiofrequency dose after seven years." *** Aydin D., Feychting M., Schuz J. et al;. Mobile phone use and brain tumours in children and adolescents: a multi-center case-control study. J. Natl Cancer Inst. 2011; 103(16):1-13.** **Aydin (2011) was cited in AGNER (2012), ANSES (2013) and NIPH (2012).**	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2012	**Söderqvist F, Carlberg M, Hardell L. Review of four publications on the Danish cohort study on mobile phone subscribers and risk of brain tumors. Rev Environ Health. 2012;27(1):51–8.** BACKGROUND: Since the International Agency for Research on Cancer recently classified radiofrequency electromagnetic fields, such as those emanating from mobile and cordless phones, as possibly carcinogenic to humans (group 2B), two additional reports relevant to the topic have been published. Both articles were new updates of a Danish cohort on mobile phone subscribers and concern the possible association between assumed use of mobile phones and risk of brain tumors. The aim of the present review is to reexamine all four publications on this cohort. METHODS: In brief, publications were scrutinized, and in particular, if the authors made explicit claims to have either proved or disproved their hypothesis, such claims were reviewed in light of applied methods and study design, and in principle, the stronger the claims, the more careful our review. RESULTS: The nationwide Danish cohort study on mobile phone subscribers and risk of brain tumors, including at best 420,095 persons (58% of the initial cohort), is the only one of its kind. In comparison with previous investigations, i.e., case-control studies, its strength lies in the possibility to eliminate non-response, selection, and recall bias. Although at least non-response and recall bias can be excluded, the study has serious limitations related to exposure assessment. In fact, these limitations cloud the findings of the four reports to such an extent that render them uninformative at best. At worst, they may be used in a seemingly solid argument against an increased risk--as reassuring results from a large nationwide cohort study, which rules out not only non-response and recall bias but also an increased risk as indicated by tight confidence intervals. CONCLUSION: Although two of the most comprehensive case-control studies on the matter both have methodological limitations that need to be carefully considered, type I errors are not the only threats to the validity of studies on this topic--the Danish cohort study is a textbook example of that.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2011	**Hardell L, Carlberg M, Hansson Mild K. Re-analysis of risk for glioma in relation to mobile telephone use: comparison with the results of the Interphone international case-control study. Int J Epidemiol. 2011 Aug;40(4):1126–8.** [The Interphone study included 16 research centres from 13 countries. It looked at cases aged 30-59 years of age diagnosed during study periods of 2-4 years between 2000 and 2004.] "In contrast to the Interphone study, we also included use of cordless phones [same type of emissions]. ... It is unclear why younger cases were excluded from the final Interphone report, especially since our results indicate highest risk in the youngest age group. ... These results confirm our previous findings of an increased risk for malignant brain tumour mobile phone users (Hardell 2010)."	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

A 2. Genetic Damage

Fourteen studies reported damage to genetic material.

In people exposed to cell phones genetic damage was reported in:

- hair root cells where a phone is placed; and
- cells from inside the cheek (oral epithelium) of cell phone users;

At a somewhat higher exposure, DNA was damaged in the blood of marine workers.

In animals, evidence of genetic damage with exposure to microwave radiation was seen in:

- male rats in 2 studies (DNA damage in brain cells and liver cells; excretion of a DNA building block)
- rats of various ages. DNA damage increased with dose, and was greater in younger rats compared with mature ones;
- embryonal cells in quail eggs; and
- eggs (oocytes) in female fruit flies.

In the laboratory DNA damage from low level microwave exposure was seen in:

- human sperm exposed to mobile phones;
- a mouse sperm cell line; and
- calf thymus tissue.

Year	References and extract	Reports	Cited?
2014	**Gorpinchenko, Igor, Oleg Nikitin, Oleg Banyra, and Alexander Shulyak. The Influence of Direct Mobile Phone Radiation on Sperm Quality. Central European Journal of Urology 67, no. 1 (2014): 65–71. doi:10.5173/ceju.2014.01.art14.** **Introduction** It is impossible to imagine a modern socially–active man who does not use mobile devices and/or computers with Wi–Fi function. The effect of mobile phone radiation on male fertility is the subject of recent interest and investigations. The aim of this study was to investigate the direct in vitro influence of mobile phone radiation on sperm DNA fragmentation and motility parameters in healthy subjects with normozoospermia. **Material and methods** 32 healthy men with normal semen parameters were selected for the study. Each sperm sample was divided into two equal portions (A and B). Portions A of all involved men were placed for 5 hours in a thermostat, and portions B were placed into a second thermostat for the same period of time, where a mobile phone in standby/talk mode was placed. After 5 hours of incubation the sperm samples from both thermostats were re–evaluated regarding basic motility parameters. The presence of DNA fragmentation in both A and B portions of each sample was determined each hour using a standard sperm chromatin dispersion test. **Results** The number of spermatozoa with progressive movement in the group, influenced by electromagnetic radiation, is statistically lower than the number of spermatozoa with progressive movement in the group under no effect of the mobile phone. The number of non–progressive movement spermatozoa was significantly higher in the group, which was influenced by cell phone radiation. The DNA fragmentation was also significantly higher in this group. **Conclusions** A correlation exists between mobile phone radiation exposure, DNA–fragmentation level and decreased sperm motility.	Reference provided to **Royal Society of Canada** (in 2013)	n/a
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	n/a
		RSC Review of Safety Code 6 (2014)	n/a
		SCENIHR (2013)	n/a
		n/a = not available at time of report publication	

Year	References and extract	Reports	Cited?
2014	**Souza L da CM, Cerqueira E de MM, Meireles JRC. Assessment of nuclear abnormalities in exfoliated cells from the oral epithelium of mobile phone users. Electromagn Biol Med. 2014 Jun;33(2):98–102.** Transmission and reception of mobile telephony signals take place through electromagnetic wave radiation, or electromagnetic radiofrequency fields, between the mobile terminal and the radio base station. Based on reports in the literature on adverse effects from exposure to this type of radiation, the objective of this study was to evaluate the genotoxic and cytotoxic potential of such exposure, by means of the micronucleus test on exfoliated cells from the oral epithelium. The sample included 45 individuals distributed in 3 groups according to the amount of time in hours per week (t) spent using mobile phones: group I, $t > 5$ h; group II, $t > 1$ h and ≤ 5 h; and group III, $t \leq 1$ h. Cells from the oral mucosa were analyzed to assess the numbers of micronuclei, broken egg structures and degenerative nuclear abnormalities indicative of apoptosis (condensed chromatin, karyorrhexis and pyknosis) or necrosis (karyolysis in addition to these changes). The occurrences of micronuclei and degenerative nuclear abnormalities did not differ between the groups, but the number of broken egg (structures that may be associated with gene amplification) was significantly greater in the individuals in group I ($p < 0.05$).	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a n/a n/a n/a n/a

Year	References and extract	Reports	Cited?
2013	**Atlı Şekeroğlu Z, Akar A, Şekeroğlu V. Evaluation of the cytogenotoxic damage in immature and mature rats exposed to 900 MHz radiofrequency electromagnetic fields. Int J Radiat Biol. 2013 Nov;89(11):985–92.** PURPOSE: One of the most important issues regarding radiofrequency electromagnetic fields (RF-EMF) is their effect on genetic material. Therefore, we investigated the cytogenotoxic effects of 900 MHz radiofrequency electromagnetic fields (RF-EMF) and the effect of a recovery period after exposure to RF-EMF on bone marrow cells of immature and mature rats. MATERIALS AND METHODS: The immature and mature rats in treatment groups were exposed to RF-EMF for 2 h/day for 45 days. Average electrical field values for immature and mature rats were 28.1 ± 4.8 V/m and 20.0 ± 3.2 V/m, respectively. Whole-body specific absorption rate (SAR) values for immature and mature rats were in the range of 0.38-0.78 W/kg, and 0.31-0.52 W/kg during the 45 days, respectively. Two recovery groups were kept for 15 days after RF-EMF exposure. RESULTS: Significant differences were observed in chromosome aberrations (CA), micronucleus (MN) frequency, mitotic index (MI) and ratio of polychromatic erythrocytes (PCE) in all treatment and recovery groups. The cytogenotoxic damage in immature rats was statistically higher than the mature rats. The recovery period did not reduce the damage to the same extent as the corresponding control groups. CONCLUSIONS: The exposure of RF-EMF leads to cytotoxic and genotoxic damage in immature and mature rats. More sensitive studies are required to elucidate the possible carcinogenic risk of EMF exposure in humans, especially children.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	n/a
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	n/a
		n/a = not available at time of report publication	

Year	References and extract	Reports	Cited?
2013	**Burlaka A, Tsybulin O, Sidorik E, Lukin S, Polishuk V, Tsehmistrenko S, et al. Overproduction of free radical species in embryonal cells exposed to low intensity radiofrequency radiation. Exp Oncol. 2013 Sep;35(3):219–25.** Aim: Long-term exposure of humans to low intensity radiofrequency electromagnetic radiation (RF-EMR) leads to a statistically significant increase in tumor incidence. Mechanisms of such the effects are unclear, but features of oxidative stress in living cells under RF-EMR exposure were previously reported. Our study aims to assess a production of initial free radical species, which lead to oxidative stress in the cell. Materials and Methods: Embryos of Japanese quails were exposed in ovo to extremely low intensity RF-EMR of GSM 900 MHz (0.25 μW/cm2) during 158-360 h discontinuously (48 c - ON, 12 c - OFF) before and in the initial stages of development. The levels of superoxide (O2·-), nitrogen oxide (NO·), thiobarbituric acid reactive substances (TBARS), 8-oxo-2'-deoxyguanosine (8-oxo-dG) and antioxidant enzymes' activities were assessed in cells/tissues of 38-h, 5- and 10-day RF-EMR exposed and unexposed embryos. Results: The exposure resulted in a significant persistent overproduction of superoxide and nitrogen oxide in embryo cells during all period of analyses. As a result, significantly increased levels of TBARS and 8-oxo-dG followed by significantly decreased levels of superoxide dismutase and catalase activities were developed in the exposed embryo cells. Conclusion: Exposure of developing quail embryos to extremely low intensity RF-EMR of GSM 900 MHz during at least one hundred and fifty-eight hours leads to a significant overproduction of free radicals/reactive oxygen species and oxidative damage of DNA in embryo cells. These oxidative changes may lead to pathologies up to oncogenic transformation of cells.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	n/a
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
		n/a = not available at time of report publication	

Year	References and extract	Reports	Cited?
2013	**Deshmukh PS, Megha K, Banerjee BD, Ahmed RS, Chandna S, Abegaonkar MP, et al. Detection of Low Level Microwave Radiation Induced Deoxyribonucleic Acid Damage Vis-à-vis Genotoxicity in Brain of Fischer Rats. Toxicol Int. 2013 Jan;20(1):19–24.** BACKGROUND: Non-ionizing radiofrequency radiation has been increasingly used in industry, commerce, medicine and especially in mobile phone technology and has become a matter of serious concern in present time. OBJECTIVE: The present study was designed to investigate the possible deoxyribonucleic acid (DNA) damaging effects of low-level microwave radiation in brain of Fischer rats. MATERIALS AND METHODS: Experiments were performed on male Fischer rats exposed to microwave radiation for 30 days at three different frequencies: 900, 1800 and 2450 MHz. Animals were divided into 4 groups: Group I (Sham exposed): Animals not exposed to microwave radiation but kept under same conditions as that of other groups, Group II: Animals exposed to microwave radiation at frequency 900 MHz at specific absorption rate (SAR) 5.953 × 10(-4) W/kg, Group III: Animals exposed to 1800 MHz at SAR 5.835 × 10(-4) W/kg and Group IV: Animals exposed to 2450 MHz at SAR 6.672 × 10(-4) W/kg. At the end of the exposure period animals were sacrificed immediately and DNA damage in brain tissue was assessed using alkaline comet assay. RESULTS: <u>In the present study, we demonstrated DNA damaging effects of low level microwave radiation in brain.</u> CONCLUSION: We concluded that low SAR microwave radiation exposure at these frequencies may induce DNA strand breaks in brain tissue.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No No

Year	References and extract	Reports	Cited?
2013	**Hekmat A, Saboury AA, Moosavi-Movahedi AA. The toxic effects of mobile phone radiofrequency (940 MHz) on the structure of calf thymus DNA. Ecotoxicol Environ Saf. 2013 Feb;88:35–41.** Currently, the biological effects of nonionizing electromagnetic fields (EMFs) including radiofrequency (RF) radiation have been the subject of numerous experimental and theoretical studies. The aim of this study is to evaluate the possible biological effects of mobile phone RF (940 MHz, 15 V/m and SAR=40 mW/kg) on the structure of calf thymus DNA (ct DNA) immediately after exposure and 2 h after 45 min exposure via diverse range of spectroscopic instruments. The UV-vis and circular dichroism (CD) experiments depict that mobile phone EMFs can remarkably cause disturbance on ct DNA structure. In addition, the DNA samples, immediately after exposure and 2 h after 45 min exposure, are relatively thermally unstable compared to the DNA solution, which was placed in a small shielded box (unexposed ct DNA). Furthermore, the exposed DNA samples (the DNA samples that were exposed to 940 MHz EMF) have more fluorescence emission when compared with the unexposed DNA, which may have occurred attributable to expansion of the exposed DNA structure. The results of dynamic light scattering (DLS) and zeta potential experiments demonstrate that RF-EMFs lead to increment in the surface charge and size of DNA. The structure of DNA immediately after exposure is not significantly different from the DNA sample 2 h after 45 min exposure. In other words, <u>the EMF-induced conformational changes are irreversible. Collectively, our results reveal that 940 MHz can alter the structure of DNA</u>. The displacement of electrons in DNA by EMFs may lead to conformational changes of DNA and DNA disaggregation. Results from this study could have an important implication on the health effects of RF-EMFs exposure. In addition, this finding could proffer a novel strategy for the development of next generation of mobile phone.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	n/a
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
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Year	References and extract	Reports	Cited?
2013	**Liu C, Gao P, Xu S-C, Wang Y, Chen C-H, He M-D, et al. Mobile phone radiation induces mode-dependent DNA damage in a mouse spermatocyte-derived cell line: A protective role of melatonin. Int J Radiat Biol. 2013 Sep 3;** Purpose: To evaluate whether exposure to mobile phone radiation (MPR) can induce DNA damage in male germ cells. Materials and methods: A mouse spermatocyte-derived GC-2 cell line was exposed to a commercial mobile phone handset once every 20 min in standby, listen, dialed or dialing modes for 24 h. DNA damage was determined using an alkaline comet assay. Results: <u>The levels of DNA damage were significantly increased following exposure to MPR in the listen, dialed and dialing modes.</u> Moreover, there were significantly higher increases in the dialed and dialing modes than in the listen mode. Interestingly, these results were consistent with the radiation intensities of these modes. However, the DNA damage effects of MPR in the dialing mode were efficiently attenuated by melatonin pretreatment. Conclusions: These results regarding mode-dependent DNA damage have important implications for the safety of inappropriate mobile phone use by males of reproductive age and also suggest a simple preventive measure: Keeping mobile phones as far away from our body as possible, not only during conversations but during 'dialed' and 'dialing' operation modes. Since the 'dialed' mode is actually part of the standby mode, mobile phones should be kept at a safe distance from our body even during standby operation. Furthermore, the protective role of melatonin suggests that it may be a promising pharmacological candidate for preventing mobile phone use-related reproductive impairments.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	n/a
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
		n/a = not available at time of report publication	

Year	References and extract	Reports	Cited?
2012	**Çam ST, Seyhan N. Single-strand DNA breaks in human hair root cells exposed to mobile phone radiation. Int J Radiat Biol. 2012 May;88(5):420–4.** PURPOSE: To analyze the short-term effects of radiofrequency radiation (RFR) exposure on genomic deoxyribonucleic acid (DNA) of human hair root cells. SUBJECTS AND METHODS: Hair samples were collected from eight healthy human subjects immediately before and after using a 900-MHz GSM (Global System for Mobile Communications) mobile phone for 15 and 30 min. Single-strand DNA breaks of hair root cells from the samples were determined using the 'comet assay'. RESULTS: The data showed that talking on a mobile phone for 15 or 30 min significantly increased ($p < 0.05$) single-strand DNA breaks in cells of hair roots close to the phone. Comparing the 15-min and 30-min data using the paired t-test also showed that significantly more damages resulted after 30 min than after 15 min of phone use. CONCLUSIONS: A short-term exposure (15 and 30 min) to RFR (900-MHz) from a mobile phone caused a significant increase in DNA single-strand breaks in human hair root cells located around the ear which is used for the phone calls.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2012	**Khalil AM, Gagaa MH, Alshamali AM. 8-Oxo-7, 8-dihydro-2'-deoxyguanosine as a biomarker of DNA damage by mobile phone radiation. Hum Exp Toxicol. 2012 Jul;31(7):734–40.** We examined the effect of exposure to mobile phone 1800 MHz radio frequency radiation (RFR) upon the urinary excretion of 8-oxo-7, 8-dihydro-2'-deoxyguanosine (8-oxodG), one major form of oxidative DNA damage, in adult male Sprague-Dawley rats. Twenty-four rats were used in three independent experiments (RFR exposed and control, 12 rats, each). The animals were exposed to RFR for 2 h from Global System for Mobile Communications (GSM) signal generator with whole-body-specific absorption rate of 1.0 W/kg. Urine samples were collected from the rat while housed in a metabolic cage during the exposure period over a 4-h period at 0.5, 1.0, 2.0 and 4.0 h from the beginning of exposure. In the control group, the signal generator was left in the turn-off position. The creatinine-standardized concentrations of 8-oxodG were measured. With the exception of the urine collected in the last half an hour of exposure, significant elevations were noticed in the levels of 8-oxodG in urine samples from rats exposed to RFR when compared to control animals. Significant differences were seen overall across time points of urine collection with a maximum at 1 h after exposure, suggesting repair of the DNA lesions leading to 8-oxodG formation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2012	**Panagopoulos DJ. Effect of microwave exposure on the ovarian development of Drosophila melanogaster. Cell Biochem Biophys. 2012 Jun;63(2):121–32** In the present experiments the effect of GSM radiation on ovarian development of virgin Drosophila melanogaster female insects was studied. Newly emerged adult female flies were collected and divided into separate identical groups. After the a lapse of certain number of hours-different for each group-the insects (exposed and sham-exposed) were dissected and their intact ovaries were collected and photographed under an optical microscope with the same magnification. The size of the ovaries was compared between exposed and sham-exposed virgin female insects, during the time needed for the completion of oogenesis and maturation of the first eggs in the ovarioles. Immediately after the intact ovaries were photographed, they were further dissected into individual ovarioles and treated for TUNEL and acridine-orange assays to determine the degree of DNA damage in the egg chamber cells. The study showed that the ovarian size of the exposed insects is significantly smaller than that of the corresponding sham-exposed insects, due to destruction of egg chambers by the GSM radiation, after DNA damage and consequent cell death induction in the egg chamber cells of the virgin females as shown in previous experiments on inseminated females. The difference in ovarian size between sham-exposed and exposed virgin female flies becomes most evident 39-45 h after eclosion when the first eggs within the ovaries are at the late vitellogenic and post-vitellogenic stages (mid-late oogenesis). More than 45 h after eclosion, the difference in ovarian size decreases, as the first mature eggs of the sham-exposed insects are leaving the ovaries and are laid. [0.795 W/Kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2011	**Blank M, Goodman R. DNA is a fractal antenna in electromagnetic fields. Int J Radiat Biol. 2011 Apr;87(4):409–15.** PURPOSE: To review the responses of deoxyribonucleic acid (DNA) to electromagnetic fields (EMF) in different frequency ranges, and characterise the properties of DNA as an antenna. MATERIALS AND METHODS: We examined published reports of increased stress protein levels and DNA strand breaks due to EMF interactions, both of which are indicative of DNA damage. We also considered antenna properties such as electronic conduction within DNA and its compact structure in the nucleus. RESULTS: EMF interactions with DNA are similar over a range of non-ionising frequencies, i.e., extremely low frequency (ELF) and radio frequency (RF) ranges. There are similar effects in the ionising range, but the reactions are more complex. CONCLUSIONS: <u>The wide frequency range of interaction with EMF is the functional characteristic of a fractal antenna, and DNA appears to possess the two structural characteristics of fractal antennas, electronic conduction and self symmetry.</u> These properties contribute to greater reactivity of DNA with EMF in the environment, and the DNA damage could account for increases in cancer epidemiology, as well as variations in the rate of chemical evolution in early geologic history.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2011	**Esmekaya MA, Aytekin E, Ozgur E, Güler G, Ergun MA, Omeroğlu S, et al. Mutagenic and morphologic impacts of 1.8GHz radiofrequency radiation on human peripheral blood lymphocytes (hPBLs) and possible protective role of pre-treatment with Ginkgo biloba (EGb 761). Sci Total Environ. 2011 Dec 1;410-411:59–64.** The mutagenic and morphologic effects of 1.8GHz Global System for Mobile Communications (GSM) modulated RF (radiofrequency) radiation alone and in combination with Ginkgo biloba (EGb 761) pre-treatment in human peripheral blood lymphocytes (hPBLs) were investigated in this study using Sister Chromatid Exchange (SCE) and electron microscopy. Cell viability was assessed with 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) reduction assay. The lymphocyte cultures were exposed to GSM modulated RF radiation at 1.8GHz for 6, 8, 24 and 48h with and without EGb 761. We observed morphological changes in pulse-modulated RF radiated lymphocytes. Longer exposure periods led to destruction of organelle and nucleus structures. Chromatin change and the loss of mitochondrial crista occurred in cells exposed to RF for 8h and 24h and were more pronounced in cells exposed for 48h. Cytoplasmic lysis and destruction of membrane integrity of cells and nuclei were also seen in 48h RF exposed cells. There was a significant increase ($p<0.05$) in SCE frequency in RF exposed lymphocytes compared to sham controls. EGb 761 pre-treatment significantly decreased SCE from RF radiation. RF radiation also inhibited cell viability in a time dependent manner. The inhibitory effects of RF radiation on the growth of lymphoctes were marked in longer exposure periods. EGb 761 pre-treatment significantly increased cell viability in RF+EGb 761 treated groups at 8 and 24h when compared to RF exposed groups alone. <u>The results of our study showed that RF radiation affects cell morphology, increases SCE and inhibits cell proliferation. However, EGb 761 has a protective role against RF induced mutagenity. We concluded that RF radiation induces chromosomal damage in hPBLs</u> but this damage may be reduced by EGb 761 pre-treatment.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2011	**Garaj-Vrhovac V, Gajski G, Pažanin S, Sarolić A, Domijan A-M, Flajs D, et al. Assessment of cytogenetic damage and oxidative stress in personnel occupationally exposed to the pulsed microwave radiation of marine radar equipment. Int J Hyg Environ Health. 2011 Jan;214(1):59–65.** Due to increased usage of microwave radiation, there are concerns of its adverse effect in today's society. Keeping this in view, study was aimed at workers occupationally exposed to pulsed microwave radiation, originating from marine radars. Electromagnetic field strength was measured at assigned marine radar frequencies (3 GHz, 5.5 GHz and 9.4 GHz) and corresponding specific absorption rate values were determined. Parameters of the comet assay and micronucleus test were studied both in the exposed workers and in corresponding unexposed subjects. Differences between mean tail intensity (0.67 vs. 1.22) and moment (0.08 vs. 0.16) as comet assay parameters and micronucleus test parameters (micronuclei, nucleoplasmic bridges and nuclear buds) were statistically significant between the two examined groups, suggesting that cytogenetic alterations occurred after microwave exposure. Concentrations of glutathione and malondialdehyde were measured spectrophotometrically and using high performance liquid chromatography. The glutathione concentration in exposed group was significantly lower than in controls (1.24 vs. 0.53) whereas the concentration of malondialdehyde was significantly higher (1.74 vs. 3.17), indicating oxidative stress. Results suggests that pulsed microwaves from working environment can be the cause of genetic and cell alterations and that oxidative stress can be one of the possible mechanisms of DNA and cell damage.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2011	**Trosić I, Pavicić I, Milković-Kraus S, Mladinić M, Zeljezić D. Effect of electromagnetic radiofrequency radiation on the rats' brain, liver and kidney cells measured by comet assay. Coll Antropol. 2011 Dec;35(4):1259–64.** The goal of study was to evaluate DNA damage in rat's renal, liver and brain cells after in vivo exposure to radiofrequency/microwave (Rf/Mw) radiation of cellular phone frequencies range. To determine DNA damage, a single cell gel electrophoresis/comet assay was used. Wistar rats (male, 12 week old, approximate body weight 350 g) (N = 9) were exposed to the carrier frequency of 915 MHz with Global System Mobile signal modulation (GSM), power density of 2.4 W/m2, whole body average specific absorption rate SAR of 0.6 W/kg. The animals were irradiated for one hour/day, seven days/week during two weeks period. The exposure set-up was Gigahertz Transversal Electromagnetic Mode Cell (GTEM--cell). Sham irradiated controls (N = 9) were apart of the study. The body temperature was measured before and after exposure. There were no differences in temperature in between control and treated animals. Comet assay parameters such as the tail length and tail intensity were evaluated. In comparison with tail length in controls (13.5 +/- 0.7 microm), the tail was slightly elongated in brain cells of irradiated animals (14.0 +/- 0.3 microm). The tail length obtained for liver (14.5 +/- 0.3 microm) and kidney (13.9 +/- 0.5 microm) homogenates notably differs in comparison with matched sham controls (13.6 +/- 0.3 microm) and (12.9 +/- 0.9 microm). Differences in tail intensity between control and exposed animals were not significant. The results of this study suggest that, under the experimental conditions applied, repeated 915 MHz irradiation could be a cause of DNA breaks in renal and liver cells, but not affect the cell genome at the higher extent compared to the basal damage.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

B. Male and Female Infertility

Fourteen studies that were not examined during Canada's review of Safety Code 6 show strengthening evidence that phones in pockets bode poorly for future parenthood.

In 2014 a large, high-quality systematic review and meta-analysis found that cell phone radiation reduced human sperm motility and viability by a factor of 4, while effects were 2 to 4 times worse in animal studies. Another research study of human sperm then found more DNA fragmentation and less motility with exposure to a mobile phone. Early human embryonic development was also reduced with exposure to cell phone radiation.

In animals:

- mobile phone radiation reduced sperm viability and motility, with increased oxidative stress in two studies in rats;
- cell phone radiation induced testicular damage in rats;
- rats exposed in utero had fewer eggs in the ovaries; and
- fruit flies developed damaged eggs when exposed to GSM radiation.

<table>
<tr><th>Year</th><th>References and extract</th><th>Reports</th><th>Cited?</th></tr>
<tr><td>2014</td><td>Gorpinchenko, Igor, Oleg Nikitin, Oleg Banyra, and Alexander Shulyak. The Influence of Direct Mobile Phone Radiation on Sperm Quality. Central European Journal of Urology 67, no. 1 (2014): 65–71. doi:10.5173/ceju.2014.01.art14.

Introduction
It is impossible to imagine a modern socially–active man who does not use mobile devices and/or computers with Wi–Fi function. The effect of mobile phone radiation on male fertility is the subject of recent interest and investigations. The aim of this study was to investigate the direct in vitro influence of mobile phone radiation on sperm DNA fragmentation and motility parameters in healthy subjects with normozoospermia.
Material and methods
32 healthy men with normal semen parameters were selected for the study. Each sperm sample was divided into two equal portions (A and B). Portions A of all involved men were placed for 5 hours in a thermostat, and portions B were placed into a second thermostat for the same period of time, where a mobile phone in standby/talk mode was placed. After 5 hours of incubation the sperm samples from both thermostats were re–evaluated regarding basic motility parameters. The presence of DNA fragmentation in both A and B portions of each sample was determined each hour using a standard sperm chromatin dispersion test.
Results
The number of spermatozoa with progressive movement in the group, influenced by electromagnetic radiation, is statistically lower than the number of spermatozoa with progressive movement in the group under no effect of the mobile phone. The number of non–progressive movement spermatozoa was significantly higher in the group, which was influenced by cell phone radiation. The DNA fragmentation was also significantly higher in this group.
Conclusions
A correlation exists between mobile phone radiation exposure, DNA–fragmentation level and decreased sperm motility.</td><td>Reference provided to Royal Society of Canada (in 2013)</td><td>n/a</td></tr>
<tr><td></td><td></td><td>Health Canada Draft Safety Code 6 (2014)</td><td>No</td></tr>
<tr><td></td><td></td><td>Health Canada SC6 Rationale (2013)</td><td>n/a</td></tr>
<tr><td></td><td></td><td>RSC Review of Safety Code 6 (2014)</td><td>n/a</td></tr>
<tr><td></td><td></td><td>SCENIHR (2013)</td><td>n/a</td></tr>
<tr><td></td><td></td><td colspan="2">n/a = not available at time of report publication</td></tr>
</table>

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2014	**Liu K, Li Y, Zhang G, Liu J, Cao J, Ao L, et al. Association between mobile phone use and semen quality: a systemic review and meta-analysis. Andrology. 2014 Apr 3;** Possible hazardous health effects of radiofrequency electromagnetic radiations emitted from mobile phone on the reproductive system have raised public concern in recent years. This systemic review and meta-analysis was prepared following standard procedures of the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and checklist. Relevant studies published up to May 2013 were identified from five major international and Chinese literature databases: Medline/PubMed, EMBASE, CNKI, the VIP database and the Cochrane Central Register of Controlled Trials in the Cochrane Library. Eighteen studies with 3947 men and 186 rats were included in the systemic review, of which 12 studies (four human studies, four in vitro studies and four animal studies) with 1533 men and 97 rats were used in the meta-analyses. Systemic review showed that results of most of the human studies and in vitro laboratory studies indicated mobile phone use or radiofrequency exposure had negative effects on the various semen parameters studied. However, meta-analysis indicated that mobile phone use had no adverse effects on semen parameters in human studies. In the in vitro studies, meta-analysis indicated that radiofrequency radiation had detrimental effect on sperm motility and viability in vitro [pooled mean difference (MDs) (95% CI): -4.11 (-8.08, -0.13), -3.82 (-7.00, -0.65) for sperm motility and viability respectively]. As for animal studies, radiofrequency exposure had harmful effects on sperm concentration and motility [pooled MDs (95% CI): -8.75 (-17.37, -0.12), -17.72 (-32.79, -2.65) for sperm concentration and motility respectively]. Evidence from current studies suggests potential harmful effects of mobile phone use on semen parameters. A further multicentred and standardized study is needed to assess the risk of mobile phone use on the reproductive system.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a n/a n/a

Year	References and extract	Reports	Cited?
2014	**Su X-J, Yuan W, Tan H, Liu X-Y, Li D, Li D-K, et al. Correlation between Exposure to Magnetic Fields and Embryonic Development in the First Trimester. PLoS ONE. 2014 Jun 30;9(6):e101050.** Objective: To explore the correlation between maternal magnetic field (MF) exposure in daily life and embryonic development. Methods: A cross-sectional study was conducted among 149 pregnant women who were seeking induced abortion of unwanted pregnancies. Participating women were asked to wear an EMDEX Lite magnetic field meter for a 24-h period to obtain MF exposure level within 4 weeks following the abortion. Embryonic bud and sac lengths were measured through B-mode ultrasound before the surgical abortion. Embryo sections were prepared and examined for histological changes, and the apoptosis status of the deciduas was examined using the TUNEL apoptosis assay. Results: Embryonic bud length was inversely associated with maternal daily MF exposure level; the association was statistically significant at the time-weighted-average and 75th percentile of MF exposure levels, with coefficients of −3.09 (P = 0.0479) and −3.07(P = 0.0228), respectively. Logistic regression for examining the risk of higher MF exposure indicated that women with her 75th percentile of daily MF measurements ≥0.82 mG had a 3.95-fold risk of having a fetus with a shorter embryonic bud length than those whose daily MF exposure were <0.82 mG. MF exposure was associated with a higher degree of apoptosis, but the association was not statistically significant. We failed to find a statistical correlation between MF exposure and embryonic sac length and histological changes in the first trimester. Conclusion: Prenatal MF exposure may have an adverse effect on embryonic development.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a n/a n/a n/a n/a

Year	References and extract	Reports	Cited?
2013	**Ghanbari M, Mortazavi SB, Khavanin A, Khazaei M. The Effects of Cell Phone Waves (900 MHz-GSM Band) on Sperm Parameters and Total Antioxidant Capacity in Rats. Int J Fertil Steril. 2013 Apr;7(1):21–8.** BACKGROUND: There is tremendous concern regarding the possible adverse effects of cell phone microwaves. Contradictory results, however, have been reported for the effects of these waves on the body. In the present study, the effect of cell phone microwaves on sperm parameters and total antioxidant capacity was investigated with regard to the duration of exposure and the frequency of these waves. MATERIALS AND METHODS: This experimental study was performed on 28 adult male Wistar rats (200-250 g). The animals were randomly assigned to four groups (n=7): i. control; ii. two-week exposure to cell phone-simulated waves; iii. three-week exposure to cell phone simulated waves; and iv. two-week exposure to cell phone antenna waves. In all groups, sperm analysis was performed based on standard methods and we determined the mean sperm total antioxidant capacity according to the ferric reducing ability of plasma (FRAP) method. Data were analyzed by one-way ANOVA followed by Tukey's test using SPSS version 16 software. RESULTS: The results indicated that sperm viability, motility, and total antioxidant capacity in all exposure groups decreased significantly compared to the control group ($p<0.05$). Increasing the duration of exposure from 2 to 3 weeks caused a statistically significant decrease in sperm viability and motility ($p<0.05$). CONCLUSION: Exposure to cell phone waves can decrease sperm viability and motility in rats. These waves can also decrease sperm total antioxidant capacity in rats and result in oxidative stress.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

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2013	**Liu C, Gao P, Xu S-C, Wang Y, Chen C-H, He M-D, et al. Mobile phone radiation induces mode-dependent DNA damage in a mouse spermatocyte-derived cell line: A protective role of melatonin. Int J Radiat Biol. 2013 Sep 3;** Purpose: To evaluate whether exposure to mobile phone radiation (MPR) can induce DNA damage in male germ cells. Materials and methods: A mouse spermatocyte-derived GC-2 cell line was exposed to a commercial mobile phone handset once every 20 min in standby, listen, dialed or dialing modes for 24 h. DNA damage was determined using an alkaline comet assay. Results: The levels of DNA damage were significantly increased following exposure to MPR in the listen, dialed and dialing modes. Moreover, there were significantly higher increases in the dialed and dialing modes than in the listen mode. Interestingly, these results were consistent with the radiation intensities of these modes. However, the DNA damage effects of MPR in the dialing mode were efficiently attenuated by melatonin pretreatment. Conclusions: These results regarding mode-dependent DNA damage have important implications for the safety of inappropriate mobile phone use by males of reproductive age and also suggest a simple preventive measure: Keeping mobile phones as far away from our body as possible, not only during conversations but during 'dialed' and 'dialing' operation modes. Since the 'dialed' mode is actually part of the standby mode, mobile phones should be kept at a safe distance from our body even during standby operation. Furthermore, the protective role of melatonin suggests that it may be a promising pharmacological candidate for preventing mobile phone use-related reproductive impairments.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
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		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2012	**Al-Damegh MA. Rat testicular impairment induced by electromagnetic radiation from a conventional cellular telephone and the protective effects of the antioxidants vitamins C and E. Clinics (Sao Paulo). 2012 Jul;67(7):785–92.** OBJECTIVE: The aim of this study was to investigate the possible effects of electromagnetic radiation from conventional cellular phone use on the oxidant and antioxidant status in rat blood and testicular tissue and determine the possible protective role of vitamins C and E in preventing the detrimental effects of electromagnetic radiation on the testes. MATERIALS AND METHODS: The treatment groups were exposed to an electromagnetic field, electromagnetic field plus vitamin C (40 mg/kg/day) or electromagnetic field plus vitamin E (2.7 mg/kg/day). All groups were exposed to the same electromagnetic frequency for 15, 30, and 60 min daily for two weeks. RESULTS: There was a significant increase in the diameter of the seminiferous tubules with a disorganized seminiferous tubule sperm cycle interruption in the electromagnetism-exposed group. The serum and testicular tissue conjugated diene, lipid hydroperoxide, and catalase activities increased 3-fold, whereas the total serum and testicular tissue glutathione and glutathione peroxidase levels decreased 3-5 fold in the electromagnetism-exposed animals. CONCLUSION: Our results indicate that the adverse effect of the generated electromagnetic frequency had a negative impact on testicular architecture and enzymatic activity. This finding also indicated the possible role of vitamins C and E in mitigating the oxidative stress imposed on the testes and restoring normality to the testes.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
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		Health Canada **SC6 Rationale (2013)**	No
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		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2012	**Kesari KK, Behari J. Evidence for mobile phone radiation exposure effects on reproductive pattern of male rats: role of ROS. Electromagn Biol Med. 2012 Sep;31(3):213–22** The relationship between radiofrequency electromagnetic fields emitted from mobile phone and infertility is a matter of continuing debate. It is postulated that these radiations may affect the reproduction pattern spell by targeting biochemistry of sperm. In an attempt to expedite the issue, 70 days old Wistar rats (n = 6) were exposed to mobile phone radiofrequency (RF) radiation for 2 h per day for 45 days and data compared with sham exposed (n = 6) group. A significant decrease ($P < 0.05$) in the level of testosterone and an increase in caspase-3 activity were found in the RF-exposed animals. Distortions in sperm head and mid piece of sperm mitochondrial sheath were also observed as captured by Transmission Electron Microscope (TEM). In addition, progeny from RF-exposed rats showed significant decreases in number and weight as compared with that of sham-exposed animals. A reduction in testosterone, an increase in caspase-3, and distortion in spermatozoa could be caused by overproduction of reactive oxygen species (ROS) in animals under mobile phone radiation exposure. Our findings on these biomarkers are clear indications of possible health implications of repeated exposure to mobile phone radiation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2012	**Kumar S, Behari J, Sisodia R. Impact of microwave at X-Band in the aetiology of male infertility. Electromagnetic Biology and Medicine. 2012 Sep;31(3):223–32.** Reports of declining male fertility have renewed interest in assessing the role of environmental and occupational exposures to electromagnetic fields (EMFs) in the aetiology of human infertility. Testicular functions are particularly susceptible to electromagnetic fields. The aim of the present work was to investigate the effect of 10-GHz EMF on male albino rat's reproductive system and to investigate the possible causative factor for such effect of exposure. The study was carried out in two groups of 70-day old adult male albino rats: a sham-exposed and a 10-GHz-exposed group (2h a day for 45 days). Immediately after completion of the exposure, animals were sacrificed and sperms were extracted from the cauda and caput part of testis for the analysis of MDA, melatonin, and creatine kinase. Creatine kinase results revealed an increased level of phosphorylation that converts creatine to creatine phosphate in sperms after EMF exposure. EMF exposure also reduced the level of melatonin and MDA. It is concluded that microwave exposure could adversely affect male fertility by reducing availability of the above parameters. These results are indications of deleterious effects of these radiations on reproductive pattern of male rats. [0.014 W/Kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2012	**Panagopoulos DJ. Effect of microwave exposure on the ovarian development of Drosophila melanogaster. Cell Biochem Biophys. 2012 Jun;63(2):121–32** In the present experiments the effect of GSM radiation on ovarian development of virgin Drosophila melanogaster female insects was studied. Newly emerged adult female flies were collected and divided into separate identical groups. After the a lapse of certain number of hours-different for each group-the insects (exposed and sham-exposed) were dissected and their intact ovaries were collected and photographed under an optical microscope with the same magnification. The size of the ovaries was compared between exposed and sham-exposed virgin female insects, during the time needed for the completion of oogenesis and maturation of the first eggs in the ovarioles. Immediately after the intact ovaries were photographed, they were further dissected into individual ovarioles and treated for TUNEL and acridine-orange assays to determine the degree of DNA damage in the egg chamber cells. The study showed that the ovarian size of the exposed insects is significantly smaller than that of the corresponding sham-exposed insects, due to destruction of egg chambers by the GSM radiation, after DNA damage and consequent cell death induction in the egg chamber cells of the virgin females as shown in previous experiments on inseminated females. The difference in ovarian size between sham-exposed and exposed virgin female flies becomes most evident 39-45 h after eclosion when the first eggs within the ovaries are at the late vitellogenic and post-vitellogenic stages (mid-late oogenesis). More than 45 h after eclosion, the difference in ovarian size decreases, as the first mature eggs of the sham-exposed insects are leaving the ovaries and are laid. [0.795 W/Kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2011	**Kesari KK, Kumar S, Behari J. Effects of radiofrequency electromagnetic wave exposure from cellular phones on the reproductive pattern in male Wistar rats. Appl Biochem Biotechnol. 2011 Jun;164(4):546–59.** The present study investigates the effect of free radical formation due to mobile phone exposure and effect on fertility pattern in 70-day-old male Wistar rats (sham exposed and exposed). Exposure took place in Plexiglas cages for 2 h a day for 35 days to mobile phone frequency. The specific absorption rate was estimated to be 0.9 W/kg. An analysis of antioxidant enzymes glutathione peroxidase ($P < 0.001$) and superoxide dismutase ($P < 0.007$) showed a decrease, while an increase in catalase ($P < 0.005$) was observed. Malondialdehyde ($P < 0.003$) showed an increase and histone kinase ($P = 0.006$) showed a significant decrease in the exposed group. Micronuclei also show a significant decrease ($P < 0.002$) in the exposed group. A significant change in sperm cell cycle of G(0)-G(1) ($P = 0.042$) and G(2)/M ($P = 0.022$) were recorded. Generation of free radicals was recorded to be significantly increased ($P = 0.035$). Our findings on antioxidant, malondialdehyde, histone kinase, micronuclei, and sperm cell cycle are clear indications of an infertility pattern, initiated due to an overproduction of reactive oxygen species. It is concluded that radiofrequency electromagnetic wave from commercially available cell phones might affect the fertilizing potential of spermatozoa.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2010 biochem	**Kesari KK, Kumar S, Behari J. Mobile phone usage and male infertility in Wistar rats. Indian J Exp Biol. 2010 Oct;48(10):987–92.** A significant decrease in protein kinase C and total sperm count along with increased apoptosis were observed in male Wistar rats exposed to mobile phone frequencies (2 h/day x 35 days at 0.9 W/kg specific absorption rate). The results suggest that a reduction in protein kinase activity may be related to overproduction of reactive oxygen species (ROS) under microwave field exposure. Decrease in sperm count and an increase in apoptosis may be causative factor due to mobile radiation exposure leading to infertility.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2010	**Otitoloju AA, Obe IA, Adewale OA, Otubanjo OA, Osunkalu VO. Preliminary study on the induction of sperm head abnormalities in mice, Mus musculus, exposed to radiofrequency radiations from global system for mobile communication base stations. Bull Environ Contam Toxicol. 2010 Jan;84(1):51–4** The exposure of male mice to radiofrequency radiations from mobile phone (GSM) base stations at a workplace complex and residential quarters caused 39.78 and 46.03%, respectively, in sperm head abnormalities compared to 2.13% in control group. Statistical analysis of sperm head abnormality score showed that there was a significant ($p < 0.05$) difference in occurrence of sperm head abnormalities in test animals. The major abnormalities observed were knobbed hook, pin-head and banana-shaped sperm head. The occurrence of the sperm head abnormalities was also found to be dose dependent. The implications of the observed increase occurrence of sperm head abnormalities on the reproductive health of humans living in close. [0.07 - 0.1 uW/cm2]	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extract	Reports	Cited?
2009	**Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, et al. Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertil Steril. 2009 Oct;92(4):1318–25** OBJECTIVE: To evaluate effects of cellular phone radiofrequency electromagnetic waves (RF-EMW) during talk mode on unprocessed (neat) ejaculated human semen. DESIGN: Prospective pilot study. SETTING: Center for reproductive medicine laboratory in tertiary hospital setting. SAMPLES: Neat semen samples from normal healthy donors (n = 23) and infertile patients (n = 9). INTERVENTION(S): After liquefaction, neat semen samples were divided into two aliquots. One aliquot (experimental) from each patient was exposed to cellular phone radiation (in talk mode) for 1 h, and the second aliquot (unexposed) served as the control sample under identical conditions. MAIN OUTCOME MEASURE(S): Evaluation of sperm parameters (motility, viability), reactive oxygen species (ROS), total antioxidant capacity (TAC) of semen, ROS-TAC score, and sperm DNA damage. RESULT(S): Samples exposed to RF-EMW showed a significant decrease in sperm motility and viability, increase in ROS level, and decrease in ROS-TAC score. Levels of TAC and DNA damage showed no significant differences from the unexposed group. CONCLUSION(S): Radiofrequency electromagnetic waves emitted from cell phones may lead to oxidative stress in human semen. We speculate that keeping the cell phone in a trouser pocket in talk mode may negatively affect spermatozoa and impair male fertility. [1.0 W/kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extract	Reports	Cited?
2009	**Gul A, Çelebi H, Uğraş S. The effects of microwave emitted by cellular phones on ovarian follicles in rats. Arch Gynecol Obstet. 2009 Nov 1;280(5):729–33** Objective The aim of this study was to investigate whether there were any toxic effects of microwaves of cellular phones on ovaries in rats. Methods In this study, 82 female pups of rats, aged 21 days (43 in the study group and 39 in the control group) were used. Pregnant rats in the study group were exposed to mobile phones that were placed beneath the polypropylene cages during the whole period of pregnancy. The cage was free from all kinds of materials, which could affect electromagnetic fields. A mobile phone in a standby position for 11 h and 45 min was turned on to speech position for 15 min every 12 h and the battery was charged continuously. On the 21st day after the delivery, the female rat pups were killed and the right ovaries were removed. The volumes of the ovaries were measured and the number of follicles in every tenth section was counted. Results The analysis revealed that in the study group, the number of follicles was lower than that in the control group. The decreased number of follicles in pups exposed to mobile phone microwaves suggest that intrauterine exposure has toxic effects on ovaries. Conclusion We suggest that the microwaves of mobile phones might decrease the number of follicles in rats by several known and, no doubt, countless unknown mechanisms. [< 1.0 W/Kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** .	Yes No No No No

C. Impairment to Development, Learning and Behaviour from Conception to Old Age

A multitude of events orchestrate the progression from a fertilized egg to a newborn infant, through childhood and adolescence, and stages of adulthood. If radiation changes embryonic development, the trajectory of a life is altered.

This collection of 31 publications includes research that reports behaviour or cognition, and/or that involved chronic or pre-natal exposure. Cancer as a result of long term exposure is reported in Section A1 but a discussion of children's risk of brain tumours (not in Section A1) is included here. This section also includes two discussions of exposure assessment of particular relevance for children, as well as Harvard paediatrician Dr. Herbert's extensive review of EMFs and autism, that she submitted to the RSC.

In humans:

- prenatal and postnatal exposure to cell phone exposure was associated with behavioural problems during childhood. This study replicates previous findings; and
- children with higher exposure to mobile phones exhibited more symptoms of Attention Deficit Hyperactivity Disorder (ADHD), only among those who also had higher levels of lead. It is thought that greater membrane permeability with radiofrequency exposures (see section H) increases access of many toxins to the cell, and so will magnify the toxicity of many toxins including metals such as lead, mercury, etc. Examination of toxic exposures in isolation, without consideration of co-exposures, leads to under-estimation of risks.

In animals:

- in numerous studies, rats exposed to *in utero* had higher oxidative stress in the brain and liver early in life, loss of brain cells [pyramidal cells in the hippocampus], poorer learning and working memory, and lower passive avoidance (potentially associated with anti-social behaviour);
- injection of serum from exposed rats, to pregnant rats, impaired development and led to higher foetal loss, presumed due to auto-antibodies;
- cell phone radiation damaged pregnant and foetal rat brains;
- across four studies radiofrequency/microwave exposure from a GSM phone affected grooming and rearing of adolescent rats, a month of exposure (1 h/day) altered passive avoidance behaviour and hippocampal morphology, as well as learning and memory, and also decreased locomotion;
- in two studies, long term exposure of rats to a cell phone impaired memory and increased error rates, with changes in the hippocampus. One study reported an age-dependent variation. A further study reported formation of auto-antibodies;
- exposure of rats reduced the efficacy of a pain-killer;
- in two studies, mice exposed *in utero* had impaired memory and were hyperactive because neuronal programming was altered. Exposed mice embryos had impaired bone and cartilage formation;
- the neuro-immune system of middle-aged rats was affected by GSM exposure, in a manner distinct from younger rats;
- formation of the retina of the eye was deranged in chicks;
- ants' memory was severely impaired by exposure to GSM 900 MHz radiation; and
- honeybees exposed to mobile phones gave signals of warning/distress that may trigger swarming.

Year	References and extracts	Reports	Cited?
2014	**Cetin H, Nazıroğlu M, Celik O, Yüksel M, Pastacı N, Ozkaya MO. Liver antioxidant stores protect the brain from electromagnetic radiation (900 and 1800 MHz)-induced oxidative stress in rats during pregnancy and the development of offspring. J Matern Fetal Neonatal Med. 2014 Apr 9;** Abstract Objectives: The present study determined the effects of mobile phone (900 and 1800 MHz)-induced electromagnetic radiation (EMR) exposure on oxidative stress in the brain and liver as well as the element levels in growing rats from pregnancy to 6 weeks of age. Methods: Thirty-two rats and their offspring were equally divided into three different groups: the control, 900 MHz, and 1800 MHz groups. The 900 MHz and 1800 MHz groups were exposed to EMR for 60 min/d during pregnancy and neonatal development. At the 4th, 5th, and 6th weeks of the experiment, brain samples were obtained. Results: Brain and liver glutathione peroxidase activities, as well as liver vitamin A and β-carotene concentrations decreased in the EMR groups, although brain iron, vitamin A, and β-carotene concentrations increased in the EMR groups. In the 6th week, selenium concentrations in the brain decreased in the EMR groups. There were no statistically significant differences in glutathione, vitamin E, chromium, copper, magnesium, manganese, and zinc concentrations between the three groups. Conclusion: EMR-induced oxidative stress in the brain and liver was reduced during the development of offspring. Mobile phone-induced EMR could be considered as a cause of oxidative brain and liver injury in growing rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a No n/a

Year	References and extracts	Reports	Cited?
2013	**Baş O, Sönmez OF, Aslan A, İkinci A, Hancı H, Yıldırım M, et al. Pyramidal Cell Loss in the Cornu Ammonis of 32-day-old Female Rats Following Exposure to a 900 Megahertz Electromagnetic Field During Prenatal Days 13–21. NeuroQuantology [Internet]. 2013 Oct 30;11(4). Available from: http://www.neuroquantology.com/index.php/journal/article/view/701** The number of studies reporting that the electromagnetic field (EMF) emitted by mobile phones affects human health is increasing by the day. In previous studies we reported that a 900 megahertz (MHz) EMF applied throughout the prenatal period reduced the number of pyramidal cells in the cornu ammonis of rat pups in the postnatal period. In this study we investigated the effect of a 900 MHz EMF applied on days 13-21 of the prenatal period on the number of pyramidal cells in the cornu ammonis of rat pups in the postnatal period. For that purpose, pregnant rats were divided into experimental and control groups. Experimental group pregnant rats were exposed to the effect of a 900 MHz EMF on days 13-21 of pregnancy. No procedure was applied to the control group. Newborn female rat pups were added to the study, and no procedure was performed on these after birth. Five newborn female rats were obtained from the experimental group and six from the control group. All female rat pups were decapitated on the postnatal 32nd day, and histological procedures were performed on the brain tissues. Sections were stained with Cresyl fast violet. The optical dissector technique was used to estimate the total number of pyramidal cells in the cornu ammonis. Sections of cornu ammonis were subjected to histopathological evaluations. Our results showed that exposure to 900 MHz EMF during prenatal days 13-21 led to a significant decrease in the number of pyramidal cells in the cornu ammonis of the experimental group female rat pups ($P<0.05$). Histopathological examination revealed picnotic cells in the cornu ammonis in experimental female rat pups. The pyramidal cell loss in the cornu ammonis may therefore be attributed to exposure to 900 MHz EMF in days 13-21 of the prenatal period.	Reference provided to **Royal Society of Canada** (in 2013)	**No** | Health Canada Draft **Safety Code 6 (2014)**	No Health Canada **SC6 Rationale (2013)**	n/a **RSC Review of Safety Code 6 (2014)**	No **SCENIHR (2013)**	n/a n/a = not available at time of report publication

Year	References and extracts	Reports	Cited?
2013	**Byun, Yoon-Hwan, Mina Ha, Ho-Jang Kwon, Yun-Chul Hong, Jong-Han Leem, Joon Sakong, Su Young Kim, et al. Mobile Phone Use, Blood Lead Levels, and Attention Deficit Hyperactivity Symptoms in Children: A Longitudinal Study. PLoS ONE 8, no. 3 (March 21, 2013). doi:10.1371/journal.pone.0059742.** **Background** Concerns have developed for the possible negative health effects of radiofrequency electromagnetic field (RF-EMF) exposure to children's brains. The purpose of this longitudinal study was to investigate the association between mobile phone use and symptoms of Attention Deficit Hyperactivity Disorder (ADHD) considering the modifying effect of lead exposure. **Methods** A total of 2,422 children at 27 elementary schools in 10 Korean cities were examined and followed up 2 years later. Parents or guardians were administered a questionnaire including the Korean version of the ADHD rating scale and questions about mobile phone use, as well as socio-demographic factors. The ADHD symptom risk for mobile phone use was estimated at two time points using logistic regression and combined over 2 years using the generalized estimating equation model with repeatedly measured variables of mobile phone use, blood lead, and ADHD symptoms, adjusted for covariates. **Results** The ADHD symptom risk associated with mobile phone use for voice calls but the association was limited to children exposed to relatively high lead. **Conclusions** The results suggest that simultaneous exposure to lead and RF from mobile phone use was associated with increased ADHD symptom risk, although possible reverse causality could not be ruled out.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Gao X, Luo R, Ma B, Wang H, Liu T, Zhang J, et al. [Interference of vitamin E on the brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats]. Wei Sheng Yan Jiu. 2013 Jul;42(4):642–6.** OBJECTIVE: To investigate the interference of vitamin E on brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats. METHODS: 40 pregnant rats were randomly divided into five groups (positive control, negative control, low, middle and high dosage of vitamin E groups). The low, middle and high dosage of vitamin E groups were supplemented with 5, 15 and 30 mg/ml vitamin E respectively since the first day of pregnancy. And the negative control group and the positive control group were given peanut oil without vitamin E. All groups except for the negative control group were exposed to 900MHz intensity of cell phone radiation for one hour each time, three times per day for 21 days. After accouchement, the right hippocampus tissue of fetal rats in each group was taken and observed under electron microscope. The vitality of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and the content of malondialdehyde (MDA) in pregnant and fetal rats' brain tissue were tested. RESULTS: Compared with the negative control group, the chondriosomes in neuron and neuroglia of brain tissues was swelling, mild edema was found around the capillary, chromatin was concentrated and collected, and bubbles were formed in vascular endothelial cells (VEC) in the positive fetal rat control group, whereas the above phenomenon was un-conspicuous in the middle and high dosage of vitamin E groups. We can see uniform chromatin, abundant mitochondrion, rough endoplasmic reticulum and free ribosomes in the high dosage group. The apoptosis has not fond in all groups'sections. In the antioxidase activity analysis, compared with the negative control group, the vitality of SOD and GSH-Px significantly decreased and the content of MDA significantly increased both in the pregnant and fetal rats positive control group ($P < 0.05$). In fetal rats, the vitality of SOD and GSH-Px significantly increased in the brain tissues of all three different vitamin E dosages groups when compared with the positive control group, and the content of MDA was found significantly decreased in both middle and high dosage of vitamin E groups($P < 0.05$). The same results have also been found in high dosage pregnant rat group, but in middle dosage group only SOD activity was found increased with significance ($P < 0.05$). With the dosage increase of vitamin E, the vitality of SOD and GSH-Px was increasing and the content of MDA was decreasing. CONCLUSION: Under the experimental dosage, vitamin E has certain interference on damage of antioxidant capacity and energy metabolization induced by electromagnetic radiation of cell phone in pregnant rats and fetal rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Haghani M, Shabani M, Moazzami K. Maternal mobile phone exposure adversely affects the electrophysiological properties of Purkinje neurons in rat offspring. Neuroscience. 2013 Oct 10;250:588–98.** Electromagnetic field (EMF) radiations emitted from mobile phones may cause structural damage to neurons. With the increased usage of mobile phones worldwide, concerns about their possible effects on the nervous system are rising. In the present study, we aimed to elucidate the possible effects of prenatal EMF exposure on the cerebellum of offspring Wistar rats. Rats in the EMF group were exposed to 900-MHz pulse-EMF irradiation for 6h per day during all gestation period. Ten offspring per each group were evaluated for behavioral and electrophysiological evaluations. Cerebellum-related behavioral dysfunctions were analyzed using motor learning and cerebellum-dependent functional tasks (Accelerated Rotarod, Hanging and Open field tests). Whole-cell patch clamp recordings were used for electrophysiological evaluations. The results of the present study failed to show any behavioral abnormalities in rats exposed to chronic EMF radiation. However, whole-cell patch clamp recordings revealed decreased neuronal excitability of Purkinje cells in rats exposed to EMF. The most prominent changes included afterhyperpolarization amplitude, spike frequency, half width and first spike latency. In conclusion, the results of the present study show that prenatal EMF exposure results in altered electrophysiological properties of Purkinje neurons. However, these changes may not be severe enough to alter the cerebellum-dependent functional tasks.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	Yes No n/a No n/a

Year	References and extracts	Reports	Cited?
2013	**Hao D, Yang L, Chen S, Tong J, Tian Y, Su B, et al. Effects of long-term electromagnetic field exposure on spatial learning and memory in rats. Neurol Sci. 2013 Feb;34(2):157–64.** With the development of communications industry, mobile phone plays an important role in daily life. Whether or not the electromagnetic radiation emitted by mobile phone causes any adverse effects on brain function has become of a great concern. This paper investigated the effect of electromagnetic field on spatial learning and memory in rats. 32 trained Wistar rats were divided into two groups: exposure group and control group. The exposure group was exposed to 916 MHz, 10w/m2 mobile phone electromagnetic field (EMF) 6 h a day, 5 days a week, 10 weeks. The completion time, number of total errors and the neuron discharge signals were recorded while the rats were searching for food in an eight-arm radial maze at every weekend. The neuron signals of one exposed rat and one control rat in the maze were obtained by the implanted microelectrode arrays in their hippocampal regions. It can be seen that during the weeks 4-5 of the experiment, the average completion time and error rate of the exposure group were longer and larger than that of control group ($p < 0.05$). During the weeks 1-3 and 6-9, they were close to each other. The hippocampal neurons showed irregular firing patterns and more spikes with shorter interspike interval during the whole experiment period. It indicates that the 916 MHz EMF influence learning and memory in rats to some extent in a period during exposure, and the rats can adapt to long-term EMF exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Herbert MR, Sage C. Autism and EMF? Plausibility of a pathophysiological link - Part I. Pathophysiology. 2013 Jun;20(3):191–209.** Although autism spectrum conditions (ASCs) are defined behaviorally, they also involve multileveled disturbances of underlying biology that find striking parallels in the physiological impacts of electromagnetic frequency and radiofrequency exposures (EMF/RFR). Part I of this paper will review the critical contributions pathophysiology may make to the etiology, pathogenesis and ongoing generation of core features of ASCs. We will review pathophysiological damage to core cellular processes that are associated both with ASCs and with biological effects of EMF/RFR exposures that contribute to chronically disrupted homeostasis. Many studies of people with ASCs have identified oxidative stress and evidence of free radical damage, cellular stress proteins, and deficiencies of antioxidants such as glutathione. Elevated intracellular calcium in ASCs may be due to genetics or may be downstream of inflammation or environmental exposures. Cell membrane lipids may be peroxidized, mitochondria may be dysfunctional, and various kinds of immune system disturbances are common. Brain oxidative stress and inflammation as well as measures consistent with blood-brain barrier and brain perfusion compromise have been documented. Part II of this paper will review how behaviors in ASCs may emerge from alterations of electrophysiological oscillatory synchronization, how EMF/RFR could contribute to these by de-tuning the organism, and policy implications of these vulnerabilities. Changes in brain and autonomic nervous system electrophysiological function and sensory processing predominate, seizures are common, and sleep disruption is close to universal. All of these phenomena also occur with EMF/RFR exposure that can add to system overload ('allostatic load') in ASCs by increasing risk, and worsening challenging biological problems and symptoms; conversely, reducing exposure might ameliorate symptoms of ASCs by reducing obstruction of physiological repair. Various vital but vulnerable mechanisms such as calcium channels may be disrupted by environmental agents, various genes associated with autism or the interaction of both. With dramatic increases in reported ASCs that are coincident in time with the deployment of wireless technologies, we need aggressive investigation of potential ASC - EMF/RFR links. The evidence is sufficient to warrant new public exposure standards benchmarked to low-intensity (non-thermal) exposure levels now known to be biologically disruptive, and strong, interim precautionary practices are advocated. * Dr. Martha Herbert provided this reference to the RSC panel 25 October 2013 as part of the RSC public consultation process. Dr. Herbert is a pediatric neurologist and neuroscientist on the faculty of Harvard Medical School and on staff at the Massachusetts General Hospital with Board Certification in Neurology with Special Competency in Child Neurology and Subspecialty in Neurodevelopmental disorders.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** .	Yes* No No No No

Year	References and extracts	Reports	Cited?
2013	**Herbert MR, Sage C. Autism and EMF? Plausibility of a pathophysiological link Part II. Pathophysiology. 2013 Jun;20(3):211–34.** Autism spectrum conditions (ASCs) are defined behaviorally, but they also involve multileveled disturbances of underlying biology that find striking parallels in the physiological impacts of electromagnetic frequency and radiofrequency radiation exposures (EMF/RFR). Part I (Vol 776) of this paper reviewed the critical contributions pathophysiology may make to the etiology, pathogenesis and ongoing generation of behaviors currently defined as being core features of ASCs. We reviewed pathophysiological damage to core cellular processes that are associated both with ASCs and with biological effects of EMF/RFR exposures that contribute to chronically disrupted homeostasis. Many studies of people with ASCs have identified oxidative stress and evidence of free radical damage, cellular stress proteins, and deficiencies of antioxidants such as glutathione. Elevated intracellular calcium in ASCs may be due to genetics or may be downstream of inflammation or environmental exposures. Cell membrane lipids may be peroxidized, mitochondria may be dysfunctional, and various kinds of immune system disturbances are common. Brain oxidative stress and inflammation as well as measures consistent with blood-brain barrier and brain perfusion compromise have been documented. Part II of this paper documents how behaviors in ASCs may emerge from alterations of electrophysiological oscillatory synchronization, how EMF/RFR could contribute to these by de-tuning the organism, and policy implications of these vulnerabilities. It details evidence for mitochondrial dysfunction, immune system dysregulation, neuroinflammation and brain blood flow alterations, altered electrophysiology, disruption of electromagnetic signaling, synchrony, and sensory processing, de-tuning of the brain and organism, with autistic behaviors as emergent properties emanating from this pathophysiology. Changes in brain and autonomic nervous system electrophysiological function and sensory processing predominate, seizures are common, and sleep disruption is close to universal. All of these phenomena also occur with EMF/RFR exposure that can add to system overload ('allostatic load') in ASCs by increasing risk, and can worsen challenging biological problems and symptoms; conversely, reducing exposure might ameliorate symptoms of ASCs by reducing obstruction of physiological repair. Various vital but vulnerable mechanisms such as calcium channels may be disrupted by environmental agents, various genes associated with autism or the interaction of both. With dramatic increases in reported ASCs that are coincident in time with the deployment of wireless technologies, we need aggressive investigation of potential ASC-EMF/RFR links. The evidence is sufficient to warrant new public exposure standards benchmarked to low-intensity (non-thermal) exposure levels now known to be biologically disruptive, and strong, interim precautionary practices are advocated. * Dr. Martha Herbert provided this reference to the RSC panel 25 October 2013 as part of the RSC public consultation process. Dr. Herbert is a pediatric neurologist and neuroscientist on the faculty of Harvard Medical School and on staff at the Massachusetts General Hospital with Board Certification in Neurology with Special Competency in Child Neurology and Subspecialty in Neurodevelopmental disorders.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes* No No No No

Year	References and extracts	Reports	Cited?
2013	**İkinci A, Odacı E, Yıldırım M, Kaya H, Akça M, Hancı H, et al. The Effects of Prenatal Exposure to a 900 Megahertz Electromagnetic Field on Hippocampus Morphology and Learning Behavior in Rat Pups. NeuroQuantology [Internet]. 2013 Oct 28;11(4). Available from: http://www.neuroquantology.com/index.php/journal/article/view/699** The purpose of this study was to examine the effect on hippocampus morphology and learning behavior in rat pups following prenatal exposure to a 900 megahertz (MHz) electromagnetic field (EMF). Female Sprague Dawley rats weighing 180-250 g were left to mate with males. The following day, pregnant rats identified as such by the vaginal smear test were divided into two groups, control (n=3) and EMF (n=3). No procedures were performed on the control group. The rats in the EMF group were exposed to 900 MHz EMF on days 13 to 21 of pregnancy, for 1 h a day. Female rat pups were removed from their mothers at 22 days old. We then established two newborn rat groups, a 13 member control group and a 10 member EMF group. Radial arm maze and passive avoidance tests were used to measure rat pups' learning and memory performance. All rats were decapitated on the postnatal 32nd day. Routine histological procedures were performed on the brain tissues, and sections were stained with Cresyl fast violet. The radial arm maze (p=0.007) and passive avoidance (p=0.032) tests were administered to both groups under identical conditions, and compromised learning behavior was determined in the EMF group rats. Morphological compromise was also determined in the EMF group sections. <u>Our results show that the application of a 900 MHz EMF in the prenatal period adversely affected female pups' learning behavior and also resulted in histopathological changes appearing in the hippocampus.</u>	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No n/a

Year	References and extracts	Reports	Cited?
2013	**Maaroufi K, Had-Aissouni L, Melon C, Sakly M, Abdelmelek H, Poucet B, et al. Spatial learning, monoamines and oxidative stress in rats exposed to 900MHz electromagnetic field in combination with iron overload. Behav Brain Res. 2013 Oct 18;258C:80–9.** The increasing use of mobile phone technology over the last decade raises concerns about the impact of high frequency electromagnetic fields (EMF) on health. More recently, a link between EMF, iron overload in the brain and neurodegenerative disorders including Parkinson's and Alzheimer's diseases has been suggested. Co-exposure to EMF and brain iron overload may have a greater impact on brain tissues and cognitive processes than each treatment by itself. To examine this hypothesis, Long-Evans rats submitted to 900MHz exposure or combined 900MHz EMF and iron overload treatments were tested in various spatial learning tasks (navigation task in the Morris water maze, working memory task in the radial-arm maze, and object exploration task involving spatial and non spatial processing). Biogenic monoamines and metabolites (dopamine, serotonin) and oxidative stress were measured. Rats exposed to EMF were impaired in the object exploration task but not in the navigation and working memory tasks. They also showed alterations of monoamine content in several brain areas but mainly in the hippocampus. Rats that received combined treatment did not show greater behavioral and neurochemical deficits than EMF-exposed rats. None of the two treatments produced global oxidative stress. These results show that there is an impact of EMF on the brain and cognitive processes but this impact is revealed only in a task exploiting spontaneous exploratory activity. In contrast, there are no synergistic effects between EMF and a high content of iron in the brain.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Narayanan SN, Kumar RS, Paval J, Kedage V, Bhat MS, Nayak S, et al. Analysis of emotionality and locomotion in radio-frequency electromagnetic radiation exposed rats. Neurol Sci. 2013 Jul;34(7):1117–24.** In the current study the modulatory role of mobile phone radio-frequency electromagnetic radiation (RF-EMR) on emotionality and locomotion was evaluated in adolescent rats. Male albino Wistar rats (6-8 weeks old) were randomly assigned into the following groups having 12 animals in each group. Group I (Control): they remained in the home cage throughout the experimental period. Group II (Sham exposed): they were exposed to mobile phone in switch-off mode for 28 days, and Group III (RF-EMR exposed): they were exposed to RF-EMR (900 MHz) from an active GSM (Global system for mobile communications) mobile phone with a peak power density of 146.60 μW/cm(2) for 28 days. On 29th day, the animals were tested for emotionality and locomotion. Elevated plus maze (EPM) test revealed that, percentage of entries into the open arm, percentage of time spent on the open arm and distance travelled on the open arm were significantly reduced in the RF-EMR exposed rats. Rearing frequency and grooming frequency were also decreased in the RF-EMR exposed rats. Defecation boli count during the EPM test was more with the RF-EMR group. No statistically significant difference was found in total distance travelled, total arm entries, percentage of closed arm entries and parallelism index in the RF-EMR exposed rats compared to controls. Results indicate that mobile phone radiation could affect the emotionality of rats without affecting the general locomotion. [146.6 uW/cm^2]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** .	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Aldad TS, Gan G, Gao X-B, Taylor HS. Fetal radiofrequency radiation exposure from 800-1900 mhz-rated cellular telephones affects neurodevelopment and behavior in mice. Sci Rep. 2012;2:312.** Neurobehavioral disorders are increasingly prevalent in children, however their etiology is not well understood. An association between prenatal cellular telephone use and hyperactivity in children has been postulated, yet the direct effects of radiofrequency radiation exposure on neurodevelopment remain unknown. Here we used a mouse model to demonstrate that in-utero radiofrequency exposure from cellular telephones does affect adult behavior. Mice exposed in-utero were hyperactive and had impaired memory as determined using the object recognition, light/dark box and step-down assays. Whole cell patch clamp recordings of miniature excitatory postsynaptic currents (mEPSCs) revealed that these behavioral changes were due to altered neuronal developmental programming. Exposed mice had dose-responsive impaired glutamatergic synaptic transmission onto layer V pyramidal neurons of the prefrontal cortex. We present the first experimental evidence of neuropathology due to in-utero cellular telephone radiation. Further experiments are needed in humans or non-human primates to determine the risk of exposure during pregnancy.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Bodera P, Stankiewicz W, Antkowiak B, Paluch M, Kieliszek J, Sobiech J, et al. Suppressive effect of electromagnetic field on analgesic activity of tramadol in rats. Pol J Vet Sci. 2012;15(1):95–100.** The electromagnetic fields (EMFs) have been shown to alter animal and human behavior, such as directional orientation, learning, pain perception (nociception or analgesia) and anxiety-related behaviors. The aim of this study was to evaluate the influence of electromagnetic fields of high-frequency microwaves on pain perception and anti-nociceptive activity of tramadol (TRAM) - analgetic effective in the treatment of moderate to severe acute and chronic pain states. Electromagnetic fields exposures of a)1500 MHz frequency and b) modulated, 1800 MHz (which is identical to that generated by mobile phones) were applied. Paw withdrawal latency (PWL) to thermal stimulus was measured in vehicle or tramadol (TRAM) treated animals before and after 30, 60 and 90 minutes from injections. The differences in the level of pain (PWL) between control group and rats exposed to EMF alone in three measurements, were not observed. Tramadol alone significantly increased PWLs to thermal stimulus in comparison to vehicle results at 30 ($p < 0.001$) and 60 minutes ($p < 0.05$) after drug injection. EMF exposure of both frequencies transiently suppressed analgesic effect of tramadol, significantly reducing paw withdrawal latency in animals treated with this drug at 30 minutes from the drug injection.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Bouji M, Lecomte A, Hode Y, de Seze R, Villégier A-S. Effects of 900 MHz radiofrequency on corticosterone, emotional memory and neuroinflammation in middle-aged rats. Exp Gerontol. 2012 Jun;47(6):444–51.** The widespread use of mobile phones raises the question of the effects of electromagnetic fields (EMF, 900 MHz) on the brain. Previous studies reported increased levels of the glial fibrillary acidic protein (GFAP) in the rat's brain after a single exposure to 900 MHz global system for mobile (GSM) signal, suggesting a potential inflammatory process. While this result was obtained in adult rats, no data is currently available in older animals. Since the transition from middle-age to senescence is highly dependent on environment and lifestyle, we studied the reactivity of middle-aged brains to EMF exposure. We assessed the effects of a single 15 min GSM exposure (900 MHz; specific absorption rate (SAR)=6 W/kg) on GFAP expression in young adults (6 week-old) and middle-aged rats (12 month-old). Brain interleukin (IL)-1β and IL-6, plasmatic levels of corticosterone (CORT), and emotional memory were also assessed. Our data indicated that, in contrast to previously published work, acute GSM exposure did not induce astrocyte activation. Our results showed an IL-1β increase in the olfactory bulb and enhanced contextual emotional memory in GSM-exposed middle-aged rats, and increased plasmatic levels of CORT in GSM-exposed young adults. Altogether, our data showed an age dependency of reactivity to GSM exposure in neuro-immunity, stress and behavioral parameters. Reproducing these effects and studying their mechanisms may allow a better understanding of mobile phone EMF effects on neurobiological parameters.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Cammaerts M-C, De Doncker P, Patris X, Bellens F, Rachidi Z, Cammaerts D. GSM 900 MHz radiation inhibits ants' association between food sites and encountered cues. Electromagn Biol Med. 2012 Jun;31(2):151–65.** The kinetics of the acquisition and loss of the use of olfactory and visual cues were previously obtained in six experimental colonies of the ant Myrmica sabuleti meinert 1861, under normal conditions. In the present work, the same experiments were conducted on six other naive identical colonies of M. sabuleti, under electromagnetic radiation similar to those surrounding GSM and communication masts. In this situation, no association between food and either olfactory or visual cues occurred. After a recovery period, the ants were able to make such an association but never reached the expected score. Such ants having acquired a weaker olfactory or visual score and still undergoing olfactory or visual training were again submitted to electromagnetic waves. Not only did they lose all that they had memorized, but also they lost it in a few hours instead of in a few days (as under normal conditions when no longer trained). They kept no visual memory at all (instead of keeping 10% of it as they normally do). The impact of GSM 900 MHz radiation was greater on the visual memory than on the olfactory one. These communication waves may have such a disastrous impact on a wide range of insects using olfactory and/or visual memory, i.e., on bees.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Divan HA, Kheifets L, Obel C, Olsen J. Cell phone use and behavioural problems in young children. J Epidemiol Community Health. 2012 Jun 1;66(6):524–9.** **BACKGROUND:** Potential health effects of cell phone use in children have not been adequately examined. As children are using cell phones at earlier ages, research among this group has been identified as the highest priority by both national and international organisations. The authors previously reported results from the Danish National Birth Cohort (DNBC), which looked at prenatal and postnatal exposure to cell phone use and behavioural problems at age 7 years. Exposure to cell phones prenatally, and to a lesser degree postnatally, was associated with more behavioural difficulties. The original analysis included nearly 13 000 children who reached age 7 years by November 2006. **METHODS:** To see if a larger, separate group of DNBC children would produce similar results after considering additional confounders, children of mothers who might better represent current users of cell phones were analysed. This 'new' dataset consisted of 28 745 children with completed Age-7 Questionnaires to December 2008. **RESULTS:** The highest OR for behavioural problems were for children who had both prenatal and postnatal exposure to cell phones compared with children not exposed during either time period. The adjusted effect estimate was 1.5 (95% CI 1.4 to 1.7). **CONCLUSIONS:** The findings of the previous publication were replicated in this separate group of participants demonstrating that cell phone use was associated with behavioural problems at age 7 years in children, and this association was not limited to early users of the technology. Although weaker in the new dataset, even with further control for an extended set of potential confounders, the associations remained.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Gandhi OP, Morgan LL, de Salles AA, Han Y-Y, Herberman RB, Davis DL. Exposure limits: the underestimation of absorbed cell phone radiation, especially in children. Electromagn Biol Med. 2012 Mar;31(1):34–51.** The existing cell phone certification process uses a plastic model of the head called the Specific Anthropomorphic Mannequin (SAM), representing the top 10% of U.S. military recruits in 1989 and greatly underestimating the Specific Absorption Rate (SAR) for typical mobile phone users, especially children. A superior computer simulation certification process has been approved by the Federal Communications Commission (FCC) but is not employed to certify cell phones. In the United States, the FCC determines maximum allowed exposures. Many countries, especially European Union members, use the "guidelines" of International Commission on Non-Ionizing Radiation Protection (ICNIRP), a non governmental agency. Radiofrequency (RF) exposure to a head smaller than SAM will absorb a relatively higher SAR. Also, SAM uses a fluid having the average electrical properties of the head that cannot indicate differential absorption of specific brain tissue, nor absorption in children or smaller adults. The SAR for a 10-year old is up to 153% higher than the SAR for the SAM model. When electrical properties are considered, a child's head's absorption can be over two times greater, and absorption of the skull's bone marrow can be ten times greater than adults. Therefore, a new certification process is needed that incorporates different modes of use, head sizes, and tissue properties. Anatomically based models should be employed in revising safety standards for these ubiquitous modern devices and standards should be set by accountable, independent groups.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** *** this reference was noted in the written (email) submission of Dr. Davis to the RSC on 25 October 2013 as part of the RSC public consultation process.**	Yes* No No No No

Year	References and extracts	Reports	Cited?
2012	**Jing J, Yuhua Z, Xiao-qian Y, Rongping J, Dong-mei G, Xi C. The influence of microwave radiation from cellular phone on fetal rat brain. Electromagn Biol Med. 2012 Mar;31(1):57–66.** The increasing use of cellular phones in our society has brought focus on the potential detrimental effects to human health by microwave radiation. The aim of our study was to evaluate the intensity of oxidative stress and the level of neurotransmitters in the brains of fetal rats chronically exposed to cellular phones. The experiment was performed on pregnant rats exposed to different intensities of microwave radiation from cellular phones. Thirty-two pregnant rats were randomly divided into four groups: CG, GL, GM, and GH. CG accepted no microwave radiation, GL group radiated 10 min each time, GM group radiated 30 min, and GH group radiated 60 min. The 3 experimental groups were radiated 3 times a day from the first pregnant day for consecutively 20 days, and on the 21st day, the fetal rats were taken and then the contents of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), malondialdehyde (MDA), noradrenaline (NE), dopamine (DA), and 5-hydroxyindole acetic acid (5-HT) in the brain were assayed. Compared with CG, there were significant differences ($P<0.05$) found in the contents of SOD, GSH-Px, and MDA in GM and GH; the contents of SOD and GSH-Px decreased and the content of MDA increased. The significant content differences of NE and DA were found in fetal rat brains in GL and GH groups, with the GL group increased and the GH group decreased. Through this study, we concluded that receiving a certain period of microwave radiation from cellular phones during pregnancy has certain harm on fetal rat brains.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Lu Y, Xu S, He M, Chen C, Zhang L, Liu C, et al. Glucose administration attenuates spatial memory deficits induced by chronic low-power-density microwave exposure. Physiol Behav. 2012 Jul 16;106(5):631–7.** Extensive evidence indicates that glucose administration attenuates memory deficits in rodents and humans, and cognitive impairment has been associated with reduced glucose metabolism and uptake in certain brain regions including the hippocampus. In the present study, we investigated whether glucose treatment attenuated memory deficits caused by chronic low-power-density microwave (MW) exposure, and the effect of MW exposure on hippocampal glucose uptake. We exposed Wistar rats to 2.45 GHz pulsed MW irradiation at a power density of 1 mW/cm(2) for 3 h/day, for up to 30 days. MW exposure induced spatial learning and memory impairments in rats. Hippocampal glucose uptake was also reduced by MW exposure in the absence or presence of insulin, but the levels of blood glucose and insulin were not affected. However, these spatial memory deficits were reversed by systemic glucose treatment. Our results indicate that glucose administration attenuates the spatial memory deficits induced by chronic low-power-density MW exposure, and reduced hippocampal glucose uptake may be associated with cognitive impairment caused by MW exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2012	**Megha K, Deshmukh PS, Banerjee BD, Tripathi AK, Abegaonkar MP. Microwave radiation induced oxidative stress, cognitive impairment and inflammation in brain of Fischer rats. Indian J Exp Biol. 2012 Dec;50(12):889–96.** Public concerns over possible adverse effects of microwave radiation emitted by mobile phones on health are increasing. To evaluate the intensity of oxidative stress, cognitive impairment and inflammation in brain of Fischer rats exposed to microwave radiation, male Fischer-344 rats were exposed to 900 MHz microwave radiation (SAR = 5.953 x 10(-4) W/kg) and 1800 MHz microwave radiation (SAR = 5.835 x 10(-4) W/kg) for 30 days (2 h/day). Significant impairment in cognitive function and induction of oxidative stress in brain tissues of microwave exposed rats were observed in comparison with sham exposed groups. Further, significant increase in level of cytokines (IL-6 and TNF-alpha) was also observed following microwave exposure. Results of the present study indicated that increased oxidative stress due to microwave exposure may contribute to cognitive impairment and inflammation in brain.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2011	**Favre D. Mobile phone-induced honeybee worker piping. Apidologie. 2011 May;42(3):270–9.** The worldwide maintenance of the honeybee has major ecological, economic, and political implications. In the present study, electromagnetic waves originating from mobile phones were tested for potential effects on honeybee behavior. Mobile phone handsets were placed in the close vicinity of honeybees. The sound made by the bees was recorded and analyzed. The audiograms and spectrograms revealed that active mobile phone handsets have a dramatic impact on the behavior of the bees, namely by inducing the worker piping signal. In natural conditions, worker piping either announces the swarming process of the bee colony or is a signal of a disturbed bee colony.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Söderqvist F, Carlberg M, Hansson Mild K, Hardell L. Childhood brain tumour risk and its association with wireless phones: a commentary. Environ Health. 2011;10:106.** Case-control studies on adults point to an increased risk of brain tumours (glioma and acoustic neuroma) associated with the long-term use of mobile phones. Recently, the first study on mobile phone use and the risk of brain tumours in children and adolescents, CEFALO, was published. It has been claimed that this relatively small study yielded reassuring results of no increased risk. We do not agree. We consider that the data contain several indications of increased risk, despite low exposure, short latency period, and limitations in the study design, analyses and interpretation. The information certainly cannot be used as reassuring evidence against an association, for reasons that we discuss in this commentary.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Fragopoulou AF, Koussoulakos SL, Margaritis LH. Cranial and postcranial skeletal variations induced in mouse embryos by mobile phone radiation. Pathophysiology. 2010 Jun;17(3):169–77.** This study focuses on foetal development following mild daily exposure of pregnant mice to near field electromagnetic radiation emitted by a mobile phone. The investigation was motivated by the fact that the potentially hazardous electromagnetic radiation emitted by mobile phones is currently of tremendous public interest. Physically comparable pregnant mice were exposed to radiofrequency radiation GSM 900MHz emitted by a mobile phone. Within 5h after birth most cubs were fixed followed by double staining in toto, and conventional paraffin histology. Other cubs remained with their mothers until teeth eruption. Structural development was assessed by examining newborns for the presence of anomalies and/or variations in soft tissues and skeletal anatomy. Electromagnetic radiofrequency exposed newborns, externally examined, displayed a normal phenotype. Histochemical and histological studies, however, revealed variations in the exposed foetuses with respect to control ones concerning the ossification of cranial bones and thoracic cage ribs, as well as displacement of Meckelian cartilage. Littermates examined after teeth eruption displayed normal phenotypes. It is concluded that mild exposure to mobile phone radiation may affect, although transiently, mouse foetal development at the ossification level. The developmental variations observed could be explained by considering the different embryonic origin and mode of ossification of the affected skeletal elements.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Fragopoulou AF, Miltiadous P, Stamatakis A, Stylianopoulou F, Koussoulakos SL, Margaritis LH. Whole body exposure with GSM 900MHz affects spatial memory in mice. Pathophysiology. 2010 Jun;17(3):179–87.** Extended work has been performed worldwide on the effects of mobile phone radiation upon rats' cognitive functions, however there is great controversy to the existence or not of deficits. The present work has been designed in order to test the effects of mobile phone radiation on spatial learning and memory in mice Mus musculus Balb/c using the Morris water maze (a hippocampal-dependent spatial memory task), since there is just one other study on mice with very low SAR level (0.05W/kg) showing no effects. We have applied a 2h daily dose of pulsed GSM 900MHz radiation from commercially available mobile phone for 4 days at SAR values ranging from 0.41 to 0.98W/kg. Statistical analysis revealed that during learning, exposed animals showed a deficit in transferring the acquired spatial information across training days (increased escape latency and distance swam, compared to the sham-exposed animals, on the first trial of training days 2-4). Moreover, during the memory probe-trial sham-exposed animals showed the expected preference for the target quadrant, while the exposed animals showed no preference, indicating that the exposed mice had deficits in consolidation and/or retrieval of the learned spatial information. Our results provide a basis for more thorough investigations considering reports on non-thermal effects of electromagnetic fields (EMFs).	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Grigoriev YG, Grigoriev OA, Ivanov AA, Lyaginskaya AM, Merkulov AV, Shagina NB, et al. Confirmation studies of Soviet research on immunological effects of microwaves: Russian immunology results. Bioelectromagnetics. 2010 Dec;31(8):589–602.** This paper presents the results of a replication study performed to investigate earlier Soviet studies conducted between 1974 and 1991 that showed immunological and reproductive effects of long-term low-level exposure of rats to radiofrequency (RF) electromagnetic fields. The early studies were used, in part, for developing exposure standards for the USSR population and thus it was necessary to confirm the Russian findings. In the present study, the conditions of RF exposure were made as similar as possible to those in the earlier experiments: Wistar rats were exposed in the far field to 2450 MHz continuous wave RF fields with an incident power density in the cages of 5 W/m² for 7 h/day, 5 days/week for a total of 30 days, resulting in a whole-body SAR of 0.16 W/kg. Effects of the exposure on immunological parameters in the brain and liver of rats were evaluated using the complement fixation test (CFT), as in the original studies, and an additional test, the more modern ELISA test. Our results, using CFT and ELISA, partly confirmed the findings of the early studies and indicated possible effects from non-thermal RF exposure on autoimmune processes. The RF exposure resulted in minor increases in formation of antibodies in brain tissue extract and the exposure did not appear to be pathological. In addition, a study was conducted to replicate a previous Soviet study on effects from the injection of blood serum from RF-exposed rats on pregnancy and foetal and offspring development of rats, using a similar animal model and protocol. Our results showed the same general trends as the earlier study, suggesting possible adverse effects of the blood serum from exposed rats on pregnancy and foetal development of intact rats, however, application of these results in developing exposure standards is limited.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Liaginskaia AM, Grigor'ev IG, Osipov VA, Grigor'ev OA, Shafirkin AV. [Autoimmune processes after long-term low-level exposure to electromagnetic fields (the results of an experiment). Part 5. Impact of the blood serum from rats exposed to low-level electromagnetic fields on pregnancy, foetus and offspring development of intact female rats]. Radiats Biol Radioecol. 2010 Feb;50(1):28–36.** This study evaluated possible adverse effects of injection of blood serum from rats exposed to microwaves at a power density of 500 microW/cm2 on pregnancy and foetal and offspring development in intact female rats. The study was performed with 59 pregnant Wistar rats. In utero mortality, embryo and foetal body weights and placenta weight were used for the evaluation of embryo and foetal development. Generally accepted integral and specific parameters were used for the evaluation of postnatal development of offspring during the first 30 days of life. It was shown that intra peritoneal injection of blood serum from IMF exposed rats (chronic 30-day RF exposure at 500 microW/cm2) to intact rats on the 10th day of pregnancy resulted in adverse effects on foetal and offspring development. Total mortality (in utero + postnatal) as well as delay in offspring development was higher in this group.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Narayanan SN, Kumar RS, Potu BK, Nayak S, Bhat PG, Mailankot M. Effect of radio-frequency electromagnetic radiations (RF-EMR) on passive avoidance behaviour and hippocampal morphology in Wistar rats. Ups J Med Sci. 2010 May;115(2):91–6.** INTRODUCTION: The interaction of mobile phone radio-frequency electromagnetic radiation (RF-EMR) with the brain is a serious concern of our society. OBJECTIVE: We evaluated the effect of RF-EMR from mobile phones on passive avoidance behaviour and hippocampal morphology in rats. MATERIALS AND METHODS: Healthy male albino Wistar rats were exposed to RF-EMR by giving 50 missed calls (within 1 hour) per day for 4 weeks, keeping a GSM (0.9 GHz/1.8 GHz) mobile phone in vibratory mode (no ring tone) in the cage. After the experimental period, passive avoidance behaviour and hippocampal morphology were studied. RESULTS: Passive avoidance behaviour was significantly affected in mobile phone RF-EMR-exposed rats demonstrated as shorter entrance latency to the dark compartment when compared to the control rats. Marked morphological changes were also observed in the CA(3) region of the hippocampus of the mobile phone-exposed rats in comparison to the control rats. CONCLUSION: Mobile phone RF-EMR exposure significantly altered the passive avoidance behaviour and hippocampal morphology in rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Blackman C. Cell phone radiation: Evidence from ELF and RF studies supporting more inclusive risk identification and assessment. Pathophysiology. 2009 Aug;16(2-3):205–16.** Many national and international exposure standards for maximum radiation exposure from the use of cell phone and other similar portable devices are ultimately based on the production of heat particularly in regions of the head, that is, thermal effects (TE). The recent elevation in some countries of the allowable exposure, that is, averaging the exposure that occurs in a 6min period over 10g of tissue rather than over 1g allows for greater heating in small portions of the 10-g volume compared to the exposure that would be allowed averaged over 1-g volume. There is concern that 'hot' spots, that is, momentary higher intensities, could occur in portions of the 10-g tissue piece, might have adverse consequences, particularly in brain tissue. There is another concern about exposure to cell phone radiation that has been virtually ignored except for the National Council of Radiation Protection and Measurements (NCRP) advice given in a publication in 1986 [National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.]. *** This NCRP review and guidance explicitly acknowledge the existence of non-thermal effects (NTE), *** and included provisions for reduced maximum-allowable limits should certain radiation characteristics occur during the exposure. If we are to take most current national and international exposure standards as completely protective of thermal injury for acute exposure only (6min time period) then the recent evidence from epidemiological studies associating increases in brain and head cancers with increased cell phone use per day and per year over 8-12 years, raises concerns about the possible health consequences on NTE first acknowledged in the NCRP 1986 report [National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.]. This paper will review some of the salient evidence that demonstrates the existence of NTE and the exposure complexities that must be considered and understood to provide appropriate, more thorough evaluation and guidance for future studies and for assessment of potential health consequences. Unfortunately, this paper is necessary because most national and international reviews of the research area since the 1986 report [National Council for Radiation Protection and Measurements, Biological Effects and Exposure Criteria for Radiofrequency Electromagnetic Fields, National Council for Radiation Protection and Measurements, 1986, 400 pp.] have not included scientists with expertise in NTE, or given appropriate attention to their requests to include NTE in the establishment of public-health-based radiation exposure standards. Thus, those standards are limited because they are not comprehensive. [*** emphasis added ***]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Daniels WMU, Pitout IL, Afullo TJO, Mabandla MV. The effect of electromagnetic radiation in the mobile phone range on the behaviour of the rat. Metab Brain Dis. 2009 Dec;24(4):629–41.** Electromagnetic radiation (EMR) is emitted from electromagnetic fields that surround power lines, household appliances and mobile phones. Research has shown that there are connections between EMR exposure and cancer and also that exposure to EMR may result in structural damage to neurons. In a study by Salford et al. (Environ Health Perspect 111:881-883, 2003) the authors demonstrated the presence of strongly stained areas in the brains of rats that were exposed to mobile phone EMR. These darker neurons were particularly prevalent in the hippocampal area of the brain. The aim of our study was to further investigate the effects of EMR. Since the hippocampus is involved in learning and memory and emotional states, we hypothesised that EMR will have a negative impact on the subject's mood and ability to learn. We subsequently performed behavioural, histological and biochemical tests on exposed and unexposed male and female rats to determine the effects of EMR on learning and memory, emotional states and corticosterone levels. We found no significant differences in the spatial memory test, and morphological assessment of the brain also yielded non-significant differences between the groups. However, in some exposed animals there were decreased locomotor activity, increased grooming and a tendency of increased basal corticosterone levels. These findings suggested that EMR exposure may lead to abnormal brain functioning.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Narayanan SN, Kumar RS, Potu BK, Nayak S, Mailankot M. Spatial memory performance of Wistar rats exposed to mobile phone. Clinics (Sao Paulo). 2009;64(3):231–4.** INTRODUCTION: With the tremendous increase in number of mobile phone users world wide, the possible risks of this technology have become a serious concern. OBJECTIVE: We tested the effects of mobile phone exposure on spatial memory performance. MATERIALS AND METHODS: Male Wistar rats (10-12 weeks old) were exposed to 50 missed calls/day for 4 weeks from a GSM (900/1800 MHz) mobile phone in vibratory mode (no ring tone). After the experimental period, the animals were tested for spatial memory performance using the Morris water maze test. RESULTS: Both phone exposed and control animals showed a significant decrease in escape time with training. Phone exposed animals had significantly (approximately 3 times) higher mean latency to reach the target quadrant and spent significantly (approximately 2 times) less time in the target quadrant than age- and sex-matched controls. CONCLUSION: Mobile phone exposure affected the acquisition of learned responses in Wistar rats. This in turn points to the poor spatial navigation and the object place configurations of the phone-exposed animals.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Zareen N, Khan MY, Ali Minhas L. Derangement of chick embryo retinal differentiation caused by radiofrequency electromagnetic fields. Congenit Anom (Kyoto). 2009 Mar;49(1):15–9.** The possible adverse effects of radiofrequency electromagnetic fields (EMF) emitted from mobile phones present a major public concern. Biological electrical activities of the human body are vulnerable to interference from oscillatory aspects of EMF, which affect fundamental cellular activities, in particular, the highly active development process of embryos. Some studies highlight the possible health hazards of EMF, while others contest the hypothesis of biological impact of EMF. The present study was designed to observe the histomorphological effects of EMF emitted by a mobile phone on the retinae of developing chicken embryos. Fertilized chicken eggs were exposed to a ringing mobile set on silent tone placed in the incubator at different ages of development. After exposure for the scheduled duration the retinae of the embryos were dissected out and processed for histological examination. The control and experimental embryos were statistically compared for retinal thickness and epithelial pigmentation grades. Contrasting effects of EMF on the retinal histomorphology were noticed, depending on the duration of exposure. The embryos exposed for 10 post-incubation days exhibited decreased retinal growth and mild pigmentation of the epithelium. Growth retardation reallocated to growth enhancement on increasing EMF exposure for 15 post-incubation days, with a shift of pigmentation grade from mild to intense. We conclude that EMF emitted by a mobile phone cause derangement of chicken embryo retinal differentiation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

D. Effects on the Brain and Nervous System

Forty-four studies address neurological effects. Many of the effects listed here were replicated in numerous studies.

Four studies of human volunteers found that:

- short term exposure to radiofrequency energy decreased spontaneous brain activity in multiple regions of the brain, measured with functional MRI;
- mobile phone exposure reduced cochlear nerve compound action potential (CNAP) during surgery;
- GSM mobile phone (cell phone) exposure caused lower amplitude of P300 waves; and
- alterations in brain wave activity with exposure were different according to gender.

Dozens of studies in rodents found that:

- exposure *in utero* led to lower levels of a range of antioxidants, smaller numbers of pyramidal cells in the hippocampus in month-old pups, inflammation, degenerative nuclear and cellular changes and edema in the brain, electrophysiological impairment of Purkinje cells (the largest neurons in the brain), impaired transmission across synapses, DNA damage, neuronal loss, changed calcium efflux (an indication of breakdown of cellular membranes), and altered electroencephalyogram (EEG) readings;
- in rats, daily exposure caused lower levels of neurotransmitters, DNA damage, degenerative changes, oxidative stress, higher beta-amaloid, extensive changes in various protein levels, altered firing of neurons, changed calcium binding and immunoreactivity along with cell loss;
- shorter term exposure caused cell death in the brain;
- a single exposure affected neuro-immunity, stress and behaviour differently in young versus middle-aged rats, and led to impaired integrity of the blood brain barrier a week later;
- sleep cycles were altered in rats exposed to a modulated radiofrequency signal; and
- in mice, chronic radiofrequency energy reduced neurotropins (chemicals for maintenance of neurons), and caused loss of pyramidal brain cells and alteration of calcium movement across cell membranes.

In two studies of insects, short term exposure affected behaviour, memory and physiology.

Laboratory studies of cell cultures revealed:

- 3 minute exposures to GHz range radiation caused a reversible 30% decrease in firing rate and bursting rate in a synthetic neural network; and
- modulation of heat shock proteins in differentiated neuroblastoma cells (neuron-like cells).

In summary, regular cell phone exposure can lead to altered structure, biochemistry and function of the brain. Function is impaired, with cell death and increased levels of compounds associated with chronic degenerative disease.

Year	References and extracts	Reports	Cited?
2014	**Cetin H, Nazıroğlu M, Celik O, Yüksel M, Pastacı N, Ozkaya MO. Liver antioxidant stores protect the brain from electromagnetic radiation (900 and 1800 MHz)-induced oxidative stress in rats during pregnancy and the development of offspring. J Matern Fetal Neonatal Med. 2014 Apr 9;** Abstract Objectives: The present study determined the effects of mobile phone (900 and 1800 MHz)-induced electromagnetic radiation (EMR) exposure on oxidative stress in the brain and liver as well as the element levels in growing rats from pregnancy to 6 weeks of age. Methods: Thirty-two rats and their offspring were equally divided into three different groups: the control, 900 MHz, and 1800 MHz groups. The 900 MHz and 1800 MHz groups were exposed to EMR for 60 min/d during pregnancy and neonatal development. At the 4th, 5th, and 6th weeks of the experiment, brain samples were obtained. Results: Brain and liver glutathione peroxidase activities, as well as liver vitamin A and β-carotene concentrations decreased in the EMR groups, although brain iron, vitamin A, and β-carotene concentrations increased in the EMR groups. In the 6th week, selenium concentrations in the brain decreased in the EMR groups. There were no statistically significant differences in glutathione, vitamin E, chromium, copper, magnesium, manganese, and zinc concentrations between the three groups. Conclusion: EMR-induced oxidative stress in the brain and liver was reduced during the development of offspring. Mobile phone-induced EMR could be considered as a cause of oxidative brain and liver injury in growing rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a No n/a

<table>
<tr><th>Year</th><th>References and extracts</th><th>Reports</th><th>Cited?</th></tr>
<tr><td>2014</td><td>Maskey D, Kim MJ. Immunohistochemical localization of brain-derived neurotrophic factor and glial cell line-derived neurotrophic factor in the superior olivary complex of mice after radiofrequency exposure. Neurosci Lett. 2014 Apr 3;564:78–82.

Raising health concerns about the biological effects from radiofrequency exposure, even with conflicting results, has prompted calls for formulation of a guideline of the biological safety level. Given the close proximity between a mobile phone and the ear, it has been suggested that the central auditory system may be detrimentally influenced by radiofrequency exposure. In the auditory system, neurotrophins are important in the regulation of neuron survival, especially mammalian cochlear neurons. Neurotrophic factors like brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) present in the auditory system are responsible for the maintenance of auditory neurons. BDNF and GDNF may protect against acoustic trauma and prevent from hearing defect. The present study applied radiofrequency at a specific absorption rate (SAR) of 1.6W/kg (E1.6) or 0W/kg group to determine the distribution of BDNF and GDNF in the nuclei of superior olivary complex (SOC). In the E1.6 group, significant decrements of BDNF immunoreactivity (IR) were noted in the lateral superior olive, medial superior olive, superior paraolivary nucleus and medial nucleus of the trapezoid body. GDNF IR was also significantly decreased ($p<0.001$) in all SOC nuclei of the E1.6 group. The decrease in the IR of these neurotrophic factors in the SOC of the E1.6 group suggests a detrimental effect of RF exposure in the auditory nuclei.</td><td>Reference provided to Royal Society of Canada (in 2013)</td><td>n/a</td></tr>
<tr><td></td><td></td><td>Health Canada Draft Safety Code 6 (2014)</td><td>No</td></tr>
<tr><td></td><td></td><td>Health Canada SC6 Rationale (2013)</td><td>n/a</td></tr>
<tr><td></td><td></td><td>RSC Review of Safety Code 6 (2014)</td><td>n/a</td></tr>
<tr><td></td><td></td><td>SCENIHR (2013)</td><td>n/a</td></tr>
<tr><td></td><td></td><td colspan="2">n/a = not available at time of report publication</td></tr>
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Year	References and extracts	Reports	Cited?
2013	**Aboul Ezz HS, Khadrawy YA, Ahmed NA, Radwan NM, El Bakry MM. The effect of pulsed electromagnetic radiation from mobile phone on the levels of monoamine neurotransmitters in four different areas of rat brain. Eur Rev Med Pharmacol Sci. 2013 Jul;17(13):1782–8.** BACKGROUND: The use of mobile phones is rapidly increasing all over the world. Few studies deal with the effect of electromagnetic radiation (EMR) on monoamine neurotransmitters in the different brain areas of adult rat. AIM: The aim of the present study was to investigate the effect of EMR on the concentrations of dopamine (DA), norepinephrine (NE) and serotonin (5-HT) in the hippocampus, hypothalamus, midbrain and medulla oblongata of adult rats. MATERIALS AND METHODS: Adult rats were exposed daily to EMR (frequency 1800 MHz, specific absorption rate 0.843 W/kg, power density 0.02 mW/cm2, modulated at 217 Hz) and sacrificed after 1, 2 and 4 months of daily EMR exposure as well as after stopping EMR for 1 month (after 4 months of daily EMR exposure). Monoamines were determined by high performance liquid chromatography coupled with fluorescence detection (HPLC-FD) using their native properties. RESULTS: The exposure to EMR resulted in significant changes in DA, NE and 5-HT in the four selected areas of adult rat brain. CONCLUSIONS: The exposure of adult rats to EMR may cause disturbances in monoamine neurotransmitters and this may underlie many of the adverse effects reported after EMR including memory, learning, and stress. [1800 MHz; SAR 0.843W/kg; 0.02 mW/cm^2]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Baş O, Sönmez OF, Aslan A, İkinci A, Hancı H, Yıldırım M, et al. Pyramidal Cell Loss in the Cornu Ammonis of 32-day-old Female Rats Following Exposure to a 900 Megahertz Electromagnetic Field During Prenatal Days 13–21. NeuroQuantology [Internet]. 2013 Oct 30;11(4). Available from: http://www.neuroquantology.com/index.php/journal/article/view/701** The number of studies reporting that the electromagnetic field (EMF) emitted by mobile phones affects human health is increasing by the day. In previous studies we reported that a 900 megahertz (MHz) EMF applied throughout the prenatal period reduced the number of pyramidal cells in the cornu ammonis of rat pups in the postnatal period. In this study we investigated the effect of a 900 MHz EMF applied on days 13-21 of the prenatal period on the number of pyramidal cells in the cornu ammonis of rat pups in the postnatal period. For that purpose, pregnant rats were divided into experimental and control groups. Experimental group pregnant rats were exposed to the effect of a 900 MHz EMF on days 13-21 of pregnancy. No procedure was applied to the control group. Newborn female rat pups were added to the study, and no procedure was performed on these after birth. Five newborn female rats were obtained from the experimental group and six from the control group. All female rat pups were decapitated on the postnatal 32nd day, and histological procedures were performed on the brain tissues. Sections were stained with Cresyl fast violet. The optical dissector technique was used to estimate the total number of pyramidal cells in the cornu ammonis. Sections of cornu ammonis were subjected to histopathological evaluations. Our results showed that exposure to 900 MHz EMF during prenatal days 13-21 led to a significant decrease in the number of pyramidal cells in the cornu ammonis of the experimental group female rat pups ($P<0.05$). Histopathological examination revealed picnotic cells in the cornu ammonis in experimental female rat pups. The pyramidal cell loss in the cornu ammonis may therefore be attributed to exposure to 900 MHz EMF in days 13-21 of the prenatal period.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Cammaerts M-C, Rachidi Z, Bellens F, De Doncker P. Food collection and response to pheromones in an ant species exposed to electromagnetic radiation. Electromagn Biol Med. 2013 Sep;32(3):315–32.** We used the ant species Myrmica sabuleti as a model to study the impact of electromagnetic waves on social insects' response to their pheromones and their food collection. We quantified M. sabuleti workers' response to their trail, area marking and alarm pheromone under normal conditions. Then, we quantified the same responses while under the influence of electromagnetic waves. Under such an influence, ants followed trails for only short distances, no longer arrived at marked areas and no longer orientated themselves to a source of alarm pheromone. Also when exposed to electromagnetic waves, ants became unable to return to their nest and recruit congeners; therefore, the number of ants collecting food increases only slightly and slowly. After 180 h of exposure, their colonies deteriorated. Electromagnetic radiation obviously affects social insects' behavior and physiology.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Deshmukh PS, Megha K, Banerjee BD, Ahmed RS, Chandna S, Abegaonkar MP, et al. Detection of Low Level Microwave Radiation Induced Deoxyribonucleic Acid Damage Vis-à-vis Genotoxicity in Brain of Fischer Rats. Toxicol Int. 2013 Jan;20(1):19–24.** BACKGROUND: Non-ionizing radiofrequency radiation has been increasingly used in industry, commerce, medicine and especially in mobile phone technology and has become a matter of serious concern in present time. OBJECTIVE: The present study was designed to investigate the possible deoxyribonucleic acid (DNA) damaging effects of low-level microwave radiation in brain of Fischer rats. MATERIALS AND METHODS: Experiments were performed on male Fischer rats exposed to microwave radiation for 30 days at three different frequencies: 900, 1800 and 2450 MHz. Animals were divided into 4 groups: Group I (Sham exposed): Animals not exposed to microwave radiation but kept under same conditions as that of other groups, Group II: Animals exposed to microwave radiation at frequency 900 MHz at specific absorption rate (SAR) 5.953 × 10(-4) W/kg, Group III: Animals exposed to 1800 MHz at SAR 5.835 × 10(-4) W/kg and Group IV: Animals exposed to 2450 MHz at SAR 6.672 × 10(-4) W/kg. At the end of the exposure period animals were sacrificed immediately and DNA damage in brain tissue was assessed using alkaline comet assay. RESULTS: In the present study, we demonstrated DNA damaging effects of low level microwave radiation in brain. CONCLUSION: We concluded that low SAR microwave radiation exposure at these frequencies may induce DNA strand breaks in brain tissue.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Eser O, Songur A, Aktas C, Karavelioglu E, Caglar V, Aylak F, et al. The effect of electromagnetic radiation on the rat brain: an experimental study. Turk Neurosurg. 2013;23(6):707–15.** AIM: The aim of this study is to determine the structural changes of electromagnetic waves in the frontal cortex, brain stem and cerebellum. MATERIAL and METHODS: 24 Wistar Albino adult male rats were randomly divided into four groups: group I consisted of control rats, and groups II-IV comprised electromagnetically irradiated (EMR) with 900, 1800 and 2450 MHz. The heads of the rats were exposed to 900, 1800 and 2450 MHz microwaves irradiation for 1h per day for 2 months. RESULTS: While the histopathological changes in the frontal cortex and brain stem were normal in the control group, there were severe degenerative changes, shrunken cytoplasm and extensively dark pyknotic nuclei in the EMR groups. Biochemical analysis demonstrated that the Total Antioxidative Capacity level was significantly decreased in the EMR groups and also Total Oxidative Capacity and Oxidative Stress Index levels were significantly increased in the frontal cortex, brain stem and cerebellum. IL-1β level was significantly increased in the EMR groups in the brain stem. CONCLUSION: EMR causes to structural changes in the frontal cortex, brain stem and cerebellum and impair the oxidative stress and inflammatory cytokine system. This deterioration can cause to disease including loss of these areas function and cancer development.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2013	**Gao X, Luo R, Ma B, Wang H, Liu T, Zhang J, et al. [Interference of vitamin E on the brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats]. Wei Sheng Yan Jiu. 2013 Jul;42(4):642–6.** OBJECTIVE: To investigate the interlerence ot vitamin E on brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats. METHODS: 40 pregnant rats were randomly divided into five groups (positive control, negative control, low, middle and high dosage of vitamin E groups). The low, middle and high dosage of vitamin E groups were supplemented with 5, 15 and 30 mg/ml vitamin E respectively since the first day of pregnancy. And the negative control group and the positive control group were given peanut oil without vitamin E. All groups except for the negative control group were exposed to 900MHz intensity of cell phone radiation for one hour each time, three times per day for 21 days. After accouchement, the right hippocampus tissue of fetal rats in each group was taken and observed under electron microscope. The vitality of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and the content of malondialdehyde (MDA) in pregnant and fetal rats' brain tissue were tested. RESULTS: Compared with the negative control group, the chondriosomes in neuron and neuroglia of brain tissues was swelling, mild edema was found around the capillary, chromatin was concentrated and collected, and bubbles were formed in vascular endothelial cells (VEC) in the positive fetal rat control group, whereas the above phenomenon was un-conspicuous in the middle and high dosage of vitamin E groups. We can see uniform chromatin, abundant mitochondrion, rough endoplasmic reticulum and free ribosomes in the high dosage group. The apoptosis has not fond in all groups' sections. In the antioxidase activity analysis, compared with the negative control group, the vitality of SOD and GSH-Px significantly decreased and the content of MDA significantly increased both in the pregnant and fetal rats positive control group ($P < 0.05$). In fetal rats, the vitality of SOD and GSH-Px significantly increased in the brain tissues of all three different vitamin E dosages groups when compared with the positive control group, and the content of MDA was found significantly decreased in both middle and high dosage of vitamin E groups($P < 0.05$). The same results have also been found in high dosage pregnant rat group, but in middle dosage group only SOD activity was found increased with significance ($P < 0.05$). With the dosage increase of vitamin E, the vitality of SOD and GSH-Px was increasing and the content of MDA was decreasing. CONCLUSION: Under the experimental dosage, vitamin E has certain interference on damage of antioxidant capacity and energy metabolization induced by electromagnetic radiation of cell phone in pregnant rats and fetal rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Haghani M, Shabani M, Moazzami K. Maternal mobile phone exposure adversely affects the electrophysiological properties of Purkinje neurons in rat offspring. Neuroscience. 2013 Oct 10;250:588–98.** Electromagnetic field (EMF) radiations emitted from mobile phones may cause structural damage to neurons. With the increased usage of mobile phones worldwide, concerns about their possible effects on the nervous system are rising. In the present study, we aimed to elucidate the possible effects of prenatal EMF exposure on the cerebellum of offspring Wistar rats. Rats in the EMF group were exposed to 900-MHz pulse-EMF irradiation for 6h per day during all gestation period. Ten offspring per each group were evaluated for behavioral and electrophysiological evaluations. Cerebellum-related behavioral dysfunctions were analyzed using motor learning and cerebellum-dependent functional tasks (Accelerated Rotarod, Hanging and Open field tests). Whole-cell patch clamp recordings were used for electrophysiological evaluations. The results of the present study failed to show any behavioral abnormalities in rats exposed to chronic EMF radiation. However, whole-cell patch clamp recordings revealed decreased neuronal excitability of Purkinje cells in rats exposed to EMF. The most prominent changes included after hyperpolarization amplitude, spike frequency, half width and first spike latency. In conclusion, the results of the present study show that prenatal EMF exposure results in altered electrophysiological properties of Purkinje neurons. However, these changes may not be severe enough to alter the cerebellum-dependent functional tasks.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Hao D, Yang L, Chen S, Tong J, Tian Y, Su B, et al. Effects of long-term electromagnetic field exposure on spatial learning and memory in rats. Neurol Sci. 2013 Feb;34(2):157–64.** With the development of communications industry, mobile phone plays an important role in daily life. Whether or not the electromagnetic radiation emitted by mobile phone causes any adverse effects on brain function has become of a great concern. This paper investigated the effect of electromagnetic field on spatial learning and memory in rats. 32 trained Wistar rats were divided into two groups: exposure group and control group. The exposure group was exposed to 916 MHz, 10w/m2 mobile phone electromagnetic field (EMF) 6 h a day, 5 days a week, 10 weeks. The completion time, number of total errors and the neuron discharge signals were recorded while the rats were searching for food in an eight-arm radial maze at every weekend. The neuron signals of one exposed rat and one control rat in the maze were obtained by the implanted microelectrode arrays in their hippocampal regions. It can be seen that during the weeks 4-5 of the experiment, the average completion time and error rate of the exposure group were longer and larger than that of control group ($p < 0.05$). During the weeks 1-3 and 6-9, they were close to each other. The hippocampal neurons showed irregular firing patterns and more spikes with shorter interspike interval during the whole experiment period. It indicates that the 916 MHz EMF influence learning and memory in rats to some extent in a period during exposure, and the rats can adapt to long-term EMF exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**İkinci A, Odacı E, Yıldırım M, Kaya H, Akça M, Hancı H, et al. The Effects of Prenatal Exposure to a 900 Megahertz Electromagnetic Field on Hippocampus Morphology and Learning Behavior in Rat Pups. NeuroQuantology [Internet]. 2013 Oct 28;11(4). Available from: http://www.neuroquantology.com/index.php/journal/article/view/699** The purpose of this study was to examine the effect on hippocampus morphology and learning behavior in rat pups following prenatal exposure to a 900 megahertz (MHz) electromagnetic field (EMF). Female Sprague Dawley rats weighing 180-250 g were left to mate with males. The following day, pregnant rats identified as such by the vaginal smear test were divided into two groups, control (n=3) and EMF (n=3). No procedures were performed on the control group. The rats in the EMF group were exposed to 900 MHz EMF on days 13 to 21 of pregnancy, for 1 h a day. Female rat pups were removed from their mothers at 22 days old. We then established two newborn rat groups, a 13 member control group and a 10 member EMF group. Radial arm maze and passive avoidance tests were used to measure rat pups' learning and memory performance. All rats were decapitated on the postnatal 32nd day. Routine histological procedures were performed on the brain tissues, and sections were stained with Cresyl fast violet. The radial arm maze (p=0.007) and passive avoidance (p=0.032) tests were administered to both groups under identical conditions, and compromised learning behavior was determined in the EMF group rats. Morphological compromise was also determined in the EMF group sections. Our results show that the application of a 900 MHz EMF in the prenatal period adversely affected female pups' learning behavior and also resulted in histopathological changes appearing in the hippocampus.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Lv B, Chen Z, Wu T, Shao Q, Yan D, Ma L, et al. The alteration of spontaneous low frequency oscillations caused by acute electromagnetic fields exposure. Clin Neurophysiol. 2013 Sep 4;** OBJECTIVE: The motivation of this study is to evaluate the possible alteration of regional resting state brain activity induced by the acute radiofrequency electromagnetic field (RF-EMF) exposure (30min) of Long Term Evolution (LTE) signal. METHODS: We designed a controllable near-field LTE RF-EMF exposure environment. Eighteen subjects participated in a double-blind, crossover, randomized and counterbalanced experiment including two sessions (real and sham exposure). The radiation source was close to the right ear. Then the resting state fMRI signals of human brain were collected before and after the exposure in both sessions. We measured the amplitude of low frequency fluctuation (ALFF) and fractional ALFF (fALFF) to characterize the spontaneous brain activity. RESULTS: We found the decreased ALFF value around in left superior temporal gyrus, left middle temporal gyrus, right superior temporal gyrus, right medial frontal gyrus and right paracentral lobule after the real exposure. And the decreased fALFF value was also detected in right medial frontal gyrus and right paracentral lobule. CONCLUSIONS: The study provided the evidences that 30min LTE RF-EMF exposure modulated the spontaneous low frequency fluctuations in some brain regions. SIGNIFICANCE: With resting state fMRI, we found the alteration of spontaneous low frequency fluctuations induced by the acute LTE RF-EMF exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Maaroufi K, Had-Aissouni L, Melon C, Sakly M, Abdelmelek H, Poucet B, et al. Spatial learning, monoamines and oxidative stress in rats exposed to 900MHz electromagnetic field in combination with iron overload. Behav Brain Res. 2013 Oct 18;258C:80–9.** The increasing use of mobile phone technology over the last decade raises concerns about the impact of high frequency electromagnetic fields (EMF) on health. More recently, a link between EMF, iron overload in the brain and neurodegenerative disorders including Parkinson's and Alzheimer's diseases has been suggested. Co-exposure to EMF and brain iron overload may have a greater impact on brain tissues and cognitive processes than each treatment by itself. To examine this hypothesis, Long-Evans rats submitted to 900MHz exposure or combined 900MHz EMF and iron overload treatments were tested in various spatial learning tasks (navigation task in the Morris water maze, working memory task in the radial-arm maze, and object exploration task involving spatial and non spatial processing). Biogenic monoamines and metabolites (dopamine, serotonin) and oxidative stress were measured. Rats exposed to EMF were impaired in the object exploration task but not in the navigation and working memory tasks. They also showed alterations of monoamine content in several brain areas but mainly in the hippocampus. Rats that received combined treatment did not show greater behavioral and neurochemical deficits than EMF-exposed rats. None of the two treatments produced global oxidative stress. These results show that there is an impact of EMF on the brain and cognitive processes but this impact is revealed only in a task exploiting spontaneous exploratory activity. In contrast, there are no synergistic effects between EMF and a high content of iron in the brain.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Mandalà M, Colletti V, Sacchetto L, Manganotti P, Ramat S, Marcocci A, et al. Effect of Bluetooth headset and mobile phone electromagnetic fields on the human auditory nerve [Epub ahead of print]. Laryngoscope. 2013 Apr 25;124(1).** OBJECTIVES/HYPOTHESIS: The possibility that long-term mobile phone use increases the incidence of astrocytoma, glioma and acoustic neuroma has been investigated in several studies. Recently, our group showed that direct exposure (in a surgical setting) to cell phone electromagnetic fields (EMFs) induces deterioration of auditory evoked cochlear nerve compound action potential (CNAP) in humans. To verify whether the use of Bluetooth devices reduces these effects, we conducted the present study with the same experimental protocol. STUDY DESIGN: Randomized trial. METHODS: Twelve patients underwent retrosigmoid vestibular neurectomy to treat definite unilateral Ménière's disease while being monitored with acoustically evoked CNAPs to assess direct mobile phone exposure or alternatively the EMF effects of Bluetooth headsets. RESULTS: We found no short-term effects of Bluetooth EMFs on the auditory nervous structures, whereas direct mobile phone EMF exposure confirmed a significant decrease in CNAPs amplitude and an increase in latency in all subjects. CONCLUSIONS: The outcomes of the present study show that, contrary to the finding that the latency and amplitude of CNAPs are very sensitive to EMFs produced by the tested mobile phone, the EMFs produced by a common Bluetooth device do not induce any significant change in cochlear nerve activity. The conditions of exposure, therefore, differ from those of everyday life, in which various biological tissues may reduce the EMF affecting the cochlear nerve. Nevertheless, these novel findings may have important safety implications.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Mohammed HS, Fahmy HM, Radwan NM, Elsayed AA. Non-thermal continuous and modulated electromagnetic radiation fields effects on sleep EEG of rats. Journal of Advanced Research. 2013 Mar;4(2):181–7.** In the present study, the alteration in the sleep EEG in rats due to chronic exposure to low-level non-thermal electromagnetic radiation was investigated. Two types of radiation fields were used; 900 MHz unmodulated wave and 900 MHz modulated at 8 and 16 Hz waves. Animals has exposed to radiation fields for 1 month (1 h/day). EEG power spectral analyses of exposed and control animals during slow wave sleep (SWS) and rapid eye movement sleep (REM sleep) revealed that the REM sleep is more susceptible to modulated radiofrequency radiation fields (RFR) than the SWS. The latency of REM sleep increased due to radiation exposure indicating a change in the ultradian rhythm of normal sleep cycles. The cumulative and irreversible effect of radiation exposure was proposed and the interaction of the extremely low frequency radiation with the similar EEG frequencies was suggested.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2013	**Moretti D, Garenne A, Haro E, Poulletier de Gannes F, Lagroye I, Lévêque P, et al. In-vitro exposure of neuronal networks to the GSM-1800 signal. Bioelectromagnetics. 2013;34(8):571–8.** The central nervous system is the most likely target of mobile telephony radiofrequency (RF) field exposure in terms of biological effects. Several electroencephalography (EEG) studies have reported variations in the alpha-band power spectrum during and/or after RF exposure, in resting EEG and during sleep. In this context, the observation of the spontaneous electrical activity of neuronal networks under RF exposure can be an efficient tool to detect the occurrence of low-level RF effects on the nervous system. Our research group has developed a dedicated experimental setup in the GHz range for the simultaneous exposure of neuronal networks and monitoring of electrical activity. A transverse electromagnetic (TEM) cell was used to expose the neuronal networks to GSM-1800 signals at a SAR level of 3.2 W/kg. Recording of the neuronal electrical activity and detection of the extracellular spikes and bursts under exposure were performed using microelectrode arrays (MEAs). This work provides the proof of feasibility and preliminary results of the integrated investigation regarding exposure setup, culture of the neuronal network, recording of the electrical activity, and analysis of the signals obtained under RF exposure. In this pilot study on 16 cultures, there was a 30% reversible decrease in firing rate (FR) and bursting rate (BR) during a 3 min exposure to RF. Additional experiments are needed to further characterize this effect. Bioelectromagnetics 34:571–578, 2013.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Aldad TS, Gan G, Gao X-B, Taylor HS. Fetal radiofrequency radiation exposure from 800-1900 mhz-rated cellular telephones affects neurodevelopment and behavior in mice. Sci Rep. 2012;2:312.** Neurobehavioral disorders are increasingly prevalent in children, however their etiology is not well understood. An association between prenatal cellular telephone use and hyperactivity in children has been postulated, yet the direct effects of radiofrequency radiation exposure on neurodevelopment remain unknown. Here we used a mouse model to demonstrate that in-utero radiofrequency exposure from cellular telephones does affect adult behavior. Mice exposed in-utero were hyperactive and had impaired memory as determined using the object recognition, light/dark box and step-down assays. Whole cell patch clamp recordings of miniature excitatory postsynaptic currents (mEPSCs) revealed that these behavioral changes were due to altered neuronal developmental programming. Exposed mice had dose-responsive impaired glutamatergic synaptic transmission onto layer V pyramidal neurons of the prefrontal cortex. We present the first experimental evidence of neuropathology due to in-utero cellular telephone radiation. Further experiments are needed in humans or non-human primates to determine the risk of exposure during pregnancy.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Bouji M, Lecomte A, Hode Y, de Seze R, Villégier A-S. Effects of 900 MHz radiofrequency on corticosterone, emotional memory and neuroinflammation in middle-aged rats. Exp Gerontol. 2012 Jun;47(6):444–51.** The widespread use of mobile phones raises the question of the effects of electromagnetic fields (EMF, 900 MHz) on the brain. Previous studies reported increased levels of the glial fibrillary acidic protein (GFAP) in the rat's brain after a single exposure to 900 MHz global system for mobile (GSM) signal, suggesting a potential inflammatory process. While this result was obtained in adult rats, no data is currently available in older animals. Since the transition from middle-age to senescence is highly dependent on environment and lifestyle, we studied the reactivity of middle-aged brains to EMF exposure. We assessed the effects of a single 15 min GSM exposure (900 MHz; specific absorption rate (SAR)=6 W/kg) on GFAP expression in young adults (6 week-old) and middle-aged rats (12 month-old). Brain interleukin (IL)-1β and IL-6, plasmatic levels of corticosterone (CORT), and emotional memory were also assessed. Our data indicated that, in contrast to previously published work, acute GSM exposure did not induce astrocyte activation. Our results showed an IL-1β increase in the olfactory bulb and enhanced contextual emotional memory in GSM-exposed middle-aged rats, and increased plasmatic levels of CORT in GSM-exposed young adults. Altogether, our data showed an age dependency of reactivity to GSM exposure in neuro-immunity, stress and behavioral parameters. Reproducing these effects and studying their mechanisms may allow a better understanding of mobile phone EMF effects on neurobiological parameters.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Calabrò E, Condello S, Currò M, Ferlazzo N, Caccamo D, Magazù S, et al. Modulation of heat shock protein response in SH-SY5Y by mobile phone microwaves. World J Biol Chem. 2012 Feb 26;3(2):34–40.** AIM: To investigate putative biological damage caused by GSM mobile phone frequencies by assessing electromagnetic fields during mobile phone working. METHODS: Neuron-like cells, obtained by retinoic-acid-induced differentiation of human neuroblastoma SH-SY5Y cells, were exposed for 2 h and 4 h to microwaves at 1800 MHz frequency bands. RESULTS: Cell stress response was evaluated by MTT assay as well as changes in the heat shock protein expression (Hsp20, Hsp27 and Hsp70) and caspase-3 activity levels, as biomarkers of apoptotic pathway. Under our experimental conditions, neither cell viability nor Hsp27 expression nor caspase-3 activity was significantly changed. Interestingly, a significant decrease in Hsp20 expression was observed at both times of exposure, whereas Hsp70 levels were significantly increased only after 4 h exposure. CONCLUSION: The modulation of the expression of Hsps in neuronal cells can be an early response to radiofrequency microwaves.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Cammaerts M-C, De Doncker P, Patris X, Bellens F, Rachidi Z, Cammaerts D. GSM 900 MHz radiation inhibits ants' association between food sites and encountered cues. Electromagn Biol Med. 2012 Jun;31(2):151–65.** The kinetics of the acquisition and loss of the use of olfactory and visual cues were previously obtained in six experimental colonies of the ant Myrmica sabuleti meinert 1861, under normal conditions. In the present work, the same experiments were conducted on six other naive identical colonies of M. sabuleti, under electromagnetic radiation similar to those surrounding GSM and communication masts. In this situation, no association between food and either olfactory or visual cues occurred. After a recovery period, the ants were able to make such an association but never reached the expected score. Such ants having acquired a weaker olfactory or visual score and still undergoing olfactory or visual training were again submitted to electromagnetic waves. Not only did they lose all that they had memorized, but also they lost it in a few hours instead of in a few days (as under normal conditions when no longer trained). They kept no visual memory at all (instead of keeping 10% of it as they normally do). The impact of GSM 900 MHz radiation was greater on the visual memory than on the olfactory one. These communication waves may have such a disastrous impact on a wide range of insects using olfactory and/or visual memory, i.e., on bees.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Dasdag S, Akdag MZ, Kizil G, Kizil M, Cakir DU, Yokus B. Effect of 900 MHz radio frequency radiation on beta amyloid protein, protein carbonyl, and malondialdehyde in the brain. Electromagn Biol Med. 2012 Mar;31(1):67–74.** Recently, many studies have been carried out in relation to 900 MHz radiofrequency radiation (RF) emitted from a mobile phone on the brain. However, there is little data concerning possible mechanisms between long-term exposure of RF radiation and biomolecules in brain. Therefore, we aimed to investigate long-term effects of 900 MHz radiofrequency radiation on beta amyloid protein, protein carbonyl, and malondialdehyde in the rat brain. The study was carried out on 17 Wistar Albino adult male rats. The rat heads in a carousel were exposed to 900 MHz radiofrequency radiation emitted from a generator, simulating mobile phones. For the study group (n: 10), rats were exposed to the radiation 2 h per day (7 days a week) for 10 months. For the sham group (n: 7), rats were placed into the carousel and the same procedure was applied except that the generator was turned off. In this study, rats were euthanized after 10 months of exposure and their brains were removed. Beta amyloid protein, protein carbonyl, and malondialdehyde levels were found to be higher in the brain of rats exposed to 900 MHz radiofrequency radiation. However, only the increase of protein carbonyl in the brain of rats exposed to 900 MHz radiofrequency radiation was found to be statistically significant ($p<0.001$). In conclusion, 900 MHz radiation emitted from mobile/cellular phones can be an agent to alter some biomolecules such as protein. However, further studies are necessary.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Fragopoulou AF, Samara A, Antonelou MH, Xanthopoulou A, Papadopoulou A, Vougas K, et al. Brain proteome response following whole body exposure of mice to mobile phone or wireless DECT base radiation. Electromagn Biol Med. 2012 Dec;31(4):250–74.** The objective of this study was to investigate the effects of two sources of electromagnetic fields (EMFs) on the proteome of cerebellum, hippocampus, and frontal lobe in Balb/c mice following long-term whole body irradiation. Three equally divided groups of animals (6 animals/group) were used; the first group was exposed to a typical mobile phone, at a SAR level range of 0.17-0.37 W/kg for 3 h daily for 8 months, the second group was exposed to a wireless DECT base (Digital Enhanced Cordless Telecommunications/Telephone) at a SAR level range of 0.012-0.028 W/kg for 8 h/day also for 8 months and the third group comprised the sham-exposed animals. Comparative proteomics analysis revealed that long-term irradiation from both EMF sources altered significantly ($p < 0.05$) the expression of 143 proteins in total (as low as 0.003 fold downregulation up to 114 fold overexpression). Several neural function related proteins (i.e., Glial Fibrillary Acidic Protein (GFAP), Alpha-synuclein, Glia Maturation Factor beta (GMF), and apolipoprotein E (apoE)), heat shock proteins, and cytoskeletal proteins (i.e., Neurofilaments and tropomodulin) are included in this list as well as proteins of the brain metabolism (i.e., Aspartate aminotransferase, Glutamate dehydrogenase) to nearly all brain regions studied. Western blot analysis on selected proteins confirmed the proteomics data. The observed protein expression changes may be related to brain plasticity alterations, indicative of oxidative stress in the nervous system or involved in apoptosis and might potentially explain human health hazards reported so far, such as headaches, sleep disturbance, fatigue, memory deficits, and brain tumor long-term induction under similar exposure conditions.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Jing J, Yuhua Z, Xiao-qian Y, Rongping J, Dong-mei G, Xi C. The influence of microwave radiation from cellular phone on fetal rat brain. Electromagn Biol Med. 2012 Mar;31(1):57–66.** The increasing use of cellular phones in our society has brought focus on the potential detrimental effects to human health by microwave radiation. The aim of our study was to evaluate the intensity of oxidative stress and the level of neurotransmitters in the brains of fetal rats chronically exposed to cellular phones. The experiment was performed on pregnant rats exposed to different intensities of microwave radiation from cellular phones. Thirty-two pregnant rats were randomly divided into four groups: CG, GL, GM, and GH. CG accepted no microwave radiation, GL group radiated 10 min each time, GM group radiated 30 min, and GH group radiated 60 min. The 3 experimental groups were radiated 3 times a day from the first pregnant day for consecutively 20 days, and on the 21st day, the fetal rats were taken and then the contents of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), malondialdehyde (MDA), noradrenaline (NE), dopamine (DA), and 5-hydroxyindole acetic acid (5-HT) in the brain were assayed. Compared with CG, there were significant differences ($P<0.05$) found in the contents of SOD, GSH-Px, and MDA in GM and GH; the contents of SOD and GSH-Px decreased and the content of MDA increased. The significant content differences of NE and DA were found in fetal rat brains in GL and GH groups, with the GL group increased and the GH group decreased. Through this study, we concluded that receiving a certain period of microwave radiation from cellular phones during pregnancy has certain harm on fetal rat brains.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Lu Y, Xu S, He M, Chen C, Zhang L, Liu C, et al. Glucose administration attenuates spatial memory deficits induced by chronic low-power-density microwave exposure. Physiol Behav. 2012 Jul 16;106(5):631–7.** Extensive evidence indicates that glucose administration attenuates memory deficits in rodents and humans, and cognitive impairment has been associated with reduced glucose metabolism and uptake in certain brain regions including the hippocampus. In the present study, we investigated whether glucose treatment attenuated memory deficits caused by chronic low-power-density microwave (MW) exposure, and the effect of MW exposure on hippocampal glucose uptake. We exposed Wistar rats to 2.45 GHz pulsed MW irradiation at a power density of 1 mW/cm(2) for 3 h/day, for up to 30 days. MW exposure induced spatial learning and memory impairments in rats. Hippocampal glucose uptake was also reduced by MW exposure in the absence or presence of insulin, but the levels of blood glucose and insulin were not affected. However, these spatial memory deficits were reversed by systemic glucose treatment. Our results indicate that glucose administration attenuates the spatial memory deficits induced by chronic low-power-density MW exposure, and reduced hippocampal glucose uptake may be associated with cognitive impairment caused by MW exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2012	**Maskey D, Kim H-J, Kim HG, Kim MJ. Calcium-binding proteins and GFAP immunoreactivity alterations in murine hippocampus after 1 month of exposure to 835 MHz radiofrequency at SAR values of 1.6 and 4.0 W/kg. Neurosci Lett. 2012 Jan 11;506(2):292–6.** Widespread use of wireless mobile communication has raised concerns of adverse effect to the brain owing to the proximity during use due to the electromagnetic field emitted by mobile phones. Changes in calcium ion concentrations via binding proteins can disturb calcium homeostasis; however, the correlation between calcium-binding protein (CaBP) immunoreactivity (IR) and glial cells has not been determined with different SAR values. Different SAR values [1.6 (E1.6 group) and 4.0 (E4 group) W/kg] were applied to determine the distribution of calbindin D28-k (CB), calretinin (CR), and glial fibrillary acidic protein (GFAP) IR in murine hippocampus. Compared with sham control group, decreased CB and CR IRs, loss of CB and CR immunoreactive cells and increased GFAP IR exhibiting hypertrophic cytoplasmic processes were noted in both experimental groups. E4 group showed a prominent decrement in CB and CR IR than the E1.6 group due to down-regulation of CaBP proteins and neuronal loss. GFAP IR was more prominent in the E4 group than the E1.6 group. Decrement in the CaBPs can affect the calcium-buffering capacity leading to cell death, while increased GFAP IR and changes in astrocyte morphology, may mediate brain injury due to radiofrequency exposure. [1.6 and 4.0 W/kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Megha K, Deshmukh PS, Banerjee BD, Tripathi AK, Abegaonkar MP. Microwave radiation induced oxidative stress, cognitive impairment and inflammation in brain of Fischer rats. Indian J Exp Biol. 2012 Dec;50(12):889–96.** Public concerns over possible adverse effects of microwave radiation emitted by mobile phones on health are increasing. To evaluate the intensity of oxidative stress, cognitive impairment and inflammation in brain of Fischer rats exposed to microwave radiation, male Fischer-344 rats were exposed to 900 MHz microwave radiation (SAR = 5.953 x 10(-4) W/kg) and 1800 MHz microwave radiation (SAR = 5.835 x 10(-4) W/kg) for 30 days (2 h/day). Significant impairment in cognitive function and induction of oxidative stress in brain tissues of microwave exposed rats were observed in comparison with sham exposed groups. Further, significant increase in level of cytokines (IL-6 and TNF-alpha) was also observed following microwave exposure. Results of the present study indicated that increased oxidative stress due to microwave exposure may contribute to cognitive impairment and inflammation in brain.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Nazıroğlu M, Çelik Ö, Özgül C, Çiğ B, Doğan S, Bal R, et al. Melatonin modulates wireless (2.45 GHz)-induced oxidative injury through TRPM2 and voltage gated Ca(2+) channels in brain and dorsal root ganglion in rat. Physiol Behav. 2012 Feb 1;105(3):683–92.** We aimed to investigate the protective effects of melatonin and 2.45 GHz electromagnetic radiation (EMR) on brain and dorsal root ganglion (DRG) neuron antioxidant redox system, Ca(2+) influx, cell viability and electroencephalography (EEG) records in the rat. Thirty two rats were equally divided into four different groups namely group A1: Cage control, group A2: Sham control, group B: 2.45 GHz EMR, group C: 2.45 GHz EMR+melatonin. Groups B and C were exposed to 2.45 GHz EMR during 60 min/day for 30 days. End of the experiments, EEG records and the brain cortex and DRG samples were taken. Lipid peroxidation (LP), cell viability and cytosolic Ca(2+) values in DRG neurons were higher in group B than in groups A1 and A2 although their concentrations were increased by melatonin, 2-aminoethyldiphenyl borinate (2-APB), diltiazem and verapamil supplementation. Spike numbers of EEG records in group C were lower than in group B. Brain cortex vitamin E concentration was higher in group C than in group B. In conclusion, Melatonin supplementation in DRG neurons and brain seems to have protective effects on the 2.45 GHz-induced increase Ca(2+) influx, EEG records and cell viability of the hormone through TRPM2 and voltage gated Ca(2+) channels.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2011	**Carballo-Quintás M, Martínez-Silva I, Cadarso-Suárez C, Alvarez-Figueiras M, Ares-Pena FJ, López-Martín E. A study of neurotoxic biomarkers, c-fos and GFAP after acute exposure to GSM radiation at 900 MHz in the picrotoxin model of rat brains. Neurotoxicology. 2011 Aug;32(4):478–94.** The acute effects of microwave exposure from the Global System for Mobile Communication (GSM) were studied in rats, using 900MHz radiation at an intensity similar to mobile phone emissions. Acute subconvulsive doses of picrotoxin were then administered to the rats and an experimental model of seizure-proneness was created from the data. Seventy-two adult male Sprague-Dawley rats underwent immunochemical testing of relevant anatomical areas to measure induction of the c-fos neuronal marker after 90min and 24h, and of the glial fibrillary acidic protein (GFAP) 72h after acute exposure to a 900MHz electromagnetic field (EMF). The experimental set-up facilitated measurement of absorbed power, from which the average specific absorption rate was calculated using the finite-difference time-domain (FDTD) 2h after exposure to EMF radiation at 1.45W/kg in picrotoxin-treated rats and 1.38W/kg in untreated rats. Ninety minutes after radiation high levels of c-fos expression were recorded in the neocortex and paleocortex along with low hippocampus activation in picrotoxin treated animals. Most brain areas, except the limbic cortical region, showed important increases in neuronal activation 24h after picrotoxin and radiation. Three days after picrotoxin treatment, radiation effects were still apparent in the neocortex, dentate gyrus and CA3, but a significant decrease in activity was noted in the piriform and entorhinal cortex. During this time, glial reactivity increased with every seizure in irradiated, picrotoxin-treated brain regions. Our results reveal that c-fos and glial markers were triggered by the combined stress of non-thermal irradiation and the toxic effect of picrotoxin on cerebral tissues.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Liu M-L, Wen J-Q, Fan Y-B. Potential protection of green tea polyphenols against 1800 MHz electromagnetic radiation-induced injury on rat cortical neurons. Neurotox Res. 2011 Oct;20(3):270–6.** Radiofrequency electromagnetic fields (EMF) are harmful to public health, but the certain anti-irradiation mechanism is not clear yet. The present study was performed to investigate the possible protective effects of green tea polyphenols against electromagnetic radiation-induced injury in the cultured rat cortical neurons. In this study, green tea polyphenols were used in the cultured cortical neurons exposed to 1800 MHz EMFs by the mobile phone. We found that the mobile phone irradiation for 24 h induced marked neuronal cell death in the MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl-tetrazolium bromide) and TUNEL (TdT mediated biotin-dUTP nicked-end labeling) assay, and protective effects of green tea polyphenols on the injured cortical neurons were demonstrated by testing the content of Bcl-2 Assaciated X protein (Bax) in the immunoprecipitation assay and Western blot assay. In our study results, the mobile phone irradiation-induced increases in the content of active Bax were inhibited significantly by green tea polyphenols, while the contents of total Bax had no marked changes after the treatment of green tea polyphenols. Our results suggested a neuroprotective effect of green tea polyphenols against the mobile phone irradiation-induced injury on the cultured rat cortical neurons.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Ammari M, Gamez C, Lecomte A, Sakly M, Abdelmelek H, De Seze R. GFAP expression in the rat brain following sub-chronic exposure to a 900 MHz electromagnetic field signal. Int J Radiat Biol. 2010 May;86(5):367–75.** PURPOSE: The rapid development and expansion of mobile communications contributes to the general debate on the effects of electromagnetic fields emitted by mobile phones on the nervous system. This study aims at measuring the glial fibrillary acidic protein (GFAP) expression in 48 rat brains to evaluate reactive astrocytosis, three and 10 days after long-term head-only sub-chronic exposure to a 900 MHz electromagnetic field (EMF) signal, in male rats. METHODS: Sprague-Dawley rats were exposed for 45 min/day at a brain-averaged specific absorption rate (SAR) = 1.5 W/kg or 15 min/day at a SAR = 6 W/kg for five days per week during an eight-week period. GFAP expression was measured by the immunocytochemistry method in the following rat brain areas: Prefrontal cortex, cerebellar cortex, dentate gyrus of the hippocampus, lateral globus pallidus of the striatum, and the caudate putamen. RESULTS: Compared to the sham-treated rats, those exposed to the sub-chronic GSM (Global System for mobile communications) signal at 1.5 or 6 W/kg showed an increase in GFAP levels in the different brain areas, three and ten days after treatment. CONCLUSION: Our results show that sub-chronic exposures to a 900 MHz EMF signal for two months could adversely affect rat brain (sign of a potential gliosis).	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Bak M, Dudarewicz A, Zmyślony M, Sliwinska-Kowalska M. Effects of GSM signals during exposure to event related potentials (ERPs). Int J Occup Med Environ Health. 2010;23(2):191–9.** OBJECTIVES: The primary aim of this work was to assess the effect of electromagnetic field (EMF) from the GSM mobile phone system on human brain function. The assessment was based on the assay of event related potentials (ERPs). MATERIAL AND METHODS: The study group consisted of 15 volunteers, including 7 men and 8 women. The test protocol comprised determination of P300 wave in each volunteer during exposure to the EMF. To eliminate possible effects of the applied test procedure on the final result, the test was repeated without EMF exposure. P300 latency, amplitude, and latency of the N1, N2, P2 waves were analysed. RESULTS: The statistical analysis revealed an effect of EMF on P300 amplitude. In the experiment with EMF exposure, lower P300 amplitudes were observed only at the time in which the volunteers were exposed to EMF; when the exposure was discontinued, the values of the amplitude were the same as those observed before EMF application. No such change was observed when the experiment was repeated with sham exposure, which may be considered as an indirect proof that lower P300 amplitude values were due to EMF exposure. No statistically significant changes were noted in the latencies of the N1, N2, P2 waves that precede the P300 wave, nor in the latency of the P300 itself. CONCLUSIONS: The results suggest that exposure to GSM EMF exerts some effects on CNS, including effects on long latency ERPs.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Chizhenkova RA. [Pulse flows of populations of cortical neurons under microwave radiation: the number of burst activity]. Radiats Biol Radioecol. 2010 Apr;50(2):201–10.** In unanesthetized nonimmobilized rabbit pulse flows of populations of cortical neurons were investigated prior, during, and after 1-min microwave irradiation (wavelength 37.5 cm, power density 0.2-0.3; 0.4; 0.5; and 40 mW/cm2) on the basis of the analysis of burst activity identified by means of time levels 5, 10, and 20 ms. Changes of the number of the spike bursts resulted from these exposures. The direction of the shifts its dynamics was determined by as intensity of irradiation as the kind of the bursts themselves.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No
2010	**Imge EB, Kiliçoğlu B, Devrim E, Cetin R, Durak I. Effects of mobile phone use on brain tissue from the rat and a possible protective role of vitamin C - a preliminary study. Int J Radiat Biol. 2010 Dec;86(12):1044–9.** PURPOSE: To evaluate effects of mobile phone use on brain tissue and a possible protective role of vitamin C. MATERIALS AND METHODS: Forty female rats were divided into four groups randomly (Control, mobile phone, mobile phone plus vitamin C and, vitamin C alone). The mobile phone group was exposed to a mobile phone signal (900 MHz), the mobile phone plus vitamin C group was exposed to a mobile phone signal (900 MHz) and treated with vitamin C administered orally (per os). The vitamin C group was also treated with vitamin C per os for four weeks. Then, the animals were sacrificed and brain tissues were dissected to be used in the analyses of malondialdehyde (MDA), antioxidant potential (AOP), superoxide dismutase, catalase (CAT), glutathione peroxidase (GSH-Px), xanthine oxidase, adenosine deaminase (ADA) and 5'nucleotidase (5'-NT). RESULTS: Mobile phone use caused an inhibition in 5'-NT and CAT activities as compared to the control group. GSH-Px activity and the MDA level were also found to be reduced in the mobile phone group but not significantly. Vitamin C caused a significant increase in the activity of GSH-Px and non-significant increase in the activities of 5'-NT, ADA and CAT enzymes. CONCLUSION: Our results suggest that vitamin C may play a protective role against detrimental effects of mobile phone radiation in brain tissue.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Jorge-Mora T, Alvarez Folgueiras M, Leiro J, Jorge-Barreiro FJ, Ares-Pena FJ, Lopez-Martin E. Exposure To 2.45 Ghz Microwave Radiation Provokes Cerebral Changes In Induction Of Hsp-90 Î±/Î² Heat Shock Protein In Rat. Progress In Electromagnetics Research. 2010;100:351–79.** Physical agents such as non-ionizing continuous-wave 2.45 GHz radiation may cause damage that alters cellular homeostasis and may trigger activation of the genes that encode heat shock proteins (HSP). We used Enzyme-Linked ImmunoSorbent Assay (ELI-SA) and immunohistochemistry to analyze the changes in levels of HSP-90 and its distribution in the brain of Sprague-Dawley rats, ninety minutes and twenty-four hours after acute (30 min) continuous exposure to 2.45 GHz radiation in a the Gigahertz Transverse Electromagnetic (GTEM cell). In addition, we studied further indicators of neuronal insult: dark neurons, chromatin condensation and nucleus fragmentation, which were observed under optical conventional or fluorescence microscopy after DAPI staining. The cellular distribution of protein HSP-90 in the brain increased with each corresponding (0.034 ± 3.10^{-3}, 0.069 ± 5.10^{-3}, 0.27 ± 21.10^{-3} W/kg), in hypothalamic nuclei, limbic cortex and somatosensorial cortex after exposure to the radiation. At twenty-four hours post-irradiation, levels of HSP-90 protein remained high in all hypothalamic nuclei for all SARs, and in the parietal cortex, except the limbic system, HSP-90 levels were lower than in non-irradiated rats, almost half the levels in rats exposed to the highest power radiation. Non-apoptotic cellular nuclei and a some dark neurons were found ninety minutes and twenty-four hours after maximal SAR exposure. The results suggest that acute exposure to electromagnetic fields triggered an imbalance in anatomical HSP-90 levels but the anti-apoptotic mechanism is probably sufficient to compensate the non-ionizing stimulus. Further studies are required to determine the regional effects of chronic electromagnetic pollution on heat shock proteins and their involvement in neurological processes and neuronal damage.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Maganioti AE, Hountala CD, Papageorgiou CC, Kyprianou MA, Rabavilas AD, Capsalis CN. Principal component analysis of the P600 waveform: RF and gender effects. Neurosci Lett. 2010 Jun 30;478(1):19–23.** The aim of the present study was to examine the patterns of activation of the P600 waveform of the event-related potentials (ERP), applying principal component analysis (PCA) and repeated measures ANOVA, and whether these patterns are RF and gender dependent. The ERPs of thirty-nine healthy subjects (20 male and 19 female) were recorded during an auditory memory task in the presence and absence of RF, similar to that emitted by mobile phones. Both PCA and ANOVA produced congruent results, showing that activation of the P600 component occurs early and more intensely in the region of the posterior electrodes and in a less intense manner in the central electrodes. Conversely, the activation at the anterior electrodes arises later with a considerably reduced intensity. In the absence of RF female subjects exhibited significantly lower amplitudes at anterior electrodes and earlier latencies at central electrodes than male subjects. These differences disappear in the presence of RF. Consequently, the P600 component follows distinct patterns of activation in the anterior, central and posterior brain areas and gender differences are observed simultaneously at several electrodes within these areas. Finally, the gender-related functional architecture with regard the P600 component appears to be RF sensitive. In conclusion, the application of the PCA procedure provides an adequate model of the spatially distributed event-related dynamics that correspond to the P600 waveform.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Maskey D, Kim M, Aryal B, Pradhan J, Choi I-Y, Park K-S, et al. Effect of 835 MHz radiofrequency radiation exposure on calcium binding proteins in the hippocampus of the mouse brain. Brain Res. 2010 Feb 8;1313:232–41.** Worldwide expansion of mobile phones and electromagnetic field (EMF) exposure has raised question of their possible biological effects on the brain and nervous system. Radiofrequency (RF) radiation might alter intracellular signaling pathways through changes in calcium (Ca(2+)) permeability across cell membranes. Changes in the expression of calcium binding proteins (CaBP) like calbindin D28-k (CB) and calretinin (CR) could indicate impaired Ca(2+)homeostasis due to EMF exposure. CB and CR expression were measured with immunohistochemistry in the hippocampus of mice after EMF exposure at 835 MHz for different exposure times and absorption rates, 1 h/day for 5 days at a specific absorption rate (SAR)=1.6 W/kg, 1 h/day for 5 days at SAR=4.0 W/kg, 5 h/day for 1 day at SAR=1.6 W/kg, 5 h/day for 1 day at SAR=4.0 W/kg, daily exposure for 1 month at SAR=1.6 W/kg. Body weights did not change significantly. CB immunoreactivity (IR) displayed moderate staining of cells in the cornu ammonis (CA) areas and prominently stained granule cells. CR IR revealed prominently stained pyramidal cells with dendrites running perpendicularly in the CA area. Exposure for 1 month produced almost complete loss of pyramidal cells in the CA1 area. CaBP differences could cause changes in cellular Ca(2+)levels, which could have deleterious effect on normal hippocampal functions concerned with neuronal connectivity and integration.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Maskey D, Pradhan J, Aryal B, Lee C-M, Choi I-Y, Park K-S, et al. Chronic 835-MHz radiofrequency exposure to mice hippocampus alters the distribution of calbindin and GFAP immunoreactivity. Brain Res. 2010 Jul 30;1346:237–46.** Exponential interindividual handling in wireless communication system has raised possible doubts in the biological aspects of radiofrequency (RF) exposure on human brain owing to its close proximity to the mobile phone. In the nervous system, calcium (Ca(2+)) plays a critical role in releasing neurotransmitters, generating action potential and membrane integrity. Alterations in intracellular Ca(2+) concentration trigger aberrant synaptic action or cause neuronal apoptosis, which may exert an influence on the cellular pathology for learning and memory in the hippocampus. Calcium binding proteins like calbindin D28-K (CB) is responsible for the maintaining and controlling Ca(2+) homeostasis. Therefore, in the present study, we investigated the effect of RF exposure on rat hippocampus at 835 MHz with low energy (specific absorption rate: SAR=1.6 W/kg) for 3 months by using both CB and glial fibrillary acidic protein (GFAP) specific antibodies by immunohistochemical method. Decrease in CB immunoreactivity (IR) was noted in exposed (E1.6) group with loss of interneurons and pyramidal cells in CA1 area and loss of granule cells. Also, an overall increase in GFAP IR was observed in the hippocampus of E1.6. By TUNEL assay, apoptotic cells were detected in the CA1, CA3 areas and dentate gyrus of hippocampus, which reflects that chronic RF exposure may affect the cell viability. In addition, the increase of GFAP IR due to RF exposure could be well suited with the feature of reactive astrocytosis, which is an abnormal increase in the number of astrocytes due to the loss of nearby neurons. Chronic RF exposure to the rat brain suggested that the decrease of CB IR accompanying apoptosis and increase of GFAP IR might be morphological parameters in the hippocampus damages. [1.6W/kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Narayanan SN, Kumar RS, Potu BK, Nayak S, Bhat PG, Mailankot M. Effect of radio-frequency electromagnetic radiations (RF-EMR) on passive avoidance behaviour and hippocampal morphology in Wistar rats. Ups J Med Sci. 2010 May;115(2):91–6.** INTRODUCTION: The interaction of mobile phone radio-frequency electromagnetic radiation (RF-EMR) with the brain is a serious concern of our society. OBJECTIVE: We evaluated the effect of RF-EMR from mobile phones on passive avoidance behaviour and hippocampal morphology in rats. MATERIALS AND METHODS: Healthy male albino Wistar rats were exposed to RF-EMR by giving 50 missed calls (within 1 hour) per day for 4 weeks, keeping a GSM (0.9 GHz/1.8 GHz) mobile phone in vibratory mode (no ring tone) in the cage. After the experimental period, passive avoidance behaviour and hippocampal morphology were studied. RESULTS: Passive avoidance behaviour was significantly affected in mobile phone RF-EMR-exposed rats demonstrated as shorter entrance latency to the dark compartment when compared to the control rats. Marked morphological changes were also observed in the CA(3) region of the hippocampus of the mobile phone-exposed rats in comparison to the control rats. CONCLUSION: Mobile phone RF-EMR exposure significantly altered the passive avoidance behaviour and hippocampal morphology in rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Sonmez OF, Odaci E, Bas O, Kaplan S. Purkinje cell number decreases in the adult female rat cerebellum following exposure to 900 MHz electromagnetic field. Brain Res. 2010 Oct 14;1356:95–101.** The biological effects of electromagnetic field (EMF) exposure from mobile phones have growing concern among scientists since there are some reports showing increased risk for human health, especially in the use of mobile phones for a long duration. In the presented study, the effects on the number of Purkinje cells in the cerebellum of 16-week (16 weeks) old female rats were investigated following exposure to 900 MHz EMF. Three groups of rats, a control group (CG), sham exposed group (SG) and an electromagnetic field exposed group (EMFG) were used in this study. While EMFG group rats were exposed to 900 MHz EMF (1h/day for 28 days) in an exposure tube, SG was placed in the exposure tube but not exposed to EMF (1h/day for 28 days). The specific energy absorption rate (SAR) varied between 0.016 (whole body) and 2 W/kg (locally in the head). The CG was not placed into the exposure tube nor was it exposed to EMF during the study period. At the end of the experiment, all of the female rats were sacrificed and the number of Purkinje cells was estimated using a stereological counting technique. Histopathological evaluations were also done on sections of the cerebellum. Results showed that the total number of Purkinje cells in the cerebellum of the EMFG was significantly lower than those of CG ($p<0.004$) and SG ($p<0.002$). In addition, there was no significant difference at the 0.05 level between the rats' body and brain weights in the EMFG and CG or SG. Therefore, it is suggested that long duration exposure to 900 MHz EMF leads to decreases of Purkinje cell numbers in the female rat cerebellum.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Bas O, Odaci E, Kaplan S, Acer N, Ucok K, Colakoglu S. 900 MHz electromagnetic field exposure affects qualitative and quantitative features of hippocampal pyramidal cells in the adult female rat. Brain Res. 2009 Apr 10;1265:178–85.** The effects of electromagnetic fields (EMFs) emitted by mobile phones on humans hold special interest due to their use in close proximity to the brain. The current study investigated the number of pyramidal cells in the cornu ammonis (CA) of the 16-week-old female rat hippocampus following postnatal exposure to a 900 megahertz (MHz) EMF. In this study were three groups of 6 rats: control (Cont), sham exposed (Sham), and EMF exposed (EMF). EMF group rats were exposed to 900 MHz EMF (1 h/day for 28 days) in an exposure tube. Sham group was placed in the exposure tube but not exposed to EMF (1 h/day for 28 days). Cont group was not placed into the exposure tube nor were they exposed to EMF during the study period. In EMF group rats, the specific energy absorption rate (SAR) varied between 0.016 (whole body) and 2 W/kg (locally in the head). All of the rats were sacrificed at the end of the experiment and the number of pyramidal cells in the CA was estimated using the optical fractionator technique. Histopathological evaluations were made on sections of the CA region of the hippocampus. Results showed that postnatal EMF exposure caused a significant decrease of the pyramidal cell number in the CA of the EMF group ($P<0.05$). Additionally, cell loss can be seen in the CA region of EMF group even at qualitative observation. These results may encourage researchers to evaluate the chronic effects of 900 MHz EMF on teenagers' brains.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2009	**Daniels WMU, Pitout IL, Afullo TJO, Mabandla MV. The effect of electromagnetic radiation in the mobile phone range on the behaviour of the rat. Metab Brain Dis. 2009 Dec;24(4):629–41.** Electromagnetic radiation (EMR) is emitted from electromagnetic fields that surround power lines, household appliances and mobile phones. Research has shown that there are connections between EMR exposure and cancer and also that exposure to EMR may result in structural damage to neurons. In a study by Salford et al. (Environ Health Perspect 111:881-883, 2003) the authors demonstrated the presence of strongly stained areas in the brains of rats that were exposed to mobile phone EMR. These darker neurons were particularly prevalent in the hippocampal area of the brain. The aim of our study was to further investigate the effects of EMR. Since the hippocampus is involved in learning and memory and emotional states, we hypothesised that EMR will have a negative impact on the subject's mood and ability to learn. We subsequently performed behavioural, histological and biochemical tests on exposed and unexposed male and female rats to determine the effects of EMR on learning and memory, emotional states and corticosterone levels. We found no significant differences in the spatial memory test, and morphological assessment of the brain also yielded non-significant differences between the groups. However, in some exposed animals there were decreased locomotor activity, increased grooming and a tendency of increased basal corticosterone levels. These findings suggested that EMR exposure may lead to abnormal brain functioning.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Dasdag S, Akdag MZ, Ulukaya E, Uzunlar AK, Ocak AR. Effect of mobile phone exposure on apoptotic glial cells and status of oxidative stress in rat brain. Electromagn Biol Med. 2009;28(4):342–54.** The aim of this study was to investigate the effects of mobile phone exposure on glial cells in brain. The study carried out on 31 Wistar Albino adult male rats. The rat heads in a carousel exposed to 900 MHz microwave. For the study group (n:14), rats exposed to the radiation 2 h per day (7 days in a week) for 10 months. For the sham group (n:7), rats were placed into the carousel and the same procedure was applied except that the generator was turned off. For the cage control (n:10), nothing applied to rats in this group. In this study, rats were euthanized after 10 months of exposure periods and brains were removed. Brain tissues were immunohistochemically stained for the active (cleaved) caspase-3, which is a well-known apoptosis marker, and p53. The expression of the proteins was evaluated by a semi-quantitative scoring system. However, total antioxidative capacity (TAC), catalase, total oxidant status (TOS), and oxidative stress index were measured in rat brain. Final score for apoptosis in the exposed group was significantly lower than the sham ($p < 0.001$) and the cage control groups ($p < 0.01$). p53 was not significantly changed by the exposure ($p > 0.05$). The total antioxidant capacity and catalase in the experimental group was found higher than that in the sham group ($p < 0.001$, $p < 0.05$). In terms of the TOS and oxidative stress index, there was no statistically significant difference between exposure and sham groups ($p > 0.05$). In conclusion, the final score for apoptosis, total antioxidant capacity and catalase in rat brain might be altered by 900 MHz radiation produced by a generator to represent exposure of global systems for mobile communication (GSM) cellular phones.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**López-Martín E, Bregains J, Relova-Quinteiro JL, Cadarso-Suárez C, Jorge-Barreiro FJ, Ares-Pena FJ. The action of pulse-modulated GSM radiation increases regional changes in brain activity and c-Fos expression in cortical and subcortical areas in a rat model of picrotoxin-induced seizure proneness. J Neurosci Res. 2009 May 1;87(6):1484–99.** The action of the pulse-modulated GSM radiofrequency of mobile phones has been suggested as a physical phenomenon that might have biological effects on the mammalian central nervous system. In the present study, GSM-exposed picrotoxin-pretreated rats showed differences in clinical and EEG signs, and in c-Fos expression in the brain, with respect to picrotoxin-treated rats exposed to an equivalent dose of unmodulated radiation. Neither radiation treatment caused tissue heating, so thermal effects can be ruled out. The most marked effects of GSM radiation on c-Fos expression in picrotoxin-treated rats were observed in limbic structures, olfactory cortex areas and subcortical areas, the dentate gyrus, and the central lateral nucleus of the thalamic intralaminar nucleus group. Nonpicrotoxin-treated animals exposed to unmodulated radiation showed the highest levels of neuronal c-Fos expression in cortical areas. These results suggest a specific effect of the pulse modulation of GSM radiation on brain activity of a picrotoxin-induced seizure-proneness rat model and indicate that this mobile-phone-type radiation might induce regional changes in previous preexcitability conditions of neuronal activation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Nittby H, Brun A, Eberhardt J, Malmgren L, Persson BRR, Salford LG. Increased blood-brain barrier permeability in mammalian brain 7 days after exposure to the radiation from a GSM-900 mobile phone. Pathophysiology. 2009 Aug;16(2-3):103–12.** Microwaves were for the first time produced by humans in 1886 when radio waves were broadcasted and received. Until then microwaves had only existed as a part of the cosmic background radiation since the birth of universe. By the following utilization of microwaves in telegraph communication, radars, television and above all, in the modern mobile phone technology, mankind is today exposed to microwaves at a level up to 10(20) times the original background radiation since the birth of universe. Our group has earlier shown that the electromagnetic radiation emitted by mobile phones alters the permeability of the blood-brain barrier (BBB), resulting in albumin extravasation immediately and 14 days after 2h of exposure. In the background section of this report, we present a thorough review of the literature on the demonstrated effects (or lack of effects) of microwave exposure upon the BBB. Furthermore, we have continued our own studies by investigating the effects of GSM mobile phone radiation upon the blood-brain barrier permeability of rats 7 days after one occasion of 2h of exposure. Forty-eight rats were exposed in TEM-cells for 2h at non-thermal specific absorption rates (SARs) of 0mW/kg, 0.12mW/kg, 1.2mW/kg, 12mW/kg and 120mW/kg. Albumin extravasation over the BBB, neuronal albumin uptake and neuronal damage were assessed. Albumin extravasation was enhanced in the mobile phone exposed rats as compared to sham controls after this 7-day recovery period (Fisher's exact probability test, p=0.04 and Kruskal-Wallis, p=0.012), at the SAR-value of 12mW/kg (Mann-Whitney, p=0.007) and with a trend of increased albumin extravasation also at the SAR-values of 0.12mW/kg and 120mW/kg. There was a low, but significant correlation between the exposure level (SAR-value) and occurrence of focal albumin extravasation (r(s)=0.33; p=0.04). The present findings are in agreement with our earlier studies where we have seen increased BBB permeability immediately and 14 days after exposure. We here discuss the present findings as well as the previous results of altered BBB permeability from our and other laboratories. **[**0.12 to 120mW/kg**]**	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

E. Effects on the Eye

Six scientific publications highlight effects of low level radiofrequency energy on the eye. Cataract formation with higher levels of a broad range of electromagnetic radiation is well known, and eyes are at risk of thermal effects because they lack blood flow for cooling. Research now points to other effects at lower exposure levels that do not induce heating.

In animals it was found that:

- rat corneal epithelium (the growing layer on the cornea) was thicker in animals exposed to low intensity microwave radiation for two hours daily over three weeks;
- radiation from computer monitors caused changes in rat corneas and lenses, including oxidative stress and indications of genetic damage; and
- development of the retina in chick embryos was disrupted with radiation from a cell phone.

In two laboratory cell culture studies, lens epithelial cells exhibited oxidative stress, altered protein and decreased cell viability following short term (0.5 to 2 hours) exposure to low levels of 1.8 GHz radiofrequency radiation.

This research replicates the findings of a 2010 review, that summarized that radiofrequency exposure affects lens transparency, cell growth and cell death, inhibits intercellular communication, and induces stress responses and genetic damage.

Year	References and extracts	Reports	Cited?
2013	**Akar A, Karayiğit MÖ, Bolat D, Gültiken ME, Yarim M, Castellani G. Effects of low level electromagnetic field exposure at 2.45 GHz on rat cornea. International Journal of Radiation Biology. 2013 Jan 4;1–7.** **PURPOSE:** To investigate the effects of low level electromagnetic field (low level-EMF) exposure, as frequently encountered in daily life, on the normal rat cornea using histological and stereological method. **METHODS:** Twenty-two adult male Wistar rats were randomly divided into two groups: Study group (n = 11) and control group (n = 11). Rats in the study group were exposed to 2.45 GHz microwave (MW) radiation (11.96 ± 0.89 V/m), 0.25 W/kg specific absorption rate (SAR) for 2 hours each day for 21 days. The corneal thickness and the anterior epithelium corneal thickness were measured using two different methods. **RESULTS:** Using the histological method, the mean corneal thicknesses in the control and study group were 278.9 ± 54.5 μm, and 272.4 ± 85.6 μm, respectively. There was no statistically significant difference between the groups ($p > 0.05$). The anterior corneal epithelium thickness was 28.1 ± 4.9 μm in the control group and 31.7 ± 5.5 μm in the study group. There were statistically differences between the groups with regard to the thickness of anterior epithelium ($p < 0.05$). In the measurement made by the stereological method, the percentage of the cornea occupied by anterior corneal epithelium was 15.94% in the control group and 17.9% in the study group. Despite the fact that there was a relation between increased anterior epithelial area (AEA) and radiation exposure, no statistically significant relationship in area fraction of each compartment was found between the control and study groups. **CONCLUSIONS:** Results of this preliminary study show that exposure to MW radiation might cause alterations in the rat cornea. [2.45 M Hz]	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2013	**Ni S, Yu Y, Zhang Y, Wu W, Lai K, Yao K. Study of oxidative stress in human lens epithelial cells exposed to 1.8 GHz radiofrequency fields. PLoS ONE. 2013;8(8):e72370.** OBJECTIVES: The aims of the present study were to determine oxidative stress and to explore possible reasons of reactive oxygen species (ROS) increase in human lens epithelial (HLE) B3 cells exposed to low intensity 1.8 GHz radiofrequency fields (RF). METHODS: The HLE B3 cells were divided into RF exposure and RF sham-exposure groups. The RF exposure intensity was at specific absorption rate (SAR) of 2, 3, or 4 W/kg. The ROS levels were measured by a fluorescent probe 2'7'-dichlorofluorescin diacetate (DCFH-DA) assay in the HLE B3 cells exposed to 1.8 GHz RF for 0.5, 1, and 1.5 h. Lipid peroxidation and cellular viability were detected by an MDA test and Cell Counting Kit-8 (CCK-8) assays, respectively, in the HLE B3 cells exposed to 1.8 GHz RF for 6, 12, and 24 h, respectively. The mRNA expression of SOD1, SOD2, CAT, and GPx1 genes and the expression of SOD1, SOD2, CAT, and GPx1 proteins was measured by qRT-PCR and Western blot assays in the HLE B3 cells exposed to 1.8 GHz RF for 1 h. RESULTS: The ROS and MDA levels significantly increased ($P<0.05$) in the RF exposure group and that the cellular viability, mRNA expression of four genes, and expression of four proteins significantly decreased ($P<0.05$) compared with the RF sham-exposure group. CONCLUSIONS: Oxidative stress is present in HLE B3 cells exposed to 1.8 GHz low-intensity RF and that the increased production of ROS may be related to down-regulation of four antioxidant enzyme genes induced by RF exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Zhang Y, Yao K, Yu Y, Ni S, Zhang L, Wang W, et al. Effects of 1.8 GHz radiofrequency radiation on protein expression in human lens epithelial cells. Human & Experimental Toxicology. 2013 Aug 1;32(8):797–806.** **Objective:** The aim of the present study was to observe the effects of 1.8 GHz radiofrequency (RF) radiation on the protein expression of human lens epithelial cells (hLECs) in vitro. **Methods:** The hLECs were exposed and sham-exposed to 1.8 GHz RF radiation (specific absorption rate (SAR) of 4 W/kg) for 2 h. After exposure, the proteins extracted from LECs were loaded on the Ettan MDLC system connected to the LTQ-Orbitrap MS for screening the candidate protein biomarkers induced by RF. The quantitative real-time polymerase chain reaction (qRT-PCR) was used to detect the levels of messenger RNA of candidate biomarkers. After the hLECs were exposed to 1.8 GHz RF (SAR of 2, 3 and 4 W/kg) for 2 h, the Western blot assay was utilized to measure the expression levels of the above-screened candidate protein biomarkers. **Results:** The results of shotgun proteomic analysis indicated that there were eight proteins with differential expression between exposure and sham exposure groups. The results of qRT-PCR showed that there were three genes with expressional differences (valosin containing protein (VCP), ubiquitin specific peptidase 35 (USP35) and signal recognition particle 68 kDa (SRP68)) between exposure and sham exposure groups. The results of Western blot assay exhibited that the expressional levels of VCP and USP35 proteins significantly increased and the expressional level of protein SRP68 significantly decreased in hLECs exposed to 1.8 GHz RF radiation (SAR of 3 and 4 W/kg) for 2 h when compared with the corresponding sham groups ($p < 0.05$). **Conclusion:** The shotgun proteomics technique can be applied to screen the proteins with differential expression between hLECs exposed to 1.8 GHz RF and hLECs sham-exposed to 1.8 GHz RF, and three protein biomarkers associated with RF radiation were validated by Western blot assay.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Yu Y, Yao K. Non-thermal Cellular Effects of Low power Microwave Radiation on the Lens and Lens Epithelial Cells. The Journal of International Medical Research. 2010;38(3):729–36.** Because of the increased use of modern radiofrequency devices, public concern about the possible health effects of exposure to microwave radiation has arisen in many countries. It is well established that high-power microwave radiation can induce cataracts via its thermal effects. It remains unclear whether low-power microwave radiation, especially at levels below the current exposure limits, is cataractogenic. This review summarizes studies on the biological effects of low-power microwave radiation on lens and lens epithelial cells (LECs). It has been reported that exposure affects lens transparency, alters cell proliferation and apoptosis, inhibits gap junctional intercellular communication, and induces genetic instability and stress responses in LECs. <u>These results raise the question of whether the ambient microwave environment can induce non-thermal effects in the lens and whether such effects have potential health consequences.</u> Further in vivo studies on the effects on the lens of exposure to low-power microwave radiation are needed.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2009	**Balci M, Namuslu M, Devrim E, Durak I. Effects of computer monitor-emitted radiation on oxidant/antioxidant balance in cornea and lens from rats. Mol Vis. 2009;15:2521–5.** PURPOSE: This study aims to investigate the possible effects of computer monitor-emitted radiation on the oxidant/antioxidant balance in corneal and lens tissues and to observe any protective effects of vitamin C (vit C). METHODS: Four groups (PC monitor, PC monitor plus vitamin C, vitamin C, and control) each consisting of ten Wistar rats were studied. The study lasted for three weeks. Vitamin C was administered in oral doses of 250 mg/kg/day. The computer and computer plus vitamin C groups were exposed to computer monitors while the other groups were not. Malondialdehyde (MDA) levels and superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and catalase (CAT) activities were measured in corneal and lens tissues of the rats. RESULTS: In corneal tissue, MDA levels and CAT activity were found to increase in the computer group compared with the control group. In the computer plus vitamin C group, MDA level, SOD, and GSH-Px activities were higher and CAT activity lower than those in the computer and control groups. Regarding lens tissue, in the computer group, MDA levels and GSH-Px activity were found to increase, as compared to the control and computer plus vitamin C groups, and SOD activity was higher than that of the control group. In the computer plus vitamin C group, SOD activity was found to be higher and CAT activity to be lower than those in the control group. CONCLUSION: The results of this study suggest that computer-monitor radiation leads to oxidative stress in the corneal and lens tissues, and that vitamin C may prevent oxidative effects in the lens.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Zareen N, Khan MY, Ali Minhas L. Derangement of chick embryo retinal differentiation caused by radiofrequency electromagnetic fields. Congenit Anom (Kyoto). 2009 Mar;49(1):15–9.** The possible adverse effects of radiofrequency electromagnetic fields (EMF) emitted from mobile phones present a major public concern. Biological electrical activities of the human body are vulnerable to interference from oscillatory aspects of EMF, which affect fundamental cellular activities, in particular, the highly active development process of embryos. Some studies highlight the possible health hazards of EMF, while others contest the hypothesis of biological impact of EMF. The present study was designed to observe the histomorphological effects of EMF emitted by a mobile phone on the retinae of developing chicken embryos. Fertilized chicken eggs were exposed to a ringing mobile set on silent tone placed in the incubator at different ages of development. After exposure for the scheduled duration the retinae of the embryos were dissected out and processed for histological examination. The control and experimental embryos were statistically compared for retinal thickness and epithelial pigmentation grades. Contrasting effects of EMF on the retinal histomorphology were noticed, depending on the duration of exposure. The embryos exposed for 10 post-incubation days exhibited decreased retinal growth and mild pigmentation of the epithelium. Growth retardation reallocated to growth enhancement on increasing EMF exposure for 15 post-incubation days, with a shift of pigmentation grade from mild to intense. We conclude that EMF emitted by a mobile phone cause derangement of chicken embryo retinal differentiation.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

F. Cardiovascular Effects

Four research publications identify effects on the cardiovascular system:

- consistent with earlier findings regarding EHS (below) a 2013 study found a “non-thermal” (low exposure) vasodilator effect of cell phone radiation exposure to the jaw and cheek;
- rats exposed to 900 MHz pulse-modulated radiofrequency radiation (similar to phone “talk mode”) daily 20 minutes/day for three weeks experienced oxidative damage to the heart (as well as the lungs, testis and liver);
- a very large study of rats, with a range of exposure durations, found heart damage that increased with dose, as well as higher blood pressure and lower blood calcium levels; and
- in the laboratory, radiofrequency exposure altered the structure of hemoglobin and lowered its capacity to carry oxygen in the blood.

In summary, research indicates that radiofrequency radiation may make the blood carry less oxygen, harm the heart, increase blood pressure and affect blood vessels. Effects identified in people with electromagnetic hypersensitivity (below) include heart rate variability.

Year	References and extracts	Reports	
2013	**Loos N, Thuróczy G, Ghosn R, Brenet-Dufour V, Liabeuf S, Selmaoui B, et al. Is the effect of mobile phone radiofrequency waves on human skin perfusion non-thermal? Microcirculation. 2013 Oct;20(7):629–36.** OBJECTIVE: To establish whether SkBF can be modified by exposure to the radiofrequency waves emitted by a mobile phone when the latter is held against the jaw and ear. METHODS: Variations in SkBF and Tsk in adult volunteers were simultaneously recorded with a thermostatic laser Doppler system during a 20-minute "radiofrequency" exposure session and a 20-minute "sham" session. The skin microvessels' vasodilatory reserve was assessed with a heat challenge at the end of the protocol. RESULTS: During the radiofrequency exposure session, SkBF increased (vs. baseline) more than during the sham exposure session. The sessions did not differ significant in terms of the Tsk time-course response. The skin microvessels' vasodilatory ability was found to be greater during radiofrequency exposure than during sham exposure. CONCLUSIONS: Our results reveal the existence of a specific vasodilatory effect of mobile phone radiofrequency emission on skin perfusion.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2014)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	n/a
		n/a = not available at time of report publication	

Year	References and extracts	Reports	
2011	**Esmekaya MA, Ozer C, Seyhan N. 900 MHz pulse-modulated radiofrequency radiation induces oxidative stress on heart, lung, testis and liver tissues. Gen Physiol Biophys. 2011 Mar;30(1):84–9.** Oxidative stress may affect many cellular and physiological processes including gene expression, cell growth, and cell death. In the recent study, we aimed to investigate whether 900 MHz pulse-modulated radiofrequency (RF) fields induce oxidative damage on lung, heart and liver tissues. We assessed oxidative damage by investigating lipid peroxidation (malondialdehyde, MDA), nitric oxide (NOx) and glutathione (GSH) levels which are the indicators of tissue toxicity. A total of 30 male Wistar albino rats were used in this study. Rats were divided randomly into three groups; control group (n = 10), sham group (device off, n = 10) and 900 MHz pulsed-modulated RF radiation group (n = 10). The RF rats were exposed to 900 MHz pulsed modulated RF radiation at a specific absorption rate (SAR) level of 1.20 W/kg 20 min/day for three weeks. MDA and NOx levels were increased significantly in liver, lung, testis and heart tissues of the exposed group compared to sham and control groups ($p < 0.05$). Conversely GSH levels were significantly lower in exposed rat tissues ($p < 0.05$). No significantly difference was observed between sham and control groups. Results of our study showed that pulse-modulated RF radiation causes oxidative injury in liver, lung, testis and heart tissues mediated by lipid peroxidation, increased level of NOx and suppression of antioxidant defense mechanism.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2014)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	
2011	**Mohamed FA, Ahmed AA, El-Kafoury BM, Lasheen NN. Study of the cardiovascular effects of exposure to electromagnetic field. Life Science Journal [Internet]. 2011;8(1). Available from: http://www.lifesciencesite.com/lsj/life0801/33_4553life0801_260_274_fatma.pdf** Abstract: This study was conducted to throw light on electromagnetic radiofrequency (EMR) emitted from cell phones which was accused of causing a number of negative health effects in the form of influencing on the heart and circulatory system. 110 adult albino rats, of both sexes, weighing 180- 200 gms were used in the present study. Animals were allocated into two main groups: group I, including rats exposed to cell phone EMF for 4 weeks; and group II, including rats exposed to EMF for 8 weeks. Each group was further subdivided into four subgroups, a control group and three subgroups exposed to EMF for either 1h/day, 2hrs/day or 3hrs/day, exposure being carried out six days/ week, at fixed time of the day. All rats were subjected to measurement of the systolic blood pressure on the day prior to the day of sacrifice, ECG recording, assessment of cardiac weights, absolute& relative, and MDA level in cardiac tissue, as well as determination of plasma renin activity, plasma total antioxidant capacity and plasma calcium level. Specimens from the apex of the heart were subjected to histopathological examinations. Obtained results revealed that systolic blood pressure was significantly increased in all EMF-exposed rats compared to their respective controls. The heart rate, deduced from the ECG tracings, was non-significantly altered in all groups exposed to EMF for 4 weeks and in the 8 weeks-1hr/day exposure group, but was significantly reduced in rats exposed to EMF for 2hrs or 3hrs/day for 8 weeks. The ECG recording of rats exposed to EMF for 4 weeks revealed a significantly higher R voltage in the group exposed for 3hrs/day, a significant increase in QRS duration in the groups exposed for 2hrs and 3hrs/day and significant prolongation of QT-c interval in the group exposed for 3hrs/day. On the other hand, the ECG recording of rats exposed to EMF for 8 weeks revealed significantly higher R and T voltages, and significantly prolonged P-R and QT-c intervals in the groups exposed for 2hrs or 3hrs/day, the QRS duration being significantly increased in all the 8 weeks-exposed groups. In addition, a significant increase in the absolute and relative weights of the whole heart and of the left ventricle in rats exposed to EMF 2hrs or 3hrs/day for either 4 or 8 weeks was obtained. Plasma renin activity was increased in all exposed rats, the increase being statistically significant in rats exposed to EMF 3hrs/day for 4 weeks, and in all the groups exposed to EMF for 8 weeks. Plasma calcium level was significantly decreased in all the exposed groups except for the group exposed for 1hr/day for 4 weeks. The plasma total anti-oxidant capacity was significantly decreased in all exposed groups, for either 4 or 8 weeks, while the MDA level in the cardiac tissue was only significantly elevated in the 8 weeks-3hrs/day exposed group compared to the matched control group. The histopathological examination revealed hypertrophy, fragmentation and vacuolation of the myocardium, which were directly proportional to the exposure time. On conclusion, long-term exposure to cell phone EMF increases the liability for hypertension reflected on the ECG and cardiac weights which is accompanied by histopathological changes in the myocardium. In addition, an interaction of EMF with biological functions was achieved in the form of increased PRA, decreased plasma total antioxidant capacity and hypocalcemia.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2014)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	
2009	**Mousavy SJ, Riazi GH, Kamarei M, Aliakbarian H, Sattarahmady N, Sharifizadeh A, et al. Effects of mobile phone radiofrequency on the structure and function of the normal human hemoglobin. Int J Biol Macromol. 2009 Apr 1;44(3):278–85.** Widespread use of mobile phones has increased the human exposure to electromagnetic fields (EMFs). It is required to investigate the effect of EMFs on the biological systems. In this paper the effect of mobile phone RF (910MHz and 940 MHz) on structure and function of HbA was investigated. Oxygen affinity was measured by sodium dithionite with UV-vis spectrophotometer. Structural changes were studied by circular dichroism and fluorescence spectroscopy. The results indicated that mobile phone EMFs altered oxygen affinity and tertiary structure of HbA. Furthermore, the decrease of oxygen affinity of HbA corresponded to the EMFs intensity and time of exposure.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2014)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

G. Electrohypersensitivity (EHS)

We all have our strengths and vulnerabilities, and some people experience diverse symptoms that correlate reproducibly with exposure to electromagnetic energy. Research can tend to find no effect (be "biased to the null") with these individuals, due to delayed onset and resolution of symptoms, as well as other sensitivities that may be provoked in research settings.

Nine publications were identified, including:

- a study of more than 400 participants that identified a suite of biochemical markers for those with EHS;
- an overview of diagnosis of EHS by measuring heart rate variability, microcirculation and electric skin potentials;
- the Guideline of the Austrian Medical Association for the diagnosis and treatment of EMF- related health problems and illnesses (EMF syndrome), a consensus paper of the Austrian Medical Association's EMF Working Group (AG-EMF);
- research indicating that avoidance of radiation from video display terminals allowed affected individuals to return to productivity;
- research comparing individuals with symptoms associated specifically with cell phones, individuals with EHS and healthy controls found that those affected by a broader range of exposures were more likely also to suffer psychological distress than healthy controls or those with symptoms related to cell phones alone;
- an overview of the status of EHS, as a disability that is accommodated in Sweden. Differences in the skin may be markers of this disability; and
- research indicating a higher prevalence of thyroid and liver dysfunction, and chronic inflammation in patients presenting with EHS. It is recommended to check for treatable conditions in these patients.

Research is progressing on diagnosis (traits, symptoms and objective markers), treatment and accommodation of individuals with EHS, with clinical guidelines in place and under review.

	References and extracts	Reports	
2014	**De Luca C, Thai JCS, Raskovic D, Cesareo E, Caccamo D, Trukhanov A, et al. Metabolic and genetic screening of electromagnetic hypersensitive subjects as a feasible tool for diagnostics and intervention. Mediators Inflamm. 2014;2014:924184.** Growing numbers of "electromagnetic hypersensitive" (EHS) people worldwide self-report severely disabling, multiorgan, non-specific symptoms when exposed to low-dose electromagnetic radiations, often associated with symptoms of multiple chemical sensitivity (MCS) and/or other environmental "sensitivity-related illnesses" (SRI). This cluster of chronic inflammatory disorders still lacks validated pathogenetic mechanism, diagnostic biomarkers, and management guidelines. We hypothesized that SRI, not being merely psychogenic, may share organic determinants of impaired detoxification of common physic-chemical stressors. Based on our previous MCS studies, we tested a panel of 12 metabolic blood redox-related parameters and of selected drug-metabolizing-enzyme gene polymorphisms, on 153 EHS, 147 MCS, and 132 control Italians, confirming MCS altered ($P < 0.05$-0.0001) glutathione-(GSH), GSH-peroxidase/S-transferase, and catalase erythrocyte activities. We first described comparable-though milder-metabolic pro-oxidant/proinflammatory alterations in EHS with distinctively increased plasma coenzyme-Q10 oxidation ratio. Severe depletion of erythrocyte membrane polyunsaturated fatty acids with increased ω 6/ ω 3 ratio was confirmed in MCS, but not in EHS. We also identified significantly ($P = 0.003$) altered distribution-versus-control of the CYP2C19$*$1/$*$2 SNP variants in EHS, and a 9.7-fold increased risk (OR: 95% C.I. = 1.3-74.5) of developing EHS for the haplotype (null)GSTT1 + (null)GSTM1 variants. Altogether, results on MCS and EHS strengthen our proposal to adopt this blood metabolic/genetic biomarkers' panel as suitable diagnostic tool for SRI.	Reference provided to **Royal Society of Canada** (in 2013)	n/a
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	n/a
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	n/a
		n/a = not available at time of report publication	

	References and extracts	Reports	
2013	**Tuengler A, von Klitzing L. Hypothesis on how to measure electromagnetic hypersensitivity. Electromagn Biol Med. 2013 Sep;32(3):281–90.** Electromagnetic hypersensitivity (EHS) is an ill-defined term to describe the fact that people who experience health symptoms in the vicinity of electromagnetic fields (EMFs) regard them as causal for their complaints. Up to now most scientists assume a psychological cause for the suffering of electromagnetic hypersensitive individuals. This paper addresses reasons why most provocation studies could not find any association between EMF exposure and EHS and presents a hypothesis on diagnosis and differentiation of this condition. Simultaneous recordings of heart rate variability, microcirculation and electric skin potentials are used for classification of EHS. Thus, it could be possible to distinguish "genuine" electromagnetic hypersensitive individuals from those who suffer from other conditions.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
2012	**Austrian Medical Association. Guideline of the Austrian Medical Association for the diagnosis and treatment of EMF- related health problems and illnesses (EMF syndrome) Consensus paper of the Austrian Medical Association's EMF Working Group (AG-EMF) EMF Guideline OAK-AG 2012 03 03.pdf. Austrian Medical Association [Internet]. 2012; Available from: http://freiburger-appell-2012.info/media/EMF%20Guideline%20OAK-AG%20%202012%2003%2003.pdf** The Austrian Medical Association has developed a guideline for differential diagnosis and potential treatment of unspecific stress-related health problems associated with electrosmog. Its core element is a patient questionnaire consisting of a general assessment of stress symptoms and a specific assessment of electrosmog exposure. The guideline is intended as an aid in diagnosing and treating EMF-related health problems. **NOTE**: This document is currently being updated.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

	References and extracts	Reports	
2012	**Hagström M, Auranen J, Johansson O, Ekman R. Reducing electromagnetic irradiation and fields alleviates experienced health hazards of VDU work. Pathophysiology. 2012 Apr;19(2):81–7.** Word Heath Organisation (WHO) outlined in 2005 recommendations, how to treat people suffering from the functional impairment electrohypersensitivity in its document "Electromagnetic fields and public health". Unfortunately the reduction of electromagnetic fields was not considered as a treatment option. The aim of the current study was to shield the computer user from the emitted electromagnetic irradiation and fields and to correlate that to the subjective symptoms reported by electrohypersensitive volunteers. The irradiation of the shielding cabinets was recorded. They housed either separate computer screens or whole laptops. When the volunteers had used the shielding cabinet for 1-7 years, they were able work with their computers whole working day. Those who had used the shielding cabined for 2-3 months were partially symptom free. The person who had used the cabinet only for 1 week reported some alleviation of her nausea. In conclusion: it seems that reducing the electromagnetic irradiation of the computer can lessen the symptoms of electrohypersensitivity and permit working without problems. Further studies are needed to clarify how the symptoms of different organ systems recover and make computer users to work also professionally.	Reference provided to **Royal Society of Canada** (in 2013)	Yes*
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
		* this reference was noted in the written (email) submission of Dr. O. Johansson to the RSC on 25 October 2013 as part of the RSC public consultation process.	

	References and extracts	Reports	
2012	**Kato Y, Johansson O. The situation of electrohypersensitivity: symptoms, EMF sources, economic and social problems, and precautionary approach. Jap J Clin Ecol. 2012;21:123–30.**	Reference provided to **Royal Society of Canada** (in 2013)	Yes*
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
		* this reference was noted in the written (email) submission of Dr. O. Johansson to the RSC on 25 October 2013 as part of the RSC public consultation process.	

	References and extracts	Reports	
2010	**Dämvik M, Johansson O. Health risk assessment of electromagnetic fields: a conflict between the precautionary principle and environmental medicine methodology. Rev Environ Health. 2010 Dec;25(4):325–33.** The purpose of the precautionary principle is that legal requirements are to be made to safeguard against the possible health risks that have not yet been scientifically established. That a risk is not established cannot, therefore, be used as an excuse for not applying the principle. Yet, that rationale is exactly what is happening in the case of the possible health risks from exposure to electromagnetic fields (EMF). The scientists, representing both the World Health Organization and the European Commission, do not have at all the precautionary principle in mind when they report on health risks. Their starting point is instead to determine whether new research findings have been scientifically established and thus cannot be the basis for an amendment to the existing exposure limits. Uncertain indications of risk are ignored or played down. This approach is in conflict with European Union (EU) law, which requires that the degree of scientific uncertainty should be presented correctly. A thorough examination of the state of research shows many serious indications of possible health risks from exposure very far below existing limits for EMF. Case law, for other types of exposure, also shows that the precautionary principle can be applied on the basis of weaker evidence than that. Our investigation shows that the precautionary principle is not being used for its intended purpose in relation to exposure to EMF. The reason for this position is that decision-makers are being misled by inaccurate risk assessments.	Reference provided to **Royal Society of Canada** (in 2013)	Yes*
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
		*** this reference was noted in the written (email) submission of Dr. O. Johansson to the RSC on 25 October 2013 as part of the RSC public consultation process.**	

	References and extracts	Reports	
2010	**Johansson A, Nordin S, Heiden M, Sandström M. Symptoms, personality traits, and stress in people with mobile phone-related symptoms and electromagnetic hypersensitivity. J Psychosom Res. 2010 Jan;68(1):37–45.** OBJECTIVE Some people report symptoms that they associate with electromagnetic field (EMF) exposure. These symptoms may be related to specific EMF sources or to electrical equipment in general (perceived electromagnetic hypersensitivity, EHS). Research and clinical observations suggest a difference between mobile phone (MP)-related symptoms and EHS with respect to symptom prevalence, psychological factors, and health prognosis. This study assessed prevalence of EMF-related and EMF-nonrelated symptoms, anxiety, depression, somatization, exhaustion, and stress in people with MP-related symptoms or EHS versus a population-based sample and a control sample without EMF-related symptoms. METHODS Forty-five participants with MP-related symptoms and 71 with EHS were compared with a population-based sample (n=106) and a control group (n=63) using self-report questionnaires. RESULTS The EHS group reported more symptoms than the MP group, both EMF-related and EMF-nonrelated. The MP group reported a high prevalence of somatosensory symptoms, whereas the EHS group reported more neurasthenic symptoms. As to self-reported personality traits and stress, the case groups differed only on somatization and listlessness in a direct comparison. In comparison with the reference groups, the MP group showed increased levels of exhaustion and depression but not of anxiety, somatization, and stress; the EHS group showed increased levels for all of the conditions except for stress. CONCLUSION The findings support the idea of a difference between people with symptoms related to specific EMF sources and people with general EHS with respect to symptoms and anxiety, depression, somatization, exhaustion, and stress. The differences are likely to be important in the management of patients.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

	References and extracts	Reports	
2010	**Johansson O. Aspects of studies on the functional impairment electrohypersensitivity. IOP Conf Ser: Earth Environ Sci. 2010 Apr 1;10(1):012005.** Persons, claiming to suffer from exposure to electromagnetic fields, have been described in the literature. In Sweden, electrohypersensitivity (EHS) is an officially fully recognized functional impairment (i.e., it is not regarded as a disease). Survey studies show that somewhere between 230,000 – 290,000 Swedish men and women – out of a population of 9,000,000 – report a variety of symptoms when being in contact with electromagnetic field (EMF) sources. Swedish electrohypersensitive people have their own handicap organization, The Swedish Association for the Electrohypersensitive, which has its own website in both Swedish and English. This organization is included in the Swedish Disability Federation (Handikappförbundens SamarbetsOrgan; HSO). One aim of our studies has been to investigate possible alterations, in the cellular and neuronal systems of these persons' skin. In summary, it is evident from our preliminary data that various alterations are present in the electrohypersensitive persons' skin that are not indicated in the skin of normal healthy volunteers.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

	References and extracts	Reports	
2009	**Dahmen N, Ghezel-Ahmadi D, Engel A. Blood laboratory findings in patients suffering from self-perceived electromagnetic hypersensitivity (EHS). Bioelectromagnetics. 2009 May;30(4):299–306.** Risks from electromagnetic devices are of considerable concern. Electrohypersensitive (EHS) persons attribute a variety of rather unspecific symptoms to exposure to electromagnetic fields. The pathophysiology of EHS is unknown and therapy remains a challenge. We hypothesized that some electrosensitive individuals are suffering from common somatic health problems. Toward this end we analysed clinical laboratory parameters including thyroid-stimulating hormone (TSH), alanine transaminase (ALT), aspartate transaminase (AST), creatinine, hemoglobine, hematocrit and c-reactive protein (CRP) in subjects suffering from EHS and in controls that are routinely used in clinical medicine to identify or screen for common somatic disorders. One hundred thirty-two patients (n = 42 males and n = 90 females) and 101 controls (n = 34 males and n = 67 females) were recruited. Our results identified laboratory signs of thyroid dysfunction, liver dysfunction and chronic inflammatory processes in small but remarkable fractions of EHS sufferers as potential sources of symptoms that merit further investigation in future studies. In the cases of TSH and ALT/AST there were significant differences between cases and controls. The hypotheses of anaemia or kidney dysfunction playing a major role in EHS could be unambiguously refuted. Clinically it is recommended to check for signs of treatable somatic conditions when caring for individuals suffering from self-proclaimed EHS.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada **Safety Code 6 (2014) Draft**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

H. Biochemical Effects

Research often includes biochemical measurements, so literature touching on biochemical effects is not surprisingly the largest collection of publications indicating significant and potentially harmful effects of radiofrequency radiation. Several themes run through the 65 publications examining laboratory research that were identified, some of which were touched upon above.

In animal studies, radiofrequency radiation affects biochemical parameters that correspond to:

- increased oxidative stress;
- damage to genetic material;
- damage to cellular membranes, with reduced fluidity and increased permeability;
- cellular damage and cellular death, in the brain, heart, liver, testis, blood and reproductive cells (sperm and eggs); and
- changes in neurotransmitters that govern operation of the nervous system.

These findings are replicated and explored further in diverse cell culture systems simulating the nervous system, white blood cells [lymphocytes], sperm cells and tissues.

Year	References and extracts	Reports	Cited?
2014	**Beneduci A, Cosentino K, Romeo S, Massa R, Chidichimo G. Effect of millimetre waves on phosphatidylcholine membrane models: a non-thermal mechanism of interaction. Soft Matter. 2014 Jun 24** The nonthermal biological effects of millimeter waves have been mainly attributed to the interaction with biological membranes. Several data on biomimetic membrane systems seem to support this conclusion. In this paper a mechanistic hypothesis is evaluated to explain such an interaction taking into account experimental NMR data on deuterium-labeled phospholipid vesicles. These data showed that millimeter waves induce a time and a hydration-dependent reduction of the water ordering around the phosphocholine headgroups. This effect is here interpreted as a change in membrane water partitioning, due to the coupling of the radiation with the fast rotational dynamics of bound water molecules, that results in a measurable relocation of water molecules from the inner to the outer binding regions of the membrane interface. When millimeter wave exposure is performed in the vicinity of the transition point, this effect can lead to an upward shift of the membrane phase transition temperature from the fluid to the gel phase. At a macroscopic level, this unique sensitivity may be explained by the universal dynamic behaviour of the membranes in the vicinity of the transition point, where a pretransitional increase of membrane area fluctuations, i.e., of the mean area per phospholipid headgroup, is observed. Exposure to millimeter waves increases the above fluctuations and enhances the second order character of the transition. NOTE: this is a shorter wavelength than RF radiation, but is an illustration of an effect on a membrane by a wavelength that is much greater than the membrane thickness	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a No n/a

Year	References and extracts	Reports	Cited?
2014	**Cetin H, Nazıroğlu M, Celik O, Yüksel M, Pastacı N, Ozkaya MO. Liver antioxidant stores protect the brain from electromagnetic radiation (900 and 1800 MHz)-induced oxidative stress in rats during pregnancy and the development of offspring. J Matern Fetal Neonatal Med. 2014 Apr 9;** Abstract Objectives: The present study determined the effects of mobile phone (900 and 1800 MHz)-induced electromagnetic radiation (EMR) exposure on oxidative stress in the brain and liver as well as the element levels in growing rats from pregnancy to 6 weeks of age. Methods: Thirty-two rats and their offspring were equally divided into three different groups: the control, 900 MHz, and 1800 MHz groups. The 900 MHz and 1800 MHz groups were exposed to EMR for 60 min/d during pregnancy and neonatal development. At the 4th, 5th, and 6th weeks of the experiment, brain samples were obtained. Results: Brain and liver glutathione peroxidase activities, as well as liver vitamin A and β-carotene concentrations decreased in the EMR groups, although brain iron, vitamin A, and β-carotene concentrations increased in the EMR groups. In the 6th week, selenium concentrations in the brain decreased in the EMR groups. There were no statistically significant differences in glutathione, vitamin E, chromium, copper, magnesium, manganese, and zinc concentrations between the three groups. Conclusion: EMR-induced oxidative stress in the brain and liver was reduced during the development of offspring. Mobile phone-induced EMR could be considered as a cause of oxidative brain and liver injury in growing rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a No n/a

Year	References and extracts	Reports	Cited?
2014	**Furtado-Filho OV, Borba JB, Dallegrave A, Pizzolato TM, Henriques JAP, Moreira JCF, et al. Effect of 950 MHz UHF electromagnetic radiation on biomarkers of oxidative damage, metabolism of UFA and antioxidants in the livers of young rats of different ages. Int J Radiat Biol. 2014 Feb;90(2):159–68.** PURPOSE: To assess the effect of 950 MHz ultra-high-frequency electromagnetic radiation (UHF EMR) on biomarkers of oxidative damage, as well as to verify the concentration of unsaturated fatty acids (UFA) and the expression of the catalase in the livers of rats of different ages. MATERIALS AND METHODS: Twelve rats were equally divided into two groups as controls (CR) and exposed (ER), for each age (0, 6, 15 and 30 days). Radiation exposure lasted half an hour per day for up to 51 days (21 days of gestation and 6, 15 or 30 days of life outside the womb). The specific absorption rate (SAR) ranged from 1.3-1.0 W/kg. The damage to lipids, proteins and DNA was verified by thiobarbituric acid reactive substances (TBARS), protein carbonyls and comets, respectively. UFA were determined by gas chromatography with a flame ionization detector. The expression of catalase was by Western blotting. RESULTS: The neonates had low levels of TBARS and concentrations of UFA after exposure. There was no age difference in the accumulation of protein carbonyls for any age. The DNA damage of ER 15 or 30 days was different. The exposed neonates exhibited lower expression of catalase. CONCLUSIONS: 950 MHz UHF EMR does not cause oxidative stress (OS), and it is not genotoxic to the livers of neonates or those of 6 and 15 day old rats, <u>but it changes the concentrations of polyunsaturated fatty acid (PUFA) in neonates</u>. For rats of 30 days, no OS, but it is genotoxic to the livers of ER to total body irradiation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a No n/a

Year	References and extracts	Reports	Cited?
2014	**Maskey D, Kim MJ. Immunohistochemical localization of brain-derived neurotrophic factor and glial cell line-derived neurotrophic factor in the superior olivary complex of mice after radiofrequency exposure. Neurosci Lett. 2014 Apr 3;564:78–82.** Raising health concerns about the biological effects from radiofrequency exposure, even with conflicting results, has prompted calls for formulation of a guideline of the biological safety level. Given the close proximity between a mobile phone and the ear, it has been suggested that the central auditory system may be detrimentally influenced by radiofrequency exposure. In the auditory system, neurotrophins are important in the regulation of neuron survival, especially mammalian cochlear neurons. Neurotrophic factors like brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) present in the auditory system are responsible for the maintenance of auditory neurons. BDNF and GDNF may protect against acoustic trauma and prevent from hearing defect. The present study applied radiofrequency at a specific absorption rate (SAR) of 1.6W/kg (E1.6) or 0W/kg group to determine the distribution of BDNF and GDNF in the nuclei of superior olivary complex (SOC). In the E1.6 group, significant decrements of BDNF immunoreactivity (IR) were noted in the lateral superior olive, medial superior olive, superior paraolivary nucleus and medial nucleus of the trapezoid body. GDNF IR was also significantly decreased ($p<0.001$) in all SOC nuclei of the E1.6 group. The decrease in the IR of these neurotrophic factors in the SOC of the E1.6 group suggests a detrimental effect of RF exposure in the auditory nuclei.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2014)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a No n/a n/a n/a

Year	References and extracts	Reports	Cited?
2014	**Valbonesi P, Franzellitti S, Bersani F, Contin A, Fabbri E. Effects of the exposure to intermittent 1.8 GHz radio frequency electromagnetic fields on HSP70 expression and MAPK signaling pathways in PC12 cells. Int J Radiat Biol. 2014 May;90(5):382–91.** PURPOSE: We previously reported effects on heat shock protein 70 (HSP70) mRNA expression, a cytoprotective protein induced under stressful condition, in human trophoblast cells exposed to amplitude-modulated Global System for Mobile Communication (GSM) signals. In the present work the same experimental conditions were applied to the rat PC12 cells, in order to assess the stress responses mediated by HSP70 and by the Mitogen Activated Protein Kinases (MAPK) in neuronal-like cells, an interesting model to study possible effects of mobile phone frequencies exposure. MATERIALS AND METHODS: HSP70 gene expression level was evaluated by reverse transcriptase polymerase chain reaction, HSP70 protein expression and MAPK phosphorylation were assessed by Western blotting. PC12 cells were exposed for 4, 16 or 24 h to 1.8 GHz continuous wave signal (CW, carrier frequency without modulation) or to two different GSM modulation schemes, GSM-217Hz and GSM-Talk (which generates temporal changes between two different GSM signals, active during talking or listening phases, respectively, thus simulating a typical conversation). Specific adsorption rate (SAR) was 2 W/kg. RESULTS: <u>After PC12 cells exposure to the GSM-217Hz signal for 16 or 24 h, HSP70 transcription significantly increased,</u> whereas no effect was observed in cells exposed to the CW or GSM-Talk signals. HSP70 protein expression and three different MAPK signaling pathways were not affected by the exposure to any of the three different 1.8 GHz signals. CONCLUSION: <u>The positive effect on HSP70 mRNA expression, observed only in cells exposed to the GSM-217Hz signal, is a repeatable response previously reported in human trophoblast cells and now confirmed in PC12 cells</u>. Further investigations towards a possible role of 1.8 GHz signal modulation are therefore advisable.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	n/a n/a n/a n/a n/a

Year	References and extracts	Reports	Cited?
2013	**Aboul Ezz HS, Khadrawy YA, Ahmed NA, Radwan NM, El Bakry MM. The effect of pulsed electromagnetic radiation from mobile phone on the levels of monoamine neurotransmitters in four different areas of rat brain. Eur Rev Med Pharmacol Sci. 2013 Jul;17(13):1782–8.** BACKGROUND: The use of mobile phones is rapidly increasing all over the world. Few studies deal with the effect of electromagnetic radiation (EMR) on monoamine neurotransmitters in the different brain areas of adult rat. AIM: The aim of the present study was to investigate the effect of EMR on the concentrations of dopamine (DA), norepinephrine (NE) and serotonin (5-HT) in the hippocampus, hypothalamus, midbrain and medulla oblongata of adult rats. MATERIALS AND METHODS: Adult rats were exposed daily to EMR (frequency 1800 MHz, specific absorption rate 0.843 W/kg, power density 0.02 mW/cm2, modulated at 217 Hz) and sacrificed after 1, 2 and 4 months of daily EMR exposure as well as after stopping EMR for 1 month (after 4 months of daily EMR exposure). Monoamines were determined by high performance liquid chromatography coupled with fluorescence detection (HPLC-FD) using their native properties. RESULTS: The exposure to EMR resulted in significant changes in DA, NE and 5-HT in the four selected areas of adult rat brain. CONCLUSIONS: The exposure of adult rats to EMR may cause disturbances in monoamine neurotransmitters and this may underlie many of the adverse effects reported after EMR including memory, learning, and stress. [1800 MHz; SAR 0.843W/kg; 0.02 mW/cm^2]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Atlı Şekeroğlu Z, Akar A, Şekeroğlu V. Evaluation of the cytogenotoxic damage in immature and mature rats exposed to 900 MHz radiofrequency electromagnetic fields. Int J Radiat Biol. 2013 Nov;89(11):985–92.** PURPOSE: One of the most important issues regarding radiofrequency electromagnetic fields (RF-EMF) is their effect on genetic material. Therefore, we investigated the cytogenotoxic effects of 900 MHz radiofrequency electromagnetic fields (RF-EMF) and the effect of a recovery period after exposure to RF-EMF on bone marrow cells of immature and mature rats. MATERIALS AND METHODS: The immature and mature rats in treatment groups were exposed to RF-EMF for 2 h/day for 45 days. Average electrical field values for immature and mature rats were 28.1 ± 4.8 V/m and 20.0 ± 3.2 V/m, respectively. Whole-body specific absorption rate (SAR) values for immature and mature rats were in the range of 0.38-0.78 W/kg, and 0.31-0.52 W/kg during the 45 days, respectively. Two recovery groups were kept for 15 days after RF-EMF exposure. RESULTS: Significant differences were observed in chromosome aberrations (CA), micronucleus (MN) frequency, mitotic index (MI) and ratio of polychromatic erythrocytes (PCE) in all treatment and recovery groups. The cytogenotoxic damage in immature rats was statistically higher than the mature rats. The recovery period did not reduce the damage to the same extent as the corresponding control groups. CONCLUSIONS: The exposure of RF-EMF leads to cytotoxic and genotoxic damage in immature and mature rats. More sensitive studies are required to elucidate the possible carcinogenic risk of EMF exposure in humans, especially children.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No n/a

Year	References and extracts	Reports	Cited?
2013	**Beyer C, Christen P, Jelesarov I, Fröhlich J. Experimental system for real-time assessment of potential changes in protein conformation induced by electromagnetic fields. Bioelectromagnetics. 2013 Sep;34(6):419–28.** A novel experimental system to distinguish between potential thermal and non-thermal effects of electromagnetic fields (EMFs) on the conformational equilibrium and folding kinetics of proteins is presented. The system comprises an exposure chamber installed within the measurement compartment of a spectropolarimeter and allows real-time observation of the circular dichroism (CD) signal of the protein during EMF exposure. An optical temperature probe monitors the temperature of the protein solution at the site of irradiation. The electromagnetic, thermal, and fluid-dynamic behavior of the system is characterized by numerical and experimental means. The number of repeated EMF on/off cycles needed for achieving a certain detection limit is determined on the basis of the experimentally assessed precision of the CD measurements. The isolated thermosensor protein GrpE of the Hsp70 chaperone system of Eschericha coli serves as the test protein. Long-term experiments show high thermal reproducibility as well as thermal stability of the experimental setup.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No n/a

Year	References and extracts	Reports	Cited?
2013	**Burlaka A, Tsybulin O, Sidorik E, Lukin S, Polishuk V, Tsehmistrenko S, et al. Overproduction of free radical species in embryonal cells exposed to low intensity radiofrequency radiation. Exp Oncol. 2013 Sep;35(3):219–25.** Aim: Long-term exposure of humans to low intensity radiofrequency electromagnetic radiation (RF-EMR) leads to a statistically significant increase in tumor incidence. Mechanisms of such the effects are unclear, but features of oxidative stress in living cells under RF-EMR exposure were previously reported. Our study aims to assess a production of initial free radical species, which lead to oxidative stress in the cell. Materials and Methods: Embryos of Japanese quails were exposed in ovo to extremely low intensity RF-EMR of GSM 900 MHz (0.25 μW/cm2) during 158-360 h discontinuously (48 c - ON, 12 c - OFF) before and in the initial stages of development. The levels of superoxide (O2·-), nitrogen oxide (NO·), thiobarbituric acid reactive substances (TBARS), 8-oxo-2'-deoxyguanosine (8-oxo-dG) and antioxidant enzymes' activities were assessed in cells/tissues of 38-h, 5- and 10-day RF-EMR exposed and unexposed embryos. Results: The exposure resulted in a significant persistent overproduction of superoxide and nitrogen oxide in embryo cells during all period of analyses. As a result, significantly increased levels of TBARS and 8-oxo-dG followed by significantly decreased levels of superoxide dismutase and catalase activities were developed in the exposed embryo cells. Conclusion: Exposure of developing quail embryos to extremely low intensity RF-EMR of GSM 900 MHz during at least one hundred and fifty-eight hours leads to a significant overproduction of free radicals/reactive oxygen species and oxidative damage of DNA in embryo cells. These oxidative changes may lead to pathologies up to oncogenic transformation of cells.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	Yes No n/a No No

Year	References and extracts	Reports	Cited?
2013	**Cervellati F, Valacchi G, Lunghi L, Fabbri E, Valbonesi P, Marci R, et al. 17-β-estradiol counteracts the effects of high frequency electromagnetic fields on trophoblastic connexins and integrins. Oxid Med Cell Longev. 2013;2013:280850.** We investigated the effect of high-frequency electromagnetic fields (HF-EMFs) and 17-β-estradiol on connexins (Cxs), integrins (Ints), and estrogen receptor (ER) expression, as well as on ultrastructure of trophoblast-derived HTR-8/SVneo cells. HF-EMF, 17-β-estradiol, and their combination induced an increase of Cx40 and Cx43 mRNA expression. HF-EMF decreased Int alpha1 and β 1 mRNA levels but enhanced Int alpha5 mRNA expression. All the Ints mRNA expressions were increased by 17-β-estradiol and exposure to both stimuli. ER-β mRNA was reduced by HF-EMF but augmented by 17-β-estradiol alone or with HF-EMF. ER-β immunofluorescence showed a cytoplasmic localization in sham and HF-EMF exposed cells which became nuclear after treatment with hormone or both stimuli. Electron microscopy evidenced a loss of cellular contact in exposed cells which appeared counteracted by 17-β-estradiol. We demonstrate that 17-β-estradiol modulates Cxs and Ints as well as ER-β expression induced by HF-EMF, suggesting an influence of both stimuli on trophoblast differentiation and migration.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No n/a

Year	References and extracts	Reports	Cited?
2013	**Deshmukh PS, Megha K, Banerjee BD, Ahmed RS, Chandna S, Abegaonkar MP, et al. Detection of Low Level Microwave Radiation Induced Deoxyribonucleic Acid Damage Vis-à-vis Genotoxicity in Brain of Fischer Rats. Toxicol Int. 2013 Jan;20(1):19–24.** BACKGROUND: Non-ionizing radiofrequency radiation has been increasingly used in industry, commerce, medicine and especially in mobile phone technology and has become a matter of serious concern in present time. OBJECTIVE: The present study was designed to investigate the possible deoxyribonucleic acid (DNA) damaging effects of low-level microwave radiation in brain of Fischer rats. MATERIALS AND METHODS: Experiments were performed on male Fischer rats exposed to microwave radiation for 30 days at three different frequencies: 900, 1800 and 2450 MHz. Animals were divided into 4 groups: Group I (Sham exposed): Animals not exposed to microwave radiation but kept under same conditions as that of other groups, Group II: Animals exposed to microwave radiation at frequency 900 MHz at specific absorption rate (SAR) 5.953 × 10(-4) W/kg, Group III: Animals exposed to 1800 MHz at SAR 5.835 × 10(-4) W/kg and Group IV: Animals exposed to 2450 MHz at SAR 6.672 × 10(-4) W/kg. At the end of the exposure period animals were sacrificed immediately and DNA damage in brain tissue was assessed using alkaline comet assay. RESULTS: <u>In the present study, we demonstrated DNA damaging effects of low level microwave radiation in brain.</u> CONCLUSION: We concluded that low SAR microwave radiation exposure at these frequencies may induce DNA strand breaks in brain tissue.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No No

Year	References and extracts	Reports	Cited?
2013	**Gao X, Luo R, Ma B, Wang H, Liu T, Zhang J, et al. [Interference of vitamin E on the brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats]. Wei Sheng Yan Jiu. 2013 Jul;42(4):642–6.** OBJECTIVE: To investigate the interlerence ot vitamin E on brain tissue damage by electromagnetic radiation of cell phone in pregnant and fetal rats. METHODS: 40 pregnant rats were randomly divided into five groups (positive control, negative control, low, middle and high dosage of vitamin E groups). The low, middle and high dosage of vitamin E groups were supplemented with 5, 15 and 30 mg/ml vitamin E respectively since the first day of pregnancy. And the negative control group and the positive control group were given peanut oil without vitamin E. All groups except for the negative control group were exposed to 900MHz intensity of cell phone radiation for one hour each time, three times per day for 21 days. After accouchement, the right hippocampus tissue of fetal rats in each group was taken and observed under electron microscope. The vitality of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and the content of malondialdehyde (MDA) in pregnant and fetal rats' brain tissue were tested. RESULTS: Compared with the negative control group, the chondriosomes in neuron and neuroglia of brain tissues was swelling, mild edema was found around the capillary, chromatin was concentrated and collected, and bubbles were formed in vascular endothelial cells (VEC) in the positive fetal rat control group, whereas the above phenomenon was un-conspicuous in the middle and high dosage of vitamin E groups. We can see uniform chromatin, abundant mitochondrion, rough endoplasmic reticulum and free ribosomes in the high dosage group. The apoptosis has not fond in all groups'sections. In the antioxidase activity analysis, compared with the negative control group, the vitality of SOD and GSH-Px significantly decreased and the content of MDA significantly increased both in the pregnant and fetal rats positive control group ($P < 0.05$). In fetal rats, the vitality of SOD and GSH-Px significantly increased in the brain tissues of all three different vitamin E dosages groups when compared with the positive control group, and the content of MDA was found significantly decreased in both middle and high dosage of vitamin E groups($P < 0.05$). The same results have also been found in high dosage pregnant rat group, but in middle dosage group only SOD activity was found increased with significance ($P < 0.05$). With the dosage increase of vitamin E, the vitality of SOD and GSH-Px was increasing and the content of MDA was decreasing. CONCLUSION: Under the experimental dosage, vitamin E has certain interference on damage of antioxidant capacity and energy metabolization induced by electromagnetic radiation of cell phone in pregnant rats and fetal rats.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2013	**Haghani M, Shabani M, Moazzami K. Maternal mobile phone exposure adversely affects the electrophysiological properties of Purkinje neurons in rat offspring. Neuroscience. 2013 Oct 10;250:588–98.** Electromagnetic field (EMF) radiations emitted from mobile phones may cause structural damage to neurons. With the increased usage of mobile phones worldwide, concerns about their possible effects on the nervous system are rising. In the present study, we aimed to elucidate the possible effects of prenatal EMF exposure on the cerebellum of offspring Wistar rats. Rats in the EMF group were exposed to 900-MHz pulse-EMF irradiation for 6h per day during all gestation period. Ten offspring per each group were evaluated for behavioral and electrophysiological evaluations. Cerebellum-related behavioral dysfunctions were analyzed using motor learning and cerebellum-dependent functional tasks (Accelerated Rotarod, Hanging and Open field tests). Whole-cell patch clamp recordings were used for electrophysiological evaluations. The results of the present study failed to show any behavioral abnormalities in rats exposed to chronic EMF radiation. However, whole-cell patch clamp recordings revealed decreased neuronal excitability of Purkinje cells in rats exposed to EMF. The most prominent changes included after hyperpolarization amplitude, spike frequency, half width and first spike latency. In conclusion, the results of the present study show that prenatal EMF exposure results in altered electrophysiological properties of Purkinje neurons. However, these changes may not be severe enough to alter the cerebellum-dependent functional tasks.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Hekmat A, Saboury AA, Moosavi-Movahedi AA. The toxic effects of mobile phone radiofrequency (940 MHz) on the structure of calf thymus DNA. Ecotoxicol Environ Saf. 2013 Feb;88:35–41.** Currently, the biological effects of nonionizing electromagnetic fields (EMFs) including radiofrequency (RF) radiation have been the subject of numerous experimental and theoretical studies. The aim of this study is to evaluate the possible biological effects of mobile phone RF (940 MHz, 15 V/m and SAR=40 mW/kg) on the structure of calf thymus DNA (ct DNA) immediately after exposure and 2 h after 45 min exposure via diverse range of spectroscopic instruments. The UV-vis and circular dichroism (CD) experiments depict that mobile phone EMFs can remarkably cause disturbance on ct DNA structure. In addition, the DNA samples, immediately after exposure and 2 h after 45 min exposure, are relatively thermally unstable compared to the DNA solution, which was placed in a small shielded box (unexposed ct DNA). Furthermore, the exposed DNA samples (the DNA samples that were exposed to 940 MHz EMF) have more fluorescence emission when compared with the unexposed DNA, which may have occurred attributable to expansion of the exposed DNA structure. The results of dynamic light scattering (DLS) and zeta potential experiments demonstrate that RF-EMFs lead to increment in the surface charge and size of DNA. The structure of DNA immediately after exposure is not significantly different from the DNA sample 2 h after 45 min exposure. In other words, the EMF-induced conformational changes are irreversible. Collectively, our results reveal that 940 MHz can alter the structure of DNA. The displacement of electrons in DNA by EMFs may lead to conformational changes of DNA and DNA disaggregation. Results from this study could have an important implication on the health effects of RF-EMFs exposure. In addition, this finding could proffer a novel strategy for the development of next generation of mobile phone.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	Yes No n/a No No

Year	References and extracts	Reports	Cited?
2013	**Kesari KK, Meena R, Nirala J, Kumar J, Verma HN. Effect of 3G Cell Phone Exposure with Computer Controlled 2-D Stepper Motor on Non-thermal Activation of the hsp27/p38MAPK Stress Pathway in Rat Brain. Cell Biochem Biophys. 2013 Aug 15;** Cell phone radiation exposure and its biological interaction is the present concern of debate. Present study aimed to investigate the effect of 3G cell phone exposure with computer controlled 2-D stepper motor on 45-day-old male Wistar rat brain. Animals were exposed for 2 h a day for 60 days by using mobile phone with angular movement up to zero to 30°. The variation of the motor is restricted to 90° with respect to the horizontal plane, moving at a pre-determined rate of 2° per minute. Immediately after 60 days of exposure, animals were scarified and numbers of parameters (DNA double-strand break, micronuclei, caspase 3, apoptosis, DNA fragmentation, expression of stress-responsive genes) were performed. Result shows that microwave radiation emitted from 3G mobile phone significantly induced DNA strand breaks in brain. Meanwhile a significant increase in micronuclei, caspase 3 and apoptosis were also observed in exposed group ($P < 0.05$). Western blotting result shows that 3G mobile phone exposure causes a transient increase in phosphorylation of hsp27, hsp70, and p38 mitogen-activated protein kinase (p38MAPK), which leads to mitochondrial dysfunction-mediated cytochrome c release and subsequent activation of caspases, involved in the process of radiation-induced apoptotic cell death. Study shows that the oxidative stress is the main factor which activates a variety of cellular signal transduction pathways, among them the hsp27/p38MAPK is the pathway of principle stress response. Results conclude that 3G mobile phone radiations affect the brain function and cause several neurological disorders.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Liu C, Gao P, Xu S-C, Wang Y, Chen C-H, He M-D, et al. Mobile phone radiation induces mode-dependent DNA damage in a mouse spermatocyte-derived cell line: A protective role of melatonin. Int J Radiat Biol. 2013 Sep 3;** Purpose: To evaluate whether exposure to mobile phone radiation (MPR) can induce DNA damage in male germ cells. Materials and methods: A mouse spermatocyte-derived GC-2 cell line was exposed to a commercial mobile phone handset once every 20 min in standby, listen, dialed or dialing modes for 24 h. DNA damage was determined using an alkaline comet assay. Results: The levels of DNA damage were significantly increased following exposure to MPR in the listen, dialed and dialing modes. Moreover, there were significantly higher increases in the dialed and dialing modes than in the listen mode. Interestingly, these results were consistent with the radiation intensities of these modes. However, the DNA damage effects of MPR in the dialing mode were efficiently attenuated by melatonin pretreatment. Conclusions: These results regarding mode-dependent DNA damage have important implications for the safety of inappropriate mobile phone use by males of reproductive age and also suggest a simple preventive measure: Keeping mobile phones as far away from our body as possible, not only during conversations but during 'dialed' and 'dialing' operation modes. Since the 'dialed' mode is actually part of the standby mode, mobile phones should be kept at a safe distance from our body even during standby operation. Furthermore, the protective role of melatonin suggests that it may be a promising pharmacological candidate for preventing mobile phone use-related reproductive impairments.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	Yes No n/a No No

Year	References and extracts	Reports	Cited?
2013	**Maaroufi K, Had-Aissouni L, Melon C, Sakly M, Abdelmelek H, Poucet B, et al. Spatial learning, monoamines and oxidative stress in rats exposed to 900MHz electromagnetic field in combination with iron overload. Behav Brain Res. 2013 Oct 18;258C:80–9.** The increasing use of mobile phone technology over the last decade raises concerns about the impact of high frequency electromagnetic fields (EMF) on health. More recently, a link between EMF, iron overload in the brain and neurodegenerative disorders including Parkinson's and Alzheimer's diseases has been suggested. Co-exposure to EMF and brain iron overload may have a greater impact on brain tissues and cognitive processes than each treatment by itself. To examine this hypothesis, Long-Evans rats submitted to 900MHz exposure or combined 900MHz EMF and iron overload treatments were tested in various spatial learning tasks (navigation task in the Morris water maze, working memory task in the radial-arm maze, and object exploration task involving spatial and non spatial processing). Biogenic monoamines and metabolites (dopamine, serotonin) and oxidative stress were measured. Rats exposed to EMF were impaired in the object exploration task but not in the navigation and working memory tasks. They also showed alterations of monoamine content in several brain areas but mainly in the hippocampus. Rats that received combined treatment did not show greater behavioral and neurochemical deficits than EMF-exposed rats. None of the two treatments produced global oxidative stress. These results show that there is an impact of EMF on the brain and cognitive processes but this impact is revealed only in a task exploiting spontaneous exploratory activity. In contrast, there are no synergistic effects between EMF and a high content of iron in the brain.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2013	**Muehsam D, Lalezari P, Lekhraj R, Abruzzo P, Bolotta A, Marini M, et al. Non-thermal radio frequency and static magnetic fields increase rate of hemoglobin deoxygenation in a cell-free preparation. PLoS ONE. 2013;8(4):e61752.** The growing body of clinical and experimental data regarding electromagnetic field (EMF) bioeffects and their therapeutic applications has contributed to a better understanding of the underlying mechanisms of action. This study reports that two EMF modalities currently in clinical use, a pulse-modulated radiofrequency (PRF) signal, and a static magnetic field (SMF), applied independently, increased the rate of deoxygenation of human hemoglobin (Hb) in a cell-free assay. Deoxygenation of Hb was initiated using the reducing agent dithiothreitol (DTT) in an assay that allowed the time for deoxygenation to be controlled (from several min to several hours) by adjusting the relative concentrations of DTT and Hb. The time course of Hb deoxygenation was observed using visible light spectroscopy. Exposure for 10-30 min to either PRF or SMF increased the rate of deoxygenation occurring several min to several hours after the end of EMF exposure. The sensitivity and biochemical simplicity of the assay developed here suggest a new research tool that may help to further the understanding of basic biophysical EMF transduction mechanisms. If the results of this study were to be shown to occur at the cellular and tissue level, EMF-enhanced oxygen availability would be one of the mechanisms by which clinically relevant EMF-mediated enhancement of growth and repair processes could occur.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)** n/a = not available at time of report publication	No No n/a No n/a

Year	References and extracts	Reports	Cited?
2012	**Bouji M, Lecomte A, Hode Y, de Seze R, Villégier A-S. Effects of 900 MHz radiofrequency on corticosterone, emotional memory and neuroinflammation in middle-aged rats. Exp Gerontol. 2012 Jun;47(6):444–51.** The widespread use of mobile phones raises the question of the effects of electromagnetic fields (EMF, 900 MHz) on the brain. Previous studies reported increased levels of the glial fibrillary acidic protein (GFAP) in the rat's brain after a single exposure to 900 MHz global system for mobile (GSM) signal, suggesting a potential inflammatory process. While this result was obtained in adult rats, no data is currently available in older animals. Since the transition from middle-age to senescence is highly dependent on environment and lifestyle, we studied the reactivity of middle-aged brains to EMF exposure. We assessed the effects of a single 15 min GSM exposure (900 MHz; specific absorption rate (SAR)=6 W/kg) on GFAP expression in young adults (6 week-old) and middle-aged rats (12 month-old). Brain interleukin (IL)-1β and IL-6, plasmatic levels of corticosterone (CORT), and emotional memory were also assessed. Our data indicated that, in contrast to previously published work, acute GSM exposure did not induce astrocyte activation. Our results showed an IL-1β increase in the olfactory bulb and enhanced contextual emotional memory in GSM-exposed middle-aged rats, and increased plasmatic levels of CORT in GSM-exposed young adults. Altogether, our data showed an age dependency of reactivity to GSM exposure in neuro-immunity, stress and behavioral parameters. Reproducing these effects and studying their mechanisms may allow a better understanding of mobile phone EMF effects on neurobiological parameters.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2012	**Calabrò E, Condello S, Currò M, Ferlazzo N, Caccamo D, Magazù S, et al. Modulation of heat shock protein response in SH-SY5Y by mobile phone microwaves. World J Biol Chem. 2012 Feb 26;3(2):34–40.** AIM: To investigate putative biological damage caused by GSM mobile phone frequencies by assessing electromagnetic fields during mobile phone working. METHODS: Neuron-like cells, obtained by retinoic-acid-induced differentiation of human neuroblastoma SH-SY5Y cells, were exposed for 2 h and 4 h to microwaves at 1800 MHz frequency bands. RESULTS: Cell stress response was evaluated by MTT assay as well as changes in the heat shock protein expression (Hsp20, Hsp27 and Hsp70) and caspase-3 activity levels, as biomarkers of apoptotic pathway. Under our experimental conditions, neither cell viability nor Hsp27 expression nor caspase-3 activity was significantly changed. Interestingly, a significant decrease in Hsp20 expression was observed at both times of exposure, whereas Hsp70 levels were significantly increased only after 4 h exposure. CONCLUSION: The modulation of the expression of Hsps in neuronal cells can be an early response to radiofrequency microwaves.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012 bioc hem	**Chen G, Lu D, Chiang H, Leszczynski D, Xu Z. Using model organism Saccharomyces cerevisiae to evaluate the effects of ELF-MF and RF-EMF exposure on global gene expression. Bioelectromagnetics. 2012 Oct;33(7):550–60.** The potential health hazard of exposure to electromagnetic fields (EMF) continues to cause public concern. However, the possibility of biological and health effects of exposure to EMF remains controversial and their biophysical mechanisms are unknown. In the present study, we used Saccharomyces cerevisiae to identify genes responding to extremely low frequency magnetic fields (ELF-MF) and to radiofrequency EMF (RF-EMF) exposures. The yeast cells were exposed for 6 h to either 0.4 mT 50 Hz ELF-MF or 1800 MHz RF-EMF at a specific absorption rate of 4.7 W/kg. Gene expression was analyzed by microarray screening and confirmed using real-time reverse transcription-polymerase chain reaction (RT-PCR). We were unable to confirm microarray-detected changes in three of the ELF-MF responsive candidate genes using RT-PCR ($P > 0.05$). On the other hand, out of the 40 potential RF-EMF responsive genes, only the expressions of structural maintenance of chromosomes 3 (SMC3) and aquaporin 2 (AQY2 (m)) were confirmed, while three other genes, that is, halotolerance protein 9 (HAL9), yet another kinase 1 (YAK1) and one function-unknown gene (open reading frame: YJL171C), showed opposite changes in expression compared to the microarray data ($P < 0.05$). In conclusion, the results of this study suggest that the yeast cells did not alter gene expression in response to 50 Hz ELF-MF and that the response to RF-EMF is limited to only a very small number of genes. The possible biological consequences of the gene expression changes induced by RF-EMF await further investigation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Dasdag S, Akdag MZ, Kizil G, Kizil M, Cakir DU, Yokus B. Effect of 900 MHz radio frequency radiation on beta amyloid protein, protein carbonyl, and malondialdehyde in the brain. Electromagn Biol Med. 2012 Mar;31(1):67–74.** Recently, many studies have been carried out in relation to 900 MHz radiofrequency radiation (RF) emitted from a mobile phone on the brain. However, there is little data concerning possible mechanisms between long-term exposure of RF radiation and biomolecules in brain. Therefore, we aimed to investigate long-term effects of 900 MHz radiofrequency radiation on beta amyloid protein, protein carbonyl, and malondialdehyde in the rat brain. The study was carried out on 17 Wistar Albino adult male rats. The rat heads in a carousel were exposed to 900 MHz radiofrequency radiation emitted from a generator, simulating mobile phones. For the study group (n: 10), rats were exposed to the radiation 2 h per day (7 days a week) for 10 months. For the sham group (n: 7), rats were placed into the carousel and the same procedure was applied except that the generator was turned off. In this study, rats were euthanized after 10 months of exposure and their brains were removed. Beta amyloid protein, protein carbonyl, and malondialdehyde levels were found to be higher in the brain of rats exposed to 900 MHz radiofrequency radiation. However, only the increase of protein carbonyl in the brain of rats exposed to 900 MHz radiofrequency radiation was found to be statistically significant ($p<0.001$). In conclusion, 900 MHz radiation emitted from mobile/cellular phones can be an agent to alter some biomolecules such as protein. However, further studies are necessary.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Fragopoulou AF, Samara A, Antonelou MH, Xanthopoulou A, Papadopoulou A, Vougas K, et al. Brain proteome response following whole body exposure of mice to mobile phone or wireless DECT base radiation. Electromagn Biol Med. 2012 Dec;31(4):250–74.** The objective of this study was to investigate the effects of two sources of electromagnetic fields (EMFs) on the proteome of cerebellum, hippocampus, and frontal lobe in Balb/c mice following long-term whole body irradiation. Three equally divided groups of animals (6 animals/group) were used; the first group was exposed to a typical mobile phone, at a SAR level range of 0.17-0.37 W/kg for 3 h daily for 8 months, the second group was exposed to a wireless DECT base (Digital Enhanced Cordless Telecommunications/Telephone) at a SAR level range of 0.012-0.028 W/kg for 8 h/day also for 8 months and the third group comprised the sham-exposed animals. Comparative proteomics analysis revealed that long-term irradiation from both EMF sources altered significantly ($p < 0.05$) the expression of 143 proteins in total (as low as 0.003 fold downregulation up to 114 fold overexpression). Several neural function related proteins (i.e., Glial Fibrillary Acidic Protein (GFAP), Alpha-synuclein, Glia Maturation Factor beta (GMF), and apolipoprotein E (apoE)), heat shock proteins, and cytoskeletal proteins (i.e., Neurofilaments and tropomodulin) are included in this list as well as proteins of the brain metabolism (i.e., Aspartate aminotransferase, Glutamate dehydrogenase) to nearly all brain regions studied. Western blot analysis on selected proteins confirmed the proteomics data. The observed protein expression changes may be related to brain plasticity alterations, indicative of oxidative stress in the nervous system or involved in apoptosis and might potentially explain human health hazards reported so far, such as headaches, sleep disturbance, fatigue, memory deficits, and brain tumor long-term induction under similar exposure conditions.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Güler G, Tomruk A, Ozgur E, Sahin D, Sepici A, Altan N, et al. The effect of radiofrequency radiation on DNA and lipid damage in female and male infant rabbits. Int J Radiat Biol. 2012 Apr;88(4):367–73.** PURPOSE: We aimed to design a prolonged radiofrequency (RF) radiation exposure and investigate in an animal model, possible bio-effects of RF radiation on the ongoing developmental stages of children from conception to childhood. MATERIALS AND METHODS: A total of 72 New Zealand female and male white rabbits aged one month were used. Females were exposed to RF radiation for 15 min/day during 7 days, whereas males were exposed to the same level of radiation for 15 min/day during 14 days. Thirty-six female and 36 male infant rabbits were randomly divided into four groups: Group I [Intrauterine (IU) exposure (-); Extrauterine (EU) exposure (-)]: Sham exposure which means rabbits were exposed to 1800 MHz Global System for Mobile Telecommunication (GSM)-like RF signals neither in the IU nor in the EU periods. Group II [IU exposure (-); EU exposure (+)]: Infant rabbits were exposed to 1800 MHz GSM-like RF signals when they reached one month of age. Group III [IU exposure (+); EU exposure (-)]: Infant rabbits were exposed to 1800 MHz GSM-like RF signals in the IU period (between 15th and 22nd days of the gestational period). Group IV [IU exposure (+); EU exposure (+)]: Infant rabbits were exposed to 1800 MHz GSM-like RF signals both in the IU period (between 15th and 22nd days of the gestational period) and in the EU period when they reached one month of age. Biochemical analysis for lipid peroxidation and DNA damage were carried out in the livers of all rabbits. RESULTS: Lipid peroxidation levels in the liver tissues of female and male infant rabbits increased under RF radiation exposure. Liver 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels of female rabbits exposed to RF radiation were also found to increase when compared with the levels of non-exposed infants. However, there were no changes in liver 8-OHdG levels of male rabbits under RF exposure. CONCLUSION: Consequently, it can be concluded that GSM-like RF radiation may induce biochemical changes by increasing free radical attacks to structural biomolecules in the rabbit as an experimental animal model.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Jing J, Yuhua Z, Xiao-qian Y, Rongping J, Dong-mei G, Xi C. The influence of microwave radiation from cellular phone on fetal rat brain. Electromagn Biol Med. 2012 Mar;31(1):57–66.** The increasing use of cellular phones in our society has brought focus on the potential detrimental effects to human health by microwave radiation. The aim of our study was to evaluate the intensity of oxidative stress and the level of neurotransmitters in the brains of fetal rats chronically exposed to cellular phones. The experiment was performed on pregnant rats exposed to different intensities of microwave radiation from cellular phones. Thirty-two pregnant rats were randomly divided into four groups: CG, GL, GM, and GH. CG accepted no microwave radiation, GL group radiated 10 min each time, GM group radiated 30 min, and GH group radiated 60 min. The 3 experimental groups were radiated 3 times a day from the first pregnant day for consecutively 20 days, and on the 21st day, the fetal rats were taken and then the contents of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), malondialdehyde (MDA), noradrenaline (NE), dopamine (DA), and 5-hydroxyindole acetic acid (5-HT) in the brain were assayed. Compared with CG, there were significant differences ($P<0.05$) found in the contents of SOD, GSH-Px, and MDA in GM and GH; the contents of SOD and GSH-Px decreased and the content of MDA increased. The significant content differences of NE and DA were found in fetal rat brains in GL and GH groups, with the GL group increased and the GH group decreased. Through this study, we concluded that receiving a certain period of microwave radiation from cellular phones during pregnancy has certain harm on fetal rat brains.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Khalil AM, Gagaa MH, Alshamali AM. 8-Oxo-7, 8-dihydro-2'-deoxyguanosine as a biomarker of DNA damage by mobile phone radiation. Hum Exp Toxicol. 2012 Jul;31(7):734–40.** We examined the effect of exposure to mobile phone 1800 MHz radio frequency radiation (RFR) upon the urinary excretion of 8-oxo-7, 8-dihydro-2'-deoxyguanosine (8-oxodG), one major form of oxidative DNA damage, in adult male Sprague-Dawley rats. Twenty-four rats were used in three independent experiments (RFR exposed and control, 12 rats, each). The animals were exposed to RFR for 2 h from Global System for Mobile Communications (GSM) signal generator with whole-body-specific absorption rate of 1.0 W/kg. Urine samples were collected from the rat while housed in a metabolic cage during the exposure period over a 4-h period at 0.5, 1.0, 2.0 and 4.0 h from the beginning of exposure. In the control group, the signal generator was left in the turn-off position. The creatinine-standardized concentrations of 8-oxodG were measured. With the exception of the urine collected in the last half an hour of exposure, significant elevations were noticed in the levels of 8-oxodG in urine samples from rats exposed to RFR when compared to control animals. Significant differences were seen overall across time points of urine collection with a maximum at 1 h after exposure, suggesting repair of the DNA lesions leading to 8-oxodG formation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2012	**Lu Y, Xu S, He M, Chen C, Zhang L, Liu C, et al. Glucose administration attenuates spatial memory deficits induced by chronic low-power-density microwave exposure. Physiol Behav. 2012 Jul 16;106(5):631–7.** Extensive evidence indicates that glucose administration attenuates memory deficits in rodents and humans, and cognitive impairment has been associated with reduced glucose metabolism and uptake in certain brain regions including the hippocampus. In the present study, we investigated whether glucose treatment attenuated memory deficits caused by chronic low-power-density microwave (MW) exposure, and the effect of MW exposure on hippocampal glucose uptake. We exposed Wistar rats to 2.45 GHz pulsed MW irradiation at a power density of 1 mW/cm(2) for 3 h/day, for up to 30 days. MW exposure induced spatial learning and memory impairments in rats. Hippocampal glucose uptake was also reduced by MW exposure in the absence or presence of insulin, but the levels of blood glucose and insulin were not affected. However, these spatial memory deficits were reversed by systemic glucose treatment. Our results indicate that glucose administration attenuates the spatial memory deficits induced by chronic low-power-density MW exposure, and reduced hippocampal glucose uptake may be associated with cognitive impairment caused by MW exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2012	**Maskey D, Kim H-J, Kim HG, Kim MJ. Calcium-binding proteins and GFAP immunoreactivity alterations in murine hippocampus after 1 month of exposure to 835 MHz radiofrequency at SAR values of 1.6 and 4.0 W/kg. Neurosci Lett. 2012 Jan 11;506(2):292–6.** Widespread use of wireless mobile communication has raised concerns of adverse effect to the brain owing to the proximity during use due to the electromagnetic field emitted by mobile phones. Changes in calcium ion concentrations via binding proteins can disturb calcium homeostasis; however, the correlation between calcium-binding protein (CaBP) immunoreactivity (IR) and glial cells has not been determined with different SAR values. Different SAR values [1.6 (E1.6 group) and 4.0 (E4 group) W/kg] were applied to determine the distribution of calbindin D28-k (CB), calretinin (CR), and glial fibrillary acidic protein (GFAP) IR in murine hippocampus. Compared with sham control group, decreased CB and CR IRs, loss of CB and CR immunoreactive cells and increased GFAP IR exhibiting hypertrophic cytoplasmic processes were noted in both experimental groups. E4 group showed a prominent decrement in CB and CR IR than the E1.6 group due to down-regulation of CaBP proteins and neuronal loss. GFAP IR was more prominent in the E4 group than the E1.6 group. Decrement in the CaBPs can affect the calcium-buffering capacity leading to cell death, while increased GFAP IR and changes in astrocyte morphology, may mediate brain injury due to radiofrequency exposure. [1.6 and 4.0 W/kg]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2012	**Megha K, Deshmukh PS, Banerjee BD, Tripathi AK, Abegaonkar MP. Microwave radiation induced oxidative stress, cognitive impairment and inflammation in brain of Fischer rats. Indian J Exp Biol. 2012 Dec;50(12):889–96.** Public concerns over possible adverse effects of microwave radiation emitted by mobile phones on health are increasing. To evaluate the intensity of oxidative stress, cognitive impairment and inflammation in brain of Fischer rats exposed to microwave radiation, male Fischer-344 rats were exposed to 900 MHz microwave radiation (SAR = 5.953 x 10(-4) W/kg) and 1800 MHz microwave radiation (SAR = 5.835 x 10(-4) W/kg) for 30 days (2 h/day). Significant impairment in cognitive function and induction of oxidative stress in brain tissues of microwave exposed rats were observed in comparison with sham exposed groups. Further, significant increase in level of cytokines (IL-6 and TNF-alpha) was also observed following microwave exposure. Results of the present study indicated that increased oxidative stress due to microwave exposure may contribute to cognitive impairment and inflammation in brain.	Reference provided to **Royal Society of Canada (in 2013)** Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2012	**Misa Agustiño MJ, Leiro JM, Jorge Mora MT, Rodríguez-González JA, Jorge Barreiro FJ, Ares-Pena FJ, et al. Electromagnetic fields at 2.45 GHz trigger changes in heat shock proteins 90 and 70 without altering apoptotic activity in rat thyroid gland. Biol Open. 2012 Sep 15;1(9):831–8.** Non-ionizing radiation at 2.45 GHz may modify the expression of genes that codify heat shock proteins (HSP) in the thyroid gland. Using the enzyme-linked immunosorbent assay (ELISA) technique, we studied levels of HSP-90 and HSP-70. We also used hematoxilin eosin to look for evidence of lesions in the gland and applied the DAPI technique of fluorescence to search for evidence of chromatin condensation and nuclear fragmentation in the thyroid cells of adult female Sprague-Dawley rats. Fifty-four rats were individually exposed for 30 min to 2.45 GHz radiation in a Gigahertz transverse electromagnetic (GTEM) cell at different levels of non-thermal specific absorption rate (SAR), which was calculated using the finite difference time domain (FDTD) technique. Ninety minutes after radiation, HSP-90 and HSP-70 had decreased significantly (P<0.01) after applying a SAR of 0.046±1.10 W/Kg or 0.104±5.10(-3) W/Kg. Twenty-four hours after radiation, HSP-90 had partially recovered and HSP-70 had recovered completely. There were few indications of lesions in the glandular structure and signs of apoptosis were negative in all radiated animals. The results suggest that acute sub-thermal radiation at 2.45 GHz may alter levels of cellular stress in rat thyroid gland without initially altering their anti-apoptotic capacity.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Nazıroğlu M, Çelik Ö, Özgül C, Çiğ B, Doğan S, Bal R, et al. Melatonin modulates wireless (2.45 GHz)-induced oxidative injury through TRPM2 and voltage gated Ca(2+) channels in brain and dorsal root ganglion in rat. Physiol Behav. 2012 Feb 1;105(3):683–92.** We aimed to investigate the protective effects of melatonin and 2.45 GHz electromagnetic radiation (EMR) on brain and dorsal root ganglion (DRG) neuron antioxidant redox system, Ca(2+) influx, cell viability and electroencephalography (EEG) records in the rat. Thirty two rats were equally divided into four different groups namely group A1: Cage control, group A2: Sham control, group B: 2.45 GHz EMR, group C: 2.45 GHz EMR+melatonin. Groups B and C were exposed to 2.45 GHz EMR during 60 min/day for 30 days. End of the experiments, EEG records and the brain cortex and DRG samples were taken. Lipid peroxidation (LP), cell viability and cytosolic Ca(2+) values in DRG neurons were higher in group B than in groups A1 and A2 although their concentrations were increased by melatonin, 2-aminoethyldiphenyl borinate (2-APB), diltiazem and verapamil supplementation. Spike numbers of EEG records in group C were lower than in group B. Brain cortex vitamin E concentration was higher in group C than in group B. In conclusion, Melatonin supplementation in DRG neurons and brain seems to have protective effects on the 2.45 GHz-induced increase Ca(2+) influx, EEG records and cell viability of the hormone through TRPM2 and voltage gated Ca(2+) channels.	Reference provided to **Royal Society of Canada (in 2013)**	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2012	**Trivino Pardo JC, Grimaldi S, Taranta M, Naldi I, Cinti C. Microwave electromagnetic field regulates gene expression in T-lymphoblastoid leukemia CCRF-CEM cell line exposed to 900 MHz. Electromagn Biol Med. 2012 Mar;31(1):1–18.** Electric, magnetic, and electromagnetic fields are ubiquitous in our society, and concerns have been expressed regarding possible adverse effects of these exposures. Research on Extremely Low-Frequency (ELF) magnetic fields has been performed for more than two decades, and the methodology and quality of studies have improved over time. Studies have consistently shown increased risk for childhood leukemia associated with ELF magnetic fields. There are still inadequate data for other outcomes. More recently, focus has shifted toward Radio Frequencies (RF) exposures from mobile telephony. There are no persuasive data suggesting a health risk, but this research field is still immature with regard to the quantity and quality of available data. This technology is constantly changing and there is a need for continued research on this issue. To investigate whether exposure to high-frequency electromagnetic fields (EMF) could induce adverse health effects, we cultured acute T-lymphoblastoid leukemia cells (CCRF-CEM) in the presence of 900 MHz MW-EMF generated by a transverse electromagnetic (TEM) cell at short and long exposure times. We evaluated the effect of high-frequency EMF on gene expression and we identified functional pathways influenced by 900 MHz MW-EMF exposure.	Reference provided to **Royal Society of Canada (in 2013**)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013**)	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No
2012	**Trošić I, Pavičić I, Marjanović AM, Bušljeta I. Non-thermal biomarkers of exposure to radiofrequency/microwave radiation. Arh Hig Rada Toksikol. 2012;63 Suppl 1:67–73.** This article gives a review or several hypotheses on the biological effects of non-thermal radiofrequency/microwave (RF/MW) radiation and discusses our own findings from animal and in vitro studies performed over the last decade. We have found that RF/MW radiation disturbs cell proliferation and leads to cell differentiation in the bone marrow, which is reflected in the peripheral blood of rats. Repeated RF/MW radiation can also temporarily disrupt melatonin turnover. The observed changes seem to be a sign of adaptation to stress caused by irradiation rather than of malfunction. The article looks further into the basic mechanisms of RF/MW biological action, including cell growth parameters, colony-forming ability, viability, and the polar and apolar protein cytoskeleton structures. The observed reversible cell changes significantly obstructed cell growth. In contrast to the apolar intermediate proteins, the intracellular polar microtubule and actin fibres were damaged by radiation in a time-dependent manner. These significantly altered parameters can be considered as the biomarkers of exposure. Future research should combine dosimetry, experimental studies, and epidemiological data.	Reference provided to **Royal Society of Canada (in 2013)**	Yes
		Health Canada Draft **Safety Code 6 (2014**)	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2011	**Blank M, Goodman R. DNA is a fractal antenna in electromagnetic fields. Int J Radiat Biol. 2011 Apr;87(4):409–15.** PURPOSE: To review the responses of deoxyribonucleic acid (DNA) to electromagnetic fields (EMF) in different frequency ranges, and characterise the properties of DNA as an antenna. MATERIALS AND METHODS: We examined published reports of increased stress protein levels and DNA strand breaks due to EMF interactions, both of which are indicative of DNA damage. We also considered antenna properties such as electronic conduction within DNA and its compact structure in the nucleus. RESULTS: EMF interactions with DNA are similar over a range of non-ionising frequencies, i.e., extremely low frequency (ELF) and radio frequency (RF) ranges. There are similar effects in the ionising range, but the reactions are more complex. CONCLUSIONS: The wide frequency range of interaction with EMF is the functional characteristic of a fractal antenna, and DNA appears to possess the two structural characteristics of fractal antennas, electronic conduction and self symmetry. These properties contribute to greater reactivity of DNA with EMF in the environment, and the DNA damage could account for increases in cancer epidemiology, as well as variations in the rate of chemical evolution in early geologic history.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Chen YB, Li J, Liu JY, Zeng LH, Wan Y, Li YR, et al. Effect of Electromagnetic Pulses (EMP) on associative learning in mice and a preliminary study of mechanism. Int J Radiat Biol. 2011 Dec;87(12):1147–54.** PURPOSE: To investigate the effects of electromagnetic pulses (EMP) on associative learning in mice and test a preliminary mechanism for these effects. MATERIALS AND METHODS: A tapered parallel plate gigahertz transverse electromagnetic (GTEM) cell with a flared rectangular coaxial transmission line was used to expose male BALB/c mice to EMP (peak-intensity 400 kV/m, rise-time 10 ns, pulse-width 350 ns, 0.5 Hz and total 200 pulses). Concurrent sham-exposed mice were used as a control. Associative learning, oxidative stress in the brain, serum chemistry and the protective action of tocopherol monoglucoside (TMG) in mice were measured, respectively. RESULTS: (1) Twelve hour and 1 day post EMP exposure associative learning was reduced significantly compared with sham control ($p<0.05$) but recovered at 2 d post EMP exposure. (2) Compared with the sham control, lipid peroxidation of brain tissue and chemiluminescence (CL) intensity increased significantly ($p<0.05$), while the activity of the antioxidant enzymes Superoxide Dismutase [SOD], Glutathione [GSH], Glutathione Peroxidase [GSH-Px], Catalase [CAT]) decreased significantly ($p<0.05$) at 3 h, 6 h, 12 h and 1 d post EMP exposure. All these parameters recovered at 2 d post EMP exposure. (3) No significant differences between the sham control group and EMP exposed group were observed in serum cholesterol and triglycerides. (4) Pretreatment of mice with TMG showed protective effects to EMP exposure. CONCLUSIONS: EMP exposure significantly decreased associative learning in mice and TMG acted as an effective protective agent from EMP exposure. This mechanism could involve an increase of oxidative stress in brain by EMP exposure.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2011	**Esmekaya MA, Ozer C, Seyhan N. 900 MHz pulse-modulated radiofrequency radiation induces oxidative stress on heart, lung, testis and liver tissues. Gen Physiol Biophys. 2011 Mar;30(1):84–9.** Oxidative stress may affect many cellular and physiological processes including gene expression, cell growth, and cell death. In the recent study, we aimed to investigate whether 900 MHz pulse-modulated radiofrequency (RF) fields induce oxidative damage on lung, heart and liver tissues. We assessed oxidative damage by investigating lipid peroxidation (malondialdehyde, MDA), nitric oxide (NOx) and glutathione (GSH) levels which are the indicators of tissue toxicity. A total of 30 male Wistar albino rats were used in this study. Rats were divided randomly into three groups; control group (n = 10), sham group (device off, n = 10) and 900 MHz pulsed-modulated RF radiation group (n = 10). The RF rats were exposed to 900 MHz pulsed modulated RF radiation at a specific absorption rate (SAR) level of 1.20 W/kg 20 min/day for three weeks. MDA and NOx levels were increased significantly in liver, lung, testis and heart tissues of the exposed group compared to sham and control groups ($p < 0.05$). Conversely GSH levels were significantly lower in exposed rat tissues ($p < 0.05$). No significantly difference was observed between sham and control groups. Results of our study showed that pulse-modulated RF radiation causes oxidative injury in liver, lung, testis and heart tissues mediated by lipid peroxidation, increased level of NOx and suppression of antioxidant defense mechanism.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Esmekaya MA, Aytekin E, Ozgur E, Güler G, Ergun MA, Omeroğlu S, et al. Mutagenic and morphologic impacts of 1.8GHz radiofrequency radiation on human peripheral blood lymphocytes (hPBLs) and possible protective role of pre-treatment with Ginkgo biloba (EGb 761). Sci Total Environ. 2011 Dec 1;410-411:59–64.** The mutagenic and morphologic effects of 1.8GHz Global System for Mobile Communications (GSM) modulated RF (radiofrequency) radiation alone and in combination with Ginkgo biloba (EGb 761) pre-treatment in human peripheral blood lymphocytes (hPBLs) were investigated in this study using Sister Chromatid Exchange (SCE) and electron microscopy. Cell viability was assessed with 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) reduction assay. The lymphocyte cultures were exposed to GSM modulated RF radiation at 1.8GHz for 6, 8, 24 and 48h with and without EGb 761. We observed morphological changes in pulse-modulated RF radiated lymphocytes. Longer exposure periods led to destruction of organelle and nucleus structures. Chromatin change and the loss of mitochondrial crista occurred in cells exposed to RF for 8h and 24h and were more pronounced in cells exposed for 48h. Cytoplasmic lysis and destruction of membrane integrity of cells and nuclei were also seen in 48h RF exposed cells. There was a significant increase ($p<0.05$) in SCE frequency in RF exposed lymphocytes compared to sham controls. EGb 761 pre-treatment significantly decreased SCE from RF radiation. RF radiation also inhibited cell viability in a time dependent manner. The inhibitory effects of RF radiation on the growth of lymphoctes were marked in longer exposure periods. EGb 761 pre-treatment significantly increased cell viability in RF+EGb 761 treated groups at 8 and 24h when compared to RF exposed groups alone. <u>The results of our study showed that RF radiation affects cell morphology, increases SCE and inhibits cell proliferation. However, EGb 761 has a protective role against RF induced mutagenity. We concluded that RF radiation induces chromosomal damage in hPBLs</u> but this damage may be reduced by EGb 761 pre-treatment.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Garaj-Vrhovac V, Gajski G, Pažanin S, Sarolić A, Domijan A-M, Flajs D, et al. Assessment of cytogenetic damage and oxidative stress in personnel occupationally exposed to the pulsed microwave radiation of marine radar equipment. Int J Hyg Environ Health. 2011 Jan;214(1):59–65.** Due to increased usage of microwave radiation, there are concerns of its adverse effect in today's society. Keeping this in view, study was aimed at workers occupationally exposed to pulsed microwave radiation, originating from marine radars. Electromagnetic field strength was measured at assigned marine radar frequencies (3 GHz, 5.5 GHz and 9.4 GHz) and corresponding specific absorption rate values were determined. Parameters of the comet assay and micronucleus test were studied both in the exposed workers and in corresponding unexposed subjects. Differences between mean tail intensity (0.67 vs. 1.22) and moment (0.08 vs. 0.16) as comet assay parameters and micronucleus test parameters (micronuclei, nucleoplasmic bridges and nuclear buds) were statistically significant between the two examined groups, suggesting that cytogenetic alterations occurred after microwave exposure. Concentrations of glutathione and malondialdehyde were measured spectrophotometrically and using high performance liquid chromatography. The glutathione concentration in exposed group was significantly lower than in controls (1.24 vs. 0.53) whereas the concentration of malondialdehyde was significantly higher (1.74 vs. 3.17), indicating oxidative stress. Results suggests that pulsed microwaves from working environment can be the cause of genetic and cell alterations and that oxidative stress can be one of the possible mechanisms of DNA and cell damage.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Jorge-Mora T, Misa-Agustiño MJ, Rodríguez-González JA, Jorge-Barreiro FJ, Ares-Pena FJ, López-Martín E. The effects of single and repeated exposure to 2.45 GHz radiofrequency fields on c-Fos protein expression in the paraventricular nucleus of rat hypothalamus. Neurochem Res. 2011 Dec;36(12):2322–32.** This study investigated the effects of microwave radiation on the PVN of the hypothalamus, extracted from rat brains. Expression of c-Fos was used to study the pattern of cellular activation in rats exposed once or repeatedly (ten times in 2 weeks) to 2.45 GHz radiation in a GTEM cell. The power intensities used were 3 and 12 W and the Finite Difference Time Domain calculation was used to determine the specific absorption rate (SAR). High SAR triggered an increase of the c-Fos marker 90 min or 24 h after radiation, and low SAR resulted in c-Fos counts higher than in control rats after 24 h. Repeated irradiation at 3 W increased cellular activation of PVN by more than 100% compared to animals subjected to acute irradiation and to repeated non-radiated repeated session control animals. *** <u>The results suggest that PVN is sensitive to 2.45 GHz microwave radiation at non-thermal SAR levels</u>. *** [*** emphasis added ***]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Liu M-L, Wen J-Q, Fan Y-B. Potential protection of green tea polyphenols against 1800 MHz electromagnetic radiation-induced injury on rat cortical neurons. Neurotox Res. 2011 Oct;20(3):270–6.** Radiofrequency electromagnetic fields (EMF) are harmful to public health, but the certain anti-irradiation mechanism is not clear yet. The present study was performed to investigate the possible protective effects of green tea polyphenols against electromagnetic radiation-induced injury in the cultured rat cortical neurons. In this study, green tea polyphenols were used in the cultured cortical neurons exposed to 1800 MHz EMFs by the mobile phone. We found that the mobile phone irradiation for 24 h induced marked neuronal cell death in the MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl-tetrazolium bromide) and TUNEL (TdT mediated biotin-dUTP nicked-end labeling) assay, and protective effects of green tea polyphenols on the injured cortical neurons were demonstrated by testing the content of Bcl-2 Assaciated X protein (Bax) in the immunoprecipitation assay and Western blot assay. In our study results, the mobile phone irradiation-induced increases in the content of active Bax were inhibited significantly by green tea polyphenols, while the contents of total Bax had no marked changes after the treatment of green tea polyphenols. Our results suggested a neuroprotective effect of green tea polyphenols against the mobile phone irradiation-induced injury on the cultured rat cortical neurons.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2011	**Nittby H, Brun A, Strömblad S, Moghadam MK, Sun W, Malmgren L, et al. Nonthermal GSM RF and ELF EMF effects upon rat BBB permeability. Environmentalist [Internet]. 2011 Jun 1;31(2):140–8. Available from: http://link.springer.com/article/10.1007/s10669-011-9307-z** Since the late 1980s, our group has examined the effects of radiofrequency electromagnetic fields (RF-EMF), including pulse-modulated waves of the type emitted by mobile phones, upon the blood–brain barrier. In more than 2,000 rats, we have repeatedly demonstrated a passage of the rats' own albumin from the blood through the brain capillaries into the surrounding brain parenchyma at SAR values down to 0.1mW/kg. In most of these experiments, the animals were exposed in TEM-cells, ventilated by an external electrical fan at 50 Hz. In the present study, we examined whether the extremely low frequency (ELF) magnetic fields from the fan (50 Hz, 0.3–1.5 μT) might add to the RF effect. Sixty-four rats were divided into 4 groups: RF only, ELF only and RF + ELF exposure plus a sham group. The GSM-900 MHz RF exposure was at the very low, nonthermal, average whole-body SAR level 0.4 mW/kg. Demonstration of the normally occurring albumin extravasation in the basal hypothalamus is our inbuilt control proving that the staining is reliable. Two full series of staining of the whole material gave negative results for hypothalamus. Not until we changed to avidin, biotin, and antibodies from a third supplier, we received an acceptable staining. Twenty-five percent of the RF animals had a pathological albumin leakage, while the ELF and RF + ELF groups with three and two pathological findings, respectively, were not significantly different from the control group. We conclude that the use of external fans has had no major influence upon the result.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2011	**Noor NA, Mohammed HS, Ahmed NA, Radwan NM. Variations in amino acid neurotransmitters in some brain areas of adult and young male albino rats due to exposure to mobile phone radiation. Eur Rev Med Pharmacol Sci. 2011 Jul;15(7):729–42.** BACKGROUND AND OBJECTIVES: Mobile phone radiation and health concerns have been raised, especially following the enormous increase in the use of wireless mobile telephony throughout the world. The present study aims to investigate the effect of one hour daily exposure to electromagnetic radiation (EMR) with frequency of 900 Mz (SAR 1.165 w/kg, power density 0.02 mW/cm2) on the levels of amino acid neurotransmitters in the midbrain, cerebellum and medulla of adult and young male albino rats. MATERIALS AND METHODS: Adult and young rats were divided into two main groups (treated and control). The treated group of both adult and young rats was exposed to EMR for 1 hour daily. The other group of both adult and young animals was served as control. The determination of amino acid levels was carried out after 1 hour, 1 month, 2 months and 4 months of EMR exposure as well as after stopping radiation. RESULTS: Data of the present study showed a significant increase in both excitatory and inhibitory amino acids in the cerebellum of adult and young rats and midbrain of adult animals after 1 hour of EMR exposure. In the midbrain of adult animals, there was a significant increase in glycine level after 1 month followed by significant increase in GABA after 4 months. Young rats showed significant decreases in the midbrain excitatory amino acids. In the medulla, the equilibrium ratio percent (ER%) calculations showed a state of neurochemical inhibition after 4 months in case of adult animals, whereas in young animals, the neurochemical inhibitory state was observed after 1 month of exposure due to significant decrease in glutamate and aspartate levels. This state was converted to excitation after 4 months due to the increase in glutamate level. CONCLUSION: The present changes in amino acid concentrations may underlie the reported adverse effects of using mobile phones.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2011	**Trosić I, Pavicić I, Milković-Kraus S, Mladinić M, Zeljezić D. Effect of electromagnetic radiofrequency radiation on the rats' brain, liver and kidney cells measured by comet assay. Coll Antropol. 2011 Dec;35(4):1259–64.** The goal of study was to evaluate DNA damage in rat's renal, liver and brain cells after in vivo exposure to radiofrequency/microwave (Rf/Mw) radiation of cellular phone frequencies range. To determine DNA damage, a single cell gel electrophoresis/comet assay was used. Wistar rats (male, 12 week old, approximate body weight 350 g) (N = 9) were exposed to the carrier frequency of 915 MHz with Global System Mobile signal modulation (GSM), power density of 2.4 W/m2, whole body average specific absorption rate SAR of 0.6 W/kg. The animals were irradiated for one hour/day, seven days/week during two weeks period. The exposure set-up was Gigahertz Transversal Electromagnetic Mode Cell (GTEM--cell). Sham irradiated controls (N = 9) were apart of the study. The body temperature was measured before and after exposure. There were no differences in temperature in between control and treated animals. Comet assay parameters such as the tail length and tail intensity were evaluated. In comparison with tail length in controls (13.5 +/- 0.7 microm), the tail was slightly elongated in brain cells of irradiated animals (14.0 +/- 0.3 microm). The tail length obtained for liver (14.5 +/- 0.3 microm) and kidney (13.9 +/- 0.5 microm) homogenates notably differs in comparison with matched sham controls (13.6 +/- 0.3 microm) and (12.9 +/- 0.9 microm). Differences in tail intensity between control and exposed animals were not significant. The results of this study suggest that, under the experimental conditions applied, repeated 915 MHz irradiation could be a cause of DNA breaks in renal and liver cells, but not affect the cell genome at the higher extent compared to the basal damage.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Achudume A. Induction of Oxidative Stress in Male Rats Subchronically Exposed to Electromagnetic Fields at Non-Thermal Intensities. Journal of Electromagnetic Analysis and Applications [Internet]. 2010;03(08):482–7. Available from: http://www.scirp.org/journal/PaperInformation.aspx?paperID=2593** To investigate the oxidative stress-inducing potential of non-thermal electromagnetic fields in rats. Male Wister rats were exposed to electrical field intensity of 2.3 ± 0.82 µV/m . Exposure was in three forms: continuous waves, or modulated at 900 MHz or modulated GSM-nonDTX. The radio frequency radiation (RFR) was 1800 MHz, specific absorption radiation (SAR) (0.95-3.9 W/kg) for 40 and/or 60 days continuously. Control animals were located > 300 m from base station, while sham control animals were located in a similar environmental conditions, but in the vicinity of a non-functional base station. The rats were assessed for thiobarbituric and reactive species (TBARS), reduced glutathione (GSH) content, catalase activity, glutathione reductase (GR) and glucose residue after 40 and 60 days of exposure. At 40 days, electromagnetic radiation failed to induce any significant alterations. However, at 60 days of exposure various attributes evaluated decreased. The respective decreases in both nicotinamide adenine dinucleotide phosphate (NADPH) and Ascorbate- linked lipid peroxidation (LPO) with concomitant diminution in enzymatic antioxidative defense systems resulted in decreased glucose residue. The present studies showed some biochemical changes that may be associated with a prolong exposure to electromagnetic fields and its relationship to the activity of antioxidant system in rat. Regular assessment and early detection of antioxidative defense system among people working around the base stations are recommended.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Ammari M, Gamez C, Lecomte A, Sakly M, Abdelmelek H, De Seze R. GFAP expression in the rat brain following sub-chronic exposure to a 900 MHz electromagnetic field signal. Int J Radiat Biol. 2010 May;86(5):367–75.** PURPOSE: The rapid development and expansion of mobile communications contributes to the general debate on the effects of electromagnetic fields emitted by mobile phones on the nervous system. This study aims at measuring the glial fibrillary acidic protein (GFAP) expression in 48 rat brains to evaluate reactive astrocytosis, three and 10 days after long-term head-only sub-chronic exposure to a 900 MHz electromagnetic field (EMF) signal, in male rats. METHODS: Sprague-Dawley rats were exposed for 45 min/day at a brain-averaged specific absorption rate (SAR) = 1.5 W/kg or 15 min/day at a SAR = 6 W/kg for five days per week during an eight-week period. GFAP expression was measured by the immunocytochemistry method in the following rat brain areas: Prefrontal cortex, cerebellar cortex, dentate gyrus of the hippocampus, lateral globus pallidus of the striatum, and the caudate putamen. RESULTS: Compared to the sham-treated rats, those exposed to the sub-chronic GSM (Global System for mobile communications) signal at 1.5 or 6 W/kg showed an increase in GFAP levels in the different brain areas, three and ten days after treatment. CONCLUSION: Our results show that sub-chronic exposures to a 900 MHz EMF signal for two months could adversely affect rat brain (sign of a potential gliosis).	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Augner C, Hacker GW, Oberfeld G, Florian M, Hitzl W, Hutter J, et al. Effects of Exposure to GSM Mobile Phone Base Station Signals on Salivary Cortisol, Alpha-Amylase, and Immunoglobulin A. Biomedical and Environmental Sciences. 2010 Jun;23(3):199–207.** Objective The present study aimed to test whether exposure to radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phone base stations may have effects on salivary alpha-amylase, immunoglobulin A (IgA), and cortisol levels. Methods Fifty seven participants were randomly allocated to one of three different experimental scenarios (22 participants to scenario 1, 26 to scenario 2, and 9 to scenario 3). Each participant went through five 50-minute exposure sessions. The main RF-EMF source was a GSM-900-MHz antenna located at the outer wall of the building. In scenarios 1 and 2, the first, third, and fifth sessions were “low” (median power flux density 5.2 μW/m2) exposure. The second session was “high” (2126.8 μW/m2), and the fourth session was “medium” (153.6 μW/m2) in scenario 1, and vice versa in scenario 2. Scenario 3 had four “low” exposure conditions, followed by a “high” exposure condition. Biomedical parameters were collected by saliva samples three times a session. Exposure levels were created by shielding curtains. Results In scenario 3 from session 4 to session 5 (from “low” to “high” exposure), an increase of cortisol was detected, while in scenarios 1 and 2, a higher concentration of alpha-amylase related to the baseline was identified as compared to that in scenario 3. IgA concentration was not significantly related to the exposure. Conclusions RF-EMF in considerably lower field densities than ICNIRP-guidelines may influence certain psychobiological stress markers.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada **Safety Code 6 (2014) Draft** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Céspedes O, Inomoto O, Kai S, Nibu Y, Yamaguchi T, Sakamoto N, et al. Radio frequency magnetic field effects on molecular dynamics and iron uptake in cage proteins. Bioelectromagnetics. 2010 May;31(4):311–7.** The protein ferritin has a natural ferrihydrite nanoparticle that is superparamagnetic at room temperature. For native horse spleen ferritin, we measure the low field magnetic susceptibility of the nanoparticle as 2.2 x 10(-6) m(3) kg(-1) and its Néel relaxation time at about 10(-10) s. Superparamagnetic nanoparticles increase their internal energy when exposed to radio frequency magnetic fields due to the lag between magnetization and applied field. The energy is dissipated to the surrounding peptidic cage, altering the molecular dynamics and functioning of the protein. This leads to an increased population of low energy vibrational states under a magnetic field of 30 microT at 1 MHz, as measured via Raman spectroscopy. After 2 h of exposure, the proteins have a reduced iron intake rate of about 20%. *** Our results open a new path for the study of non-thermal bioeffects of radio frequency magnetic fields at the molecular scale. *** [*** emphasis added ***]	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2010	**Gapeev AB, Sirota NP, Kudriavtsev AA, Chemeris NK. [Responses of thymocytes and splenocytes to low-intensity extremely high-frequency electromagnetic radiation in normal mice and in mice with systemic inflammation]. Biofizika. 2010 Aug;55(4):645–51.** Changes in T cell subsets and expression of cytokine genes in thymocytes and splenocytes after exposure of BAL/c mice to low-intensity extremely high-frequency electromagnetic radiation (42.2 GHz, 0.1 mW/cm2, exposure duration 20 min) under normal conditions and in systemic inflammation were studied using flow cytometry and the methods of reverse transcription and real-time polymerase chain reaction. It was found that the number of CD4+ and CD8+ T cells statistically significantly increased in the thymus and considerably decreased in the spleen of exposed animals. Apparently, the exposure of animals leads to an intensification of the host defense, by activating the T-cellular immunity. As for effector functions, the increased expression of IL-1beta and IFNgamma genes in thymocytes and essentially enhanced expression of IL-1beta, IL-10, and TNFalpha genes in splenocytes were observed in mice exposed against the background of a progressive inflammatory process. The experimental data obtained specify that the directed (anti-inflammatory) response of an organism to a specific combination of effective exposure parameters of electromagnetic radiation can be realized by the activation of particular immunocompetent cells and changes in the cytokine profile.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Guler G, Tomruk A, Ozgur E, Seyhan N. The effect of radiofrequency radiation on DNA and lipid damage in non-pregnant and pregnant rabbits and their newborns. Gen Physiol Biophys. 2010 Mar;29(1):59–66.** The concerns of people on possible adverse health effects of radiofrequency radiation (RFR) generated from mobile phones as well as their supporting transmitters (base stations) have increased markedly. RFR effect on oversensitive people, such as pregnant women and their developing fetuses, and older people is another source of concern that should be considered. In this study, oxidative DNA damage and lipid peroxidation levels in the brain tissue of pregnant and non-pregnant New Zealand White rabbits and their newborns exposed to RFR were investigated. Thirteen-month-old rabbits were studied in four groups as non-pregnant-control, non-pregnant-RFR exposed, pregnant-control and pregnant-RFR exposed. They were exposed to RFR (1800 MHz GSM; 14 V/m as reference level) for 15 min/day during 7 days. Malondialdehyde (MDA) and 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels were analyzed. MDA and 8-OHdG levels of non-pregnant and pregnant-RFR exposed animals significantly increased with respect to controls ($p < 0.001$, Mann-Whitney test). No difference was found in the newborns ($p > 0.05$, Mann-Whitney). There exist very few experimental studies on the effects of RFR during pregnancy. It would be beneficial to increase the number of these studies in order to establish international standards for the protection of pregnant women from RFR.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Imge EB, Kiliçoğlu B, Devrim E, Cetin R, Durak I. Effects of mobile phone use on brain tissue from the rat and a possible protective role of vitamin C - a preliminary study. Int J Radiat Biol. 2010 Dec;86(12):1044–9.** PURPOSE: To evaluate effects of mobile phone use on brain tissue and a possible protective role of vitamin C. MATERIALS AND METHODS: Forty female rats were divided into four groups randomly (Control, mobile phone, mobile phone plus vitamin C and, vitamin C alone). The mobile phone group was exposed to a mobile phone signal (900 MHz), the mobile phone plus vitamin C group was exposed to a mobile phone signal (900 MHz) and treated with vitamin C administered orally (per os). The vitamin C group was also treated with vitamin C per os for four weeks. Then, the animals were sacrificed and brain tissues were dissected to be used in the analyses of malondialdehyde (MDA), antioxidant potential (AOP), superoxide dismutase, catalase (CAT), glutathione peroxidase (GSH-Px), xanthine oxidase, adenosine deaminase (ADA) and 5'nucleotidase (5'-NT). RESULTS: Mobile phone use caused an inhibition in 5'-NT and CAT activities as compared to the control group. GSH-Px activity and the MDA level were also found to be reduced in the mobile phone group but not significantly. Vitamin C caused a significant increase in the activity of GSH-Px and non-significant increase in the activities of 5'-NT, ADA and CAT enzymes. CONCLUSION: Our results suggest that vitamin C may play a protective role against detrimental effects of mobile phone radiation in brain tissue.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2010	**Jorge-Mora T, Alvarez Folgueiras M, Leiro J, Jorge-Barreiro FJ, Ares-Pena FJ, Lopez-Martin E. Exposure To 2.45 Ghz Microwave Radiation Provokes Cerebral Changes In Induction Of Hsp-90 Î±/Î² Heat Shock Protein In Rat. Progress In Electromagnetics Research. 2010;100:351–79.** Physical agents such as non-ionizing continuous-wave 2.45 GHz radiation may cause damage that alters cellular homeostasis and may trigger activation of the genes that encode heat shock proteins (HSP). We used Enzyme-Linked ImmunoSorbent Assay (ELI-SA) and immunohistochemistry to analyze the changes in levels of HSP-90 and its distribution in the brain of Sprague-Dawley rats, ninety minutes and twenty-four hours after acute (30 min) continuous exposure to 2.45 GHz radiation in a the Gigahertz Transverse Electromagnetic (GTEM cell). In addition, we studied further indicators of neuronal insult: dark neurons, chromatin condensation and nucleus fragmentation, which were observed under optical conventional or fluorescence microscopy after DAPI staining. The cellular distribution of protein HSP-90 in the brain increased with each corresponding (0.034 ± 3.10^{-3}, 0.069 ± 5.10^{-3}, 0.27 ± 21.10^{-3} W/kg), in hypothalamic nuclei, limbic cortex and somatosensorial cortex after exposure to the radiation. At twenty-four hours post-irradiation, levels of HSP-90 protein remained high in all hypothalamic nuclei for all SARs, and in the parietal cortex, except the limbic system, HSP-90 levels were lower than in non-irradiated rats, almost half the levels in rats exposed to the highest power radiation. Non-apoptotic cellular nuclei and a some dark neurons were found ninety minutes and twenty-four hours after maximal SAR exposure. The results suggest that acute exposure to electromagnetic fields triggered an imbalance in anatomical HSP-90 levels but the anti-apoptotic mechanism is probably sufficient to compensate the non-ionizing stimulus. Further studies are required to determine the regional effects of chronic electromagnetic pollution on heat shock proteins and their involvement in neurological processes and neuronal damage.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2010	**Lakshmi N, Tiwari R, Bhargava S, Ahuja Y. Investigations on DNA damage and frequency of micronuclei in occupational exposure to electromagnetic fields (EMFs) emitted from video display terminals (VDTs). Genet Mol Biol. 2010 Jan;33(1):154–8.** The potential effect of electromagnetic fields (EMFs) emitted from video display terminals (VDTs) to elicit biological response is a major concern for the public. The software professionals are subjected to cumulative EMFs in their occupational environments. This study was undertaken to evaluate DNA damage and incidences of micronuclei in such professionals. To the best of our knowledge, the present study is the first attempt to carry out cytogenetic investigations on assessing bioeffects in personal computer users. The study subjects (n = 138) included software professionals using VDTs for more than 2 years with age, gender, socioeconomic status matched controls (n = 151). DNA damage and frequency of micronuclei were evaluated using alkaline comet assay and cytochalasin blocked micronucleus assay respectively. Overall DNA damage and incidence of micronuclei showed no significant differences between the exposed and control subjects. With exposure characteristics, such as total duration (years) and frequency of use (minutes/day) sub-groups were assessed for such parameters. Although cumulative frequency of use showed no significant changes in the DNA integrity of the classified sub-groups, the long-term users (> 10 years) showed higher induction of DNA damage and increased frequency of micronuclei and micro nucleated cells.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Maskey D, Kim M, Aryal B, Pradhan J, Choi I-Y, Park K-S, et al. Effect of 835 MHz radiofrequency radiation exposure on calcium binding proteins in the hippocampus of the mouse brain. Brain Res. 2010 Feb 8;1313:232–41.** Worldwide expansion of mobile phones and electromagnetic field (EMF) exposure has raised question of their possible biological effects on the brain and nervous system. Radiofrequency (RF) radiation might alter intracellular signaling pathways through changes in calcium (Ca(2+)) permeability across cell membranes. Changes in the expression of calcium binding proteins (CaBP) like calbindin D28-k (CB) and calretinin (CR) could indicate impaired Ca(2+)homeostasis due to EMF exposure. CB and CR expression were measured with immunohistochemistry in the hippocampus of mice after EMF exposure at 835 MHz for different exposure times and absorption rates, 1 h/day for 5 days at a specific absorption rate (SAR)=1.6 W/kg, 1 h/day for 5 days at SAR=4.0 W/kg, 5 h/day for 1 day at SAR=1.6 W/kg, 5 h/day for 1 day at SAR=4.0 W/kg, daily exposure for 1 month at SAR=1.6 W/kg. Body weights did not change significantly. CB immunoreactivity (IR) displayed moderate staining of cells in the cornu ammonis (CA) areas and prominently stained granule cells. CR IR revealed prominently stained pyramidal cells with dendrites running perpendicularly in the CA area. Exposure for 1 month produced almost complete loss of pyramidal cells in the CA1 area. CaBP differences could cause changes in cellular Ca(2+)levels, which could have deleterious effect on normal hippocampal functions concerned with neuronal connectivity and integration.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Solomentsev GY, English NJ, Mooney DA. Hydrogen bond perturbation in hen egg white lysozyme by external electromagnetic fields: a nonequilibrium molecular dynamics study. J Chem Phys. 2010 Dec 21;133(23):235102.** Nonequilibrium molecular dynamics simulations of a charge-neutral mutant of hen egg white lysozyme have been performed at 300 K and 1 bar in the presence of external microwave fields (2.45 to 100 GHz) of an rms electric field intensity of 0.05 V Å(-1). A systematic study was carried out of the distributions of persistence times and energies of each intraprotein hydrogen bond in between breakage and reformation, in addition to overall persistence over 20 ns simulations, vis-á-vis equilibrium, zero-field conditions. It was found that localized translational motion for formally charged residues led to greater disruption of associated hydrogen bonds, although induced rotational motion of strongly dipolar residues also led to a degree of hydrogen bond perturbation. These effects were most apparent in the solvent exposed exterior of hen egg white lysozyme, in which the intraprotein hydrogen bonds tend to be weaker.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2010	**Yu Y, Yao K. Non-thermal Cellular Effects of Lowpower Microwave Radiation on the Lens and Lens Epithelial Cells. The Journal of International Medical Research. 2010;38(3):729–36.** Because of the increased use of modern radiofrequency devices, public concern about the possible health effects of exposure to microwave radiation has arisen in many countries. It is well established that high-power microwave radiation can induce cataracts via its thermal effects. It remains unclear whether low-power microwave radiation, especially at levels below the current exposure limits, is cataractogenic. This review summarizes studies on the biological effects of low-power microwave radiation on lens and lens epithelial cells (LECs). It has been reported that exposure affects lens transparency, alters cell proliferation and apoptosis, inhibits gap junctional intercellular communication, and induces genetic instability and stress responses in LECs. <u>These results raise the question of whether the ambient microwave environment can induce non-thermal effects in the lens and whether such effects have potential health consequences.</u> Further in vivo studies on the effects on the lens of exposure to low-power microwave radiation are needed.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Agarwal A, Desai NR, Makker K, Varghese A, Mouradi R, Sabanegh E, et al. Effects of radiofrequency electromagnetic waves (RF-EMW) from cellular phones on human ejaculated semen: an in vitro pilot study. Fertil Steril. 2009 Oct;92(4):1318–25.** OBJECTIVE: To evaluate effects of cellular phone radiofrequency electromagnetic waves (RF-EMW) during talk mode on unprocessed (neat) ejaculated human semen. DESIGN: Prospective pilot study. SETTING: Center for reproductive medicine laboratory in tertiary hospital setting. SAMPLES: Neat semen samples from normal healthy donors (n = 23) and infertile patients (n = 9). INTERVENTION(S): After liquefaction, neat semen samples were divided into two aliquots. One aliquot (experimental) from each patient was exposed to cellular phone radiation (in talk mode) for 1 h, and the second aliquot (unexposed) served as the control sample under identical conditions. MAIN OUTCOME MEASURE(S): Evaluation of sperm parameters (motility, viability), reactive oxygen species (ROS), total antioxidant capacity (TAC) of semen, ROS-TAC score, and sperm DNA damage. RESULT(S): Samples exposed to RF-EMW showed a significant decrease in sperm motility and viability, increase in ROS level, and decrease in ROS-TAC score. Levels of TAC and DNA damage showed no significant differences from the unexposed group. CONCLUSION(S): Radiofrequency electromagnetic waves emitted from cell phones may lead to oxidative stress in human semen. We speculate that keeping the cell phone in a trouser pocket in talk mode may negatively affect spermatozoa and impair male fertility.	Reference provided to **Royal Society of Canada** (in 2013)	Yes
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2009	**Belyaev I, Markova E, Malmgren L. Microwaves from Mobile Phones Inhibit 53BP1 Focus Formation in Human Stem Cells Stronger than in Differentiated Cells: Possible Mechanistic Link to Cancer Risk. Environ Health Perspect. 2009 Oct 22;** **Background** It is widely accepted that DNA double-strand breaks (DSBs) and their misrepair in stem cells are critical events in the multistage origination of various leukemias and tumors, including gliomas. **Objectives** We studied whether microwaves from mobile telephones of the Global System for Mobile Communication (GSM) and the Universal Global Telecommunications System (UMTS) induce DSBs or affect DSB repair in stem cells. **Methods** We analyzed tumor suppressor TP53 binding protein 1 (53BP1) foci that are typically formed at the sites of DSB location (referred to as DNA repair foci) by laser confocal microscopy. **Results** Microwaves from mobile phones inhibited formation of 53BP1 foci in human primary fibroblasts and mesenchymal stem cells. These data parallel our previous findings for human lymphocytes. Importantly, the same GSM carrier frequency (915 MHz) and UMTS frequency band (1947.4 MHz) were effective for all cell types. Exposure at 905 MHz did not inhibit 53BP1 foci in differentiated cells, either fibroblasts or lymphocytes, whereas some effects were seen in stem cells at 905 MHz. Contrary to fibroblasts, stem cells did not adapt to chronic exposure during 2 weeks. **Conclusions** The strongest microwave effects were always observed in stem cells. This result may suggest both significant misbalance in DSB repair and severe stress response. Our findings that stem cells are most sensitive to microwave exposure and react to more frequencies than do differentiated cells may be important for cancer risk assessment and indicate that stem cells are the most relevant cellular model for validating safe mobile communication signals.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	No No No No No

Year	References and extracts	Reports	Cited?
2009	**Blank M, Goodman R. Electromagnetic fields stress living cells. Pathophysiology. 2009 Aug;16(2-3):71–8.** Electromagnetic fields (EMF), in both ELF (extremely low frequency) and radio frequency (RF) ranges, activate the cellular stress response, a protective mechanism that induces the expression of stress response genes, e.g., HSP70, and increased levels of stress proteins, e.g., hsp70. The 20 different stress protein families are evolutionarily conserved and act as 'chaperones' in the cell when they 'help' repair and refold damaged proteins and transport them across cell membranes. Induction of the stress response involves activation of DNA, and despite the large difference in energy between ELF and RF, the same cellular pathways respond in both frequency ranges. Specific DNA sequences on the promoter of the HSP70 stress gene are responsive to EMF, and studies with model biochemical systems suggest that EMF could interact directly with electrons in DNA. While low energy EMF interacts with DNA to induce the stress response, increasing EMF energy in the RF range can lead to breaks in DNA strands. It is clear that in order to protect living cells, EMF safety limits must be changed from the current thermal standard, based on energy, to one based on biological responses that occur long before the threshold for thermal changes.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Crouzier D, Perrin A, Torres G, Dabouis V, Debouzy J-C. Pulsed electromagnetic field at 9.71 GHz increase free radical production in yeast (Saccharomyces cerevisiae). Pathol Biol. 2009 May;57(3):245–51.** Potential human health hazards have been reported after exposure to electromagnetic fields at low power density. Increased oxidative stress has been suggested as a potential mechanism involved in long-term effect of such exposure. In the present work, yeast cultures were exposed for 20 min to a 9.71 GHz pulsed electromagnetic field at specific absorption rates (SAR) from 0.5 W/kg to 16 W/kg. Oxidative perturbations were investigated using ESR spin trapping experiments and their impacts on membrane fluidity were assessed using spin label five nitroxide stearate. The experiments using the water-soluble spin trap alpha-(4-pyridyl-1-oxide)-N-t-butylnitrone and the lipid-soluble N-tert-butyl-alpha-phenylnitrone showed an increase of spin adduct production both in low power density exposure (SAR<4 W/kg) and in thermal conditions (SAR>4 W/kg). The membrane fluidity diminutions after exposure in all the conditions were consistent with lipid peroxidation. The overall results suggest an increase of the free radical production in the intra cellular compartment; however no effect on the yeast vitality was found.	Reference provided to **Royal Society of Canada** (in 2013)	No
		Health Canada Draft **Safety Code 6 (2014)**	No
		Health Canada **SC6 Rationale (2013)**	No
		RSC Review of Safety Code 6 (2014)	No
		SCENIHR (2013)	No

Year	References and extracts	Reports	Cited?
2009	**Daniels WMU, Pitout IL, Afullo TJO, Mabandla MV. The effect of electromagnetic radiation in the mobile phone range on the behaviour of the rat. Metab Brain Dis. 2009 Dec;24(4):629–41.** Electromagnetic radiation (EMR) is emitted from electromagnetic fields that surround power lines, household appliances and mobile phones. Research has shown that there are connections between EMR exposure and cancer and also that exposure to EMR may result in structural damage to neurons. In a study by Salford et al. (Environ Health Perspect 111:881-883, 2003) the authors demonstrated the presence of strongly stained areas in the brains of rats that were exposed to mobile phone EMR. These darker neurons were particularly prevalent in the hippocampal area of the brain. The aim of our study was to further investigate the effects of EMR. Since the hippocampus is involved in learning and memory and emotional states, we hypothesised that EMR will have a negative impact on the subject's mood and ability to learn. We subsequently performed behavioural, histological and biochemical tests on exposed and unexposed male and female rats to determine the effects of EMR on learning and memory, emotional states and corticosterone levels. We found no significant differences in the spatial memory test, and morphological assessment of the brain also yielded non-significant differences between the groups. However, in some exposed animals there were decreased locomotor activity, increased grooming and a tendency of increased basal corticosterone levels. These findings suggested that EMR exposure may lead to abnormal brain functioning.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Dasdag S, Akdag MZ, Ulukaya E, Uzunlar AK, Ocak AR. Effect of mobile phone exposure on apoptotic glial cells and status of oxidative stress in rat brain. Electromagn Biol Med. 2009;28(4):342–54.** The aim of this study was to investigate the effects of mobile phone exposure on glial cells in brain. The study carried out on 31 Wistar Albino adult male rats. The rat heads in a carousel exposed to 900 MHz microwave. For the study group (n:14), rats exposed to the radiation 2 h per day (7 days in a week) for 10 months. For the sham group (n:7), rats were placed into the carousel and the same procedure was applied except that the generator was turned off. For the cage control (n:10), nothing applied to rats in this group. In this study, rats were euthanized after 10 months of exposure periods and brains were removed. Brain tissues were immunohistochemically stained for the active (cleaved) caspase-3, which is a well-known apoptosis marker, and p53. The expression of the proteins was evaluated by a semi-quantitative scoring system. However, total antioxidative capacity (TAC), catalase, total oxidant status (TOS), and oxidative stress index were measured in rat brain. Final score for apoptosis in the exposed group was significantly lower than the sham ($p < 0.001$) and the cage control groups ($p < 0.01$). p53 was not significantly changed by the exposure ($p > 0.05$). The total antioxidant capacity and catalase in the experimental group was found higher than that in the sham group ($p < 0.001$, $p < 0.05$). In terms of the TOS and oxidative stress index, there was no statistically significant difference between exposure and sham groups ($p > 0.05$). In conclusion, the final score for apoptosis, total antioxidant capacity and catalase in rat brain might be altered by 900 MHz radiation produced by a generator to represent exposure of global systems for mobile communication (GSM) cellular phones.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Desai NR, Kesari KK, Agarwal A. Pathophysiology of cell phone radiation: oxidative stress and carcinogenesis with focus on male reproductive system. Reprod Biol Endocrinol [Internet]. 2009 Oct 22;7:114. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2776019/** Hazardous health effects stemming from exposure to radiofrequency electromagnetic waves (RF-EMW) emitted from cell phones have been reported in the literature. However, the cellular target of RF-EMW is still controversial. This review identifies the plasma membrane as a target of RF-EMW. In addition, the effects of RF-EMW on plasma membrane structures (i.e. NADH oxidase, phosphatidylserine, ornithine decarboxylase) and voltage-gated calcium channels are discussed. We explore the disturbance in reactive oxygen species (ROS) metabolism caused by RF-EMW and delineate NADH oxidase mediated ROS formation as playing a central role in oxidative stress (OS) due to cell phone radiation (with a focus on the male reproductive system). This review also addresses: 1) the controversial effects of RF-EMW on mammalian cells and sperm DNA as well as its effect on apoptosis, 2) epidemiological, in vivo animal and in vitro studies on the effect of RF-EMW on male reproductive system, and 3) finally, exposure assessment and dosimetry by computational biomodeling.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**López-Martín E, Bregains J, Relova-Quinteiro JL, Cadarso-Suárez C, Jorge-Barreiro FJ, Ares-Pena FJ. The action of pulse-modulated GSM radiation increases regional changes in brain activity and c-Fos expression in cortical and subcortical areas in a rat model of picrotoxin-induced seizure proneness. J Neurosci Res. 2009 May 1;87(6):1484–99.** The action of the pulse-modulated GSM radiofrequency of mobile phones has been suggested as a physical phenomenon that might have biological effects on the mammalian central nervous system. In the present study, GSM-exposed picrotoxin-pretreated rats showed differences in clinical and EEG signs, and in c-Fos expression in the brain, with respect to picrotoxin-treated rats exposed to an equivalent dose of unmodulated radiation. Neither radiation treatment caused tissue heating, so thermal effects can be ruled out. The most marked effects of GSM radiation on c-Fos expression in picrotoxin-treated rats were observed in limbic structures, olfactory cortex areas and subcortical areas, the dentate gyrus, and the central lateral nucleus of the thalamic intralaminar nucleus group. Nonpicrotoxin-treated animals exposed to unmodulated radiation showed the highest levels of neuronal c-Fos expression in cortical areas. These results suggest a specific effect of the pulse modulation of GSM radiation on brain activity of a picrotoxin-induced seizure-proneness rat model and indicate that this mobile-phone-type radiation might induce regional changes in previous preexcitability conditions of neuronal activation.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No
2009	**Mousavy SJ, Riazi GH, Kamarei M, Aliakbarian H, Sattarahmady N, Sharifizadeh A, et al. Effects of mobile phone radiofrequency on the structure and function of the normal human hemoglobin. Int J Biol Macromol. 2009 Apr 1;44(3):278–85.** Widespread use of mobile phones has increased the human exposure to electromagnetic fields (EMFs). It is required to investigate the effect of EMFs on the biological systems. In this paper the effect of mobile phone RF (910MHz and 940 MHz) on structure and function of HbA was investigated. Oxygen affinity was measured by sodium dithionite with UV-vis spectrophotometer. Structural changes were studied by circular dichroism and fluorescence spectroscopy. The results indicated that mobile phone EMFs altered oxygen affinity and tertiary structure of HbA. Furthermore, the decrease of oxygen affinity of HbA corresponded to the EMFs intensity and time of exposure.	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No

Year	References and extracts	Reports	Cited?
2009	**Nittby H, Brun A, Eberhardt J, Malmgren L, Persson BRR, Salford LG. Increased blood-brain barrier permeability in mammalian brain 7 days after exposure to the radiation from a GSM-900 mobile phone. Pathophysiology. 2009 Aug;16(2-3):103–12.** Microwaves were for the first time produced by humans in 1886 when radio waves were broadcasted and received. Until then microwaves had only existed as a part of the cosmic background radiation since the birth of universe. By the following utilization of microwaves in telegraph communication, radars, television and above all, in the modern mobile phone technology, mankind is today exposed to microwaves at a level up to 10(20) times the original background radiation since the birth of universe. Our group has earlier shown that the electromagnetic radiation emitted by mobile phones alters the permeability of the blood-brain barrier (BBB), resulting in albumin extravasation immediately and 14 days after 2h of exposure. In the background section of this report, we present a thorough review of the literature on the demonstrated effects (or lack of effects) of microwave exposure upon the BBB. Furthermore, we have continued our own studies by investigating the effects of GSM mobile phone radiation upon the blood-brain barrier permeability of rats 7 days after one occasion of 2h of exposure. Forty-eight rats were exposed in TEM-cells for 2h at non-thermal specific absorption rates (SARs) of 0mW/kg, 0.12mW/kg, 1.2mW/kg, 12mW/kg and 120mW/kg. Albumin extravasation over the BBB, neuronal albumin uptake and neuronal damage were assessed. Albumin extravasation was enhanced in the mobile phone exposed rats as compared to sham controls after this 7-day recovery period (Fisher's exact probability test, p=0.04 and Kruskal-Wallis, p=0.012), at the SAR-value of 12mW/kg (Mann-Whitney, p=0.007) and with a trend of increased albumin extravasation also at the SAR-values of 0.12mW/kg and 120mW/kg. There was a low, but significant correlation between the exposure level (SAR-value) and occurrence of focal albumin extravasation (r(s)=0.33; p=0.04). The present findings are in agreement with our earlier studies where we have seen increased BBB permeability immediately and 14 days after exposure. We here discuss the present findings as well as the previous results of altered BBB permeability from our and other laboratories. **[**0.12 to 120mW/kg**]**	Reference provided to **Royal Society of Canada** (in 2013) Health Canada Draft **Safety Code 6 (2014)** Health Canada **SC6 Rationale (2013)** **RSC Review of Safety Code 6 (2014)** **SCENIHR (2013)**	Yes No No No No