Appendix G1

EMF Research Updates

Exponent®

Health Sciences Practice

Research on Extremely Low Frequency Electric and Magnetic Fields and Health

Research on Extremely Low Frequency Electric and Magnetic Fields and Health

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Acronyms and Abbreviations

AC	Alternating current
ACGIH	American Conference of Governmental Industrial Hygienists
ACRBR	Australian Centre for Radiofrequency Bioeffects Research
ALL	Acute lymphoblastic leukemia
BPA	Bonneville Power Administration
CI	Confidence interval
DMBA	7, 12-dimethylbenz[a]anthracene
ELF	Extremely low frequency
EMF	Electric and magnetic fields
EMI	Electromagnetic interference
EPRI	Electric Power Research Institute
G	Gauss
GD	Gestational day
HCN	Health Council of the Netherlands
Hz	Hertz
IARC	International Agency for Research on Cancer
ICD	Implanted cardiac device
ICNIRP	International Commission on Non-Ionizing Radiation Protection
IGF-1	Insulin-like growth factor 1
m	Meter
mg	Milligram
mg/kg	Milligram per kilogram
mG	Milligauss
NRPB	National Radiological Protection Board
NIEHS	National Institute of Environmental Health Sciences
OR	Odds ratio
PND	Post-natal day
RF	Radiofrequency
ROW	Right-of-way
RR	Relative risk

SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SES	Socioeconomic status
SSI	Swedish Radiation Protection Authority
SSM	Swedish Radiation Safety Authority
WHO	World Health Organization

Introduction

Electrical objects produce two field types—electric fields and magnetic fields. The term field is used to describe the way an object influences its surrounding area. A temperature field, for example, surrounds a warm object, such as a space heater or campfire. Electric and magnetic fields (EMF) surround any object that generates, transmits, or uses electricity, including appliances, electrical wiring, office equipment, generators, and any other electrical devices. These fields are invisible, and they cannot be felt or heard.

Electric fields occur as a result of the electric potential (i.e., voltage) on these objects, and **magnetic fields** occur as a result of current flow through these objects.[1] Just like a temperature field, both electric fields and magnetic fields can be measured, and their levels depend on the properties of the source of the field (e.g., voltage, current, and configuration) and the distance from the source of the field, among other things.

Both electric fields and magnetic fields decrease rapidly with distance from the source. For example, a magnetic field of 300 milligauss (mG) within 6 inches of a vacuum cleaner diminishes to 1 mG at 4 feet (NIEHS, 2002). This is similar to the way that the heat generated by a space heater or a campfire diminishes as a person moves farther away from it. Although ordinary objects do not block magnetic fields, objects such as trees and buildings easily block electric fields.

The electrical power system in the United States produces alternating current (AC) EMF that changes direction and intensity 60 times per second—i.e., a frequency of 60 Hertz (Hz).[2] This frequency is in the extremely low frequency (ELF) range of the electromagnetic spectrum. Electricity produced by generating stations flows as 60-Hz current through transmission and distribution lines and provides power to the many appliances and electrical devices that we use in our homes, schools, and workplaces. Magnetic fields are found throughout our environment

[1] The electric field is expressed in measurement units of volts per meter (V/m) or kilovolts per meter (kV/m); 1 kilovolt per meter is equal to 1,000 V/m. The strength of magnetic fields is expressed as magnetic flux density in units called gauss (G), or in milligauss (mG), where 1 G is equal to 1,000 mG.

[2] Europe's electrical system produces 50-Hz EMF. Since 50-Hz EMF is also in the ELF range, research on 50-Hz EMF is relevant to questions on 60-Hz EMF.

because electricity is needed for many things in our daily lives, from lighting, heating, and cooling our homes to powering our refrigerators and computers.

Questions about whether these ubiquitous exposures could affect our health began to be raised in the 1970s. Since then, researchers from many different scientific disciplines have investigated this question, and hundreds of studies have been conducted. The public frequently expresses concern about ELF EMF, particularly in the context of new transmission lines. The intent of this report is to provide an update to previously prepared reports that had summarized the large body of scientific research on ELF EMF and health (Exponent, 2007, 2011). The current report also provides a summary of recent evaluations and recommendations with respect to the precautions, if any, of public health agencies

In July 2007, Exponent provided a report to the Bonneville Power Administration (BPA) that described the conclusions of a comprehensive, weight-of-evidence review published by the World Health Organization (WHO) in June 2007; the portion of Exponent's 2007 report that describes the conclusions of the WHO report is attached as Appendix 1 for reference.[3] The WHO review still represents the most recent comprehensive review of the literature by a multidisciplinary scientific panel. The WHO assembled a multidisciplinary Task Group of 21 scientists from around the world to draft a Monograph that summarized the research and provided conclusions as to whether there are risks associated with ELF EMF and, if so, at what exposure levels (WHO, 2007a). The report concluded that the only established effects of ELF EMF exposure are acute neurostimulatory effects (i.e., shock-like effects) that occur at very high levels of exposure; these exposure levels are not encountered in ordinary residential or occupational environments. The fact sheet from the WHO review is attached as Appendix 2 (WHO, 2007b).

In January 2011, Exponent provided an update to BPA on scientific research related to ELF EMF and potential health effects. The 2011 report gave a detailed overview of the relevant body of research published between January 1, 2006, and October 1, 2010.[4] In light of

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[3] Exponent. Assessment of Research Regarding EMF and Health and Environmental Effects. Olympic Peninsula Reinforcement Transmission Line Project. © Exponent, Inc., July 2007.

[4] Exponent. Research on Extremely Low Frequency Electric and Magnetic Fields and Health. © Exponent, Inc., January 2011.

additional research results since 2010, the conclusion remains that the scientific evidence does not confirm the existence of long-term health consequences of exposure to ELF EMF.

Research is a constantly evolving process. Despite the volume of research available on ELF EMF and the large reduction in uncertainty that research has achieved over the years, scientists continue research in this area with the goal of clarifying and replicating old findings and testing new hypotheses. New studies on ELF EMF are published every month. While the WHO review provides a comprehensive and relatively up-to-date summary of the status of research on this topic, new research has the potential to modify or strengthen conclusions. The BPA has, therefore, requested an update on the research with regard to ELF EMF and health. This report provides an overview of the cumulative body of research published since our previous update and covers the relevant scientific literature published during the period between October 1, 2010, and April 1, 2015.

A summary of the methods scientists use to conduct studies and make decisions about health risks is included in Section 1 as a framework for understanding later discussions. In Section 2, the discussion of new research is broadly grouped by health outcome—cancer, reproductive effects, developmental effects, and neurodegenerative diseases. This discussion summarizes two types of research—epidemiologic studies and experimental studies in animals (*in vivo*)—within each health outcome category. Experimental studies in cells and tissues (*in vitro*) of carcinogenesis are discussed briefly in Section 2. Other areas of research not reviewed by WHO are discussed in Section 3, including the possible effects of ELF EMF on the functioning of pacemakers, on flora and fauna, and on marine life. Finally, guidelines for ELF EMF exposure developed by scientific organizations to prevent against established health effects are summarized in Section 4.

1 Scientific Methods

Weight-of-evidence review

Most of what we encounter in our everyday environment has no effect on our health. Other exposures, however, may affect our health in either a beneficial or a harmful way, including such ubiquitous interactions with our environment as the air we breathe, the water we drink, and our exposure to sunlight. Much time and money is spent by scientists around the world designing, conducting, and publishing research to determine what factors may affect our health, including environmental exposures (like ELF EMF), infectious agents, and our genetics. The process for arriving at a conclusion about whether there is a health risk associated with any of these factors often is not straightforward or definitive. Rather, it is a long process that requires repeated hypothesis generation and testing.

The process begins when a scientist forms a hypothesis and conducts a study to test that hypothesis. Studies are conducted by scientists at academic universities and scientific institutions around the world. Once a study is complete, the authors submit it to a scientific journal for publication, where it undergoes peer review prior to publication. The evidence to evaluate any health risk includes all of the relevant studies published in the peer-reviewed literature.

These individual research studies can be thought of as puzzle pieces. When all of the research is placed together, we have some understanding of possible health effects; no conclusions can be reached, however, by looking at only one study, just as no picture can be formed with just one puzzle piece. Each study provides a different piece of information to the puzzle because of its unique strengths and weaknesses—if the study used valid methods and had no obvious sources of bias, it may provide a wealth of information or, if the study was not well conducted, it may add little or no information to our understanding.

This process of evaluating all of the research together to determine whether something poses either a health benefit or health risk is referred to as a weight-of-evidence review. There are three types of research that are considered in a weight-of-evidence review: epidemiology studies of people, experimental studies in animals (*in vivo* research), and experimental studies in cells and tissues (*in vitro* research). It is important to consider all three types of research together because they provide complementary information:

- Epidemiologic studies collect observational data about human populations in their everyday environments to determine whether there are patterns between exposures and diseases. These studies measure statistical associations to evaluate whether a disease and exposure occur together more often than expected. An important limitation of these studies is that, if an association is measured, they do not tell scientists how the exposure is truly related to the disease, and whether the exposure is causally related to the disease. That conclusion can only be reached by considering the entire body of research. Most of the studies evaluating ELF EMF examine whether people with a particular disease have had higher estimates of ELF EMF exposure in the past compared to people without that disease.

- Experimental studies in which scientists expose animals (*in vivo*) to varying levels of electric or magnetic fields (some as high as 50,000 mG) are an important source of information. These studies compare the amount of disease they observe in exposed animals to the amount of disease they observe in animals that have not been exposed. The strength of animal studies is that scientists are able to control all aspects of the animals' lives to minimize the potential confounding effects of factors other than the exposure of interest. The most valuable experimental studies for understanding disease are those in which the animals receive life-long exposures. The main limitation of laboratory animal studies, however, is that they are conducted in a species other than human, and thus require interspecies extrapolation for a human health risk assessment.

- Experimental studies *in vitro* involve the exposure of isolated cells and tissues to the agent of interest, in this case ELF EMF, and compare the characteristics of exposed and unexposed samples to look for differences that are indicative of a disease process. These studies are limited because what occurs to exposed cells or tissues outside of a human body may not be the same as what occurs to cells and tissues inside a body.

The weight-of-evidence approach is the standard process used worldwide by scientists, scientific organizations, and regulatory agencies to assess the possible health benefits and risks associated with exposures. A weight-of-evidence review begins with a systematic identification and review of relevant published, peer-reviewed epidemiologic, *in vivo*, and *in vitro* research. The weight that individual studies provide to the overall conclusions is not equal—studies vary widely in terms of the sophistication and validity of their methods. Therefore, each study from each discipline must be evaluated critically and assigned a weight. A final conclusion is then reached by considering the cumulative body of research, giving more weight to studies of higher quality (Figure 1).

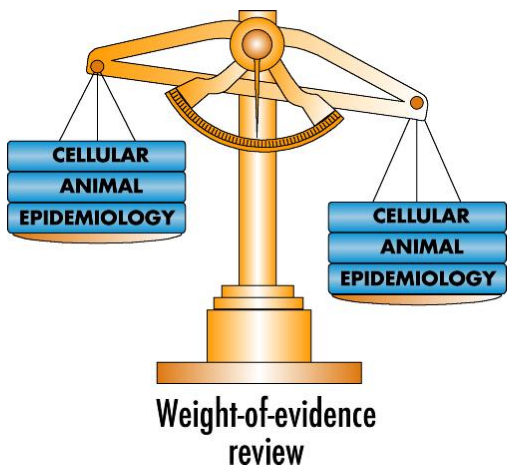

Figure 1. Weight-of-evidence reviews consider three types of research

Continuing with the puzzle example from above, the picture that is formed when the individual studies are assembled can take on many different shapes. In some cases (e.g., smoking and lung cancer), a clear picture of an adverse health effect was presented by the research within a relatively short time. In most cases, however, the picture is unclear and more questions are raised than answered. It is impossible to prove the negative in science—i.e., to say that any exposure is completely safe—therefore, research studies can only reduce the uncertainty about whether there is a health effect associated with a particular exposure through continued research. The only way to reduce this uncertainty is to conduct high quality studies with meaningful results that are replicated across study populations (in the case of epidemiologic studies) and by different laboratories (in the case of *in vivo* and *in vitro* research). Thus, in most areas of research, unless the data clearly indicate an increased risk at defined exposure levels, scientific panels will conclude that the research is inadequate or limited and requires further study until the uncertainty has been reduced below an acceptable level. While the public may interpret this conclusion as indicating concern, it is natural for scientists to recommend future research to reduce uncertainty around a largely negative body of research or to replicate findings that appear positive.

Scientific and health organizations put together panels of scientists to conduct weight-of-evidence reviews. These panels consist of experts from around the world in the areas of interest (e.g., epidemiology, neurophysiology, toxicology, etc.) and they follow standard scientific methods for arriving at conclusions about possible health risks. The conclusions of these reviews are looked to for the current scientific consensus on a particular topic and form the basis of recommendations made by organizations and governments on exposure standards and precautionary measures.

Scientific reviews on ELF EMF

Numerous national and international organizations responsible for public health have convened multidisciplinary panels of scientists to conduct weight-of-evidence reviews and arrive at conclusions about the possible risks associated with ELF EMF. These organizations include the following (in ascending, chronological order of their most recent publication):

- The **National Institute for Environmental Health Sciences** (**NIEHS**) in the United States assembled a 30-person Working Group to review the cumulative body of epidemiologic and experimental data on ELF EMF and provide conclusions and recommendations to the government (NIEHS, 1998, 1999).

- The **International Agency for Research on Cancer** (**IARC**) completed a full carcinogenic evaluation of ELF EMF in 2002 (IARC, 2002).

- The **WHO** released a review in June 2007 as part of its International EMF Program to assess the scientific evidence related to ELF EMF in the frequency range from 0 to 300 GHz (WHO, 2007a). Appendix 1 summarizes the conclusions of this review.

- The **Swedish Radiation Protection Authority (SSI),** using other major scientific reviews as a starting point, evaluated new studies in consecutive annual reports (SSI, 2007; SSI, 2008). The **Swedish Radiation Safety Authority** (SSM) superseded the SSI on June 30, 2008, and continued to publish reports on ELF EMF (SSM 2010, 2013, 2014, 2015).

- The **National Radiological Protection Board** (**NRPB**)[5] of Great Britain issued full evaluations of the research in 1992, 2001, and 2004 (NRPB 1992, 2001a, 2004), with supplemental updates (NRPB, 1993; NRPB, 1994a) and topic-specific reports (NRPB, 1994b; NRPB, 2001b; HPA, 2006) published in the interim. In a letter addressing a related topic, the Director of the Health Protection Agency of Great Britain (HPA) reiterated their position on ELF EMF and appropriate precautionary measures (HMG, 2009).

- The **International Commission on Non-Ionizing Radiation Protection** (**ICNIRP**), the formally recognized organization for providing guidance on standards for non-ionizing radiation exposure for the WHO**,** published a review of the cumulative body of epidemiologic and experimental data on ELF EMF in 2003. The ICNIRP released draft exposure guidelines for ELF EMF in July 2009 (ICNIRP, 2009). While the ICNIRP panel stated that they relied heavily on previous reviews of the literature related to long-term ELF EMF exposures, they provided relevant conclusions as part of the drafting of these guidelines. Final guidelines for ELF EMF exposure were issued in late 2010 (ICNIRP, 2010).

- The **Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)**, a scientific committee commissioned by the European Commission issued its most recent report in March 2015 (SCENIHR, 2015) updating its previous reports and conclusions (SCENIHR, 2007; SCENIHR, 2009) to the Health Directorate of the European Commission.

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[5] The NRPB merged with the HPA in April 2005 to form its new Radiation Protection Division, and subsequently, the HPA merged into Public Health England in 2013.

Dissenting opinion on ELF EMF

In August 2007, an *ad hoc*, self-organized group of 14 scientists and public health and policy consultants published an on-line report titled "*The BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF)*." An updated version of the report was subsequently published on-line in 2012. The updated report incorporates several new sections into the 2007 report. The 2012 version was authored by some of the same individuals, with some additional authors. The group's objective was to "assess scientific evidence on health impacts from electromagnetic radiation below current public exposure limits and evaluate what changes in these limits are warranted now to reduce possible public health risks in the future" (BioInitiative 2012, p. 4). The original report was followed by several publications related to ELF EMF that summarized some of the on-line report's conclusions (Hardell and Sage, 2008; Davanipour and Sobel, 2009; Johansson 2009). The individuals who comprised this group did not represent any well-established regulatory agency nor were they convened by a recognized scientific authority.

The report has been criticized by scientific agencies because it did not follow the methods of a standard weight-of-evidence review. The main criticisms included, among others, the lack of consideration of study quality when evaluating individual studies, selective referencing of positive studies in support of a specific conclusion, and heavy reliance on *in vitro* studies, which typically play a secondary role in proper human health risk assessments due to their limitations discussed above (ACRBR, 2008; HCN, 2008). Contrary to proper health risk evaluations conducted by other health and scientific agencies, neither of the BioInitiative Reports represented a consensus opinion, but included the conclusions of the individual authors of the various chapters. For these reasons, its conclusions and recommendations are not considered further in this report. Appendix 3 provides a detailed scientific commentary on the report.

Basics of epidemiology

This section briefly describes the main types of epidemiologic studies and the major issues that are relevant to evaluating their results. The two, main types of epidemiologic studies are cohort studies and case-control studies (Figure 2).

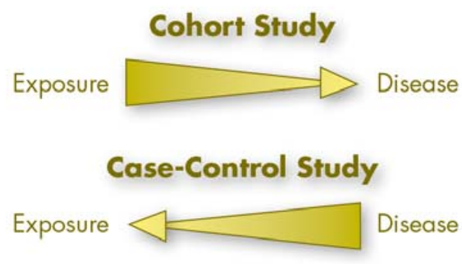


Figure 2. Basic design of cohort and case-control studies

A case-control study compares the characteristics of people that have been diagnosed with a disease (i.e., cases) to a similar group of people who do not have the disease (i.e., controls). The prevalence and extent of past exposure to a particular agent is estimated in both groups and compared to assess whether the cases have a higher exposure level than the controls, or vice versa.

In a case-control study, this comparison (or statistical association) is estimated quantitatively with an odds ratio (OR). An OR is the ratio of the odds of exposure among persons with a disease to the odds of exposure among persons without a disease. The general interpretation of an OR equal to 1.0 is that the odds of exposure are the same in the case and control groups (i.e., there is no statistical association between the exposure and disease). If the OR is greater than 1.0, the inference is that the odds of exposure are greater in the case group or, in other words, the exposure is statistically associated with an increase in the risk of the disease (Figure 3).

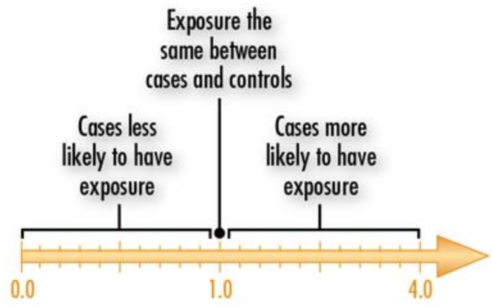


Figure 3. Interpretation of an odds ratio in a case-control study

Each OR is reported with a confidence interval (CI). A CI is a range of potential OR values that have a specified probability of including the true measure of association in the population if the study was to be repeated a large number of times. A 95% CI, for example, provides the range of potential values that has a probability of 95% to include the underlying population value the scientists are estimating with their study if the study was conducted a large number of times. In short, a CI indicates how certain (or confident) the researcher is about the OR calculated from his or her data; if the CI includes 1.0, the researcher cannot statistically exclude the possibility that the OR is 1.0, meaning the odds of exposure are the same in the case and control groups.

A cohort study is conducted in the reverse manner—in the most traditional sense, researchers study a population *without disease* and follow them over time to see if persons with a certain exposure develop disease at a higher rate than unexposed persons. The comparisons conducted in cohort studies are similar to the comparisons conducted in case-control studies, although the risk estimate is referred to as a relative risk (RR) rather than an OR. The RR is equal to rate of disease in the exposed group divided by the rate of disease in the unexposed group, with values greater than 1.0 suggesting that the exposed group has a higher rate of disease.

The resulting RR or OR is simply a comparative measure of how often a disease and exposure occur together in exposed and unexposed study populations—it does not mean that there is a known or causal relationship. Before any conclusions can be drawn, all studies considering a particular exposure and disease must be identified, and each study must be evaluated to determine the possible role that factors such as chance, bias, and confounding may have played in the study's results.

- *Chance* refers to a random event (i.e., a coincidence). An association can be observed between an exposure and disease that simply is the result of a chance occurrence. Statistics, such as the CI, are calculated to determine whether chance is a likely explanation for the findings. The CI does not include other sources of variability in the data other that those related to statistical sampling error such as might arise from bias and confounding, discussed below.
- *Bias* refers to any systematic error in the design, conduct, or analysis of a study that would cause a distorted estimate of an exposure's effect on the risk of disease. There are many different types of bias; for example, selection bias may occur if the characteristics of persons that participate in a study differ in a meaningful way from the characteristics of those subjects that do not participate (e.g., cases living near power lines might be more likely to participate than controls because the cases are concerned about this possible exposure).
- *Confounding* is a situation in which an association is distorted because the exposure being studied is associated with other risk factors for the disease. For example, a link between coffee drinking in mothers and low birth weight babies may be observed in a study, but some women who drink coffee also smoke cigarettes. When the smoking habits of mothers are taken into account, coffee drinking may not be associated with low birth weight babies because the confounding effect of smoking has been removed.

As part of the weight-of-evidence review process, each study's design and methods are evaluated critically to determine if and how chance, bias, and confounding may have affected the results and, subsequently, the weight that should be placed on the study's findings.

IARC classifications

This section briefly describes the method that the IARC uses following a weight-of-evidence review to classify exposures based on the evidence in support of carcinogenicity. The WHO adopted this method for both cancer and non-cancer health outcomes in their 2007 review on ELF EMF, and other scientific agencies refer to this classification system, as well.

First, each research type (epidemiology, *in vivo*, and *in vitro*) is evaluated to determine the strength of evidence in support of carcinogenicity (as defined in Figure 4). Epidemiologic studies are characterized as having *sufficient evidence* for carcinogenicity if an association is found and chance, bias, and confounding can be ruled out with "reasonable confidence." *Limited evidence* is used to describe a body of research where the findings are inconsistent or where an association is observed but there are outstanding questions about study design or other methodological issues that preclude making strong conclusions. *Inadequate evidence* describes a body of research where it is unclear whether the data is supportive or unsupportive of causation because there is a lack of data or there are major quantitative or qualitative issues. The same overall categories apply for *in vivo* research. *In vitro* research is not described in Figure 4 because it provides ancillary information and, therefore, is used to a lesser degree in evaluating carcinogenicity and is classified simply as strong, moderate, or weak.

Agents are then classified into five overall categories using the combined categories from epidemiologic, *in vivo*, and *in vitro* research (listed from highest to lowest risk): (1) known carcinogen, (2) probable carcinogen, (3) possible carcinogen, (4) non-classifiable, and (5) probably not a carcinogen.

As summarized in Figure 4, the category possible carcinogen typically denotes exposures for which there is limited evidence of carcinogenicity in epidemiologic studies, and *in vivo* studies provide limited or inadequate evidence of carcinogenicity.

The IARC has reviewed close to 1,000 substances and exposure circumstances to evaluate their potential carcinogenicity. About 80% of exposures fall in the categories possible carcinogen (29%) or non-classifiable (51%). This occurs because, as described above, it is nearly impossible to prove that something is completely safe and few exposures show a clear-cut or probable risk, so most agents will end up in either of these two categories. Throughout the history of the IARC, only one agent has been classified as probably not a carcinogen, which illustrates the conservatism of the evaluations and the difficulty in proving the absence of an effect beyond all doubt.

Over half of the agents are non-classifiable in terms of carcinogenicity, i.e., it is unclear whether they can cause cancer—hair coloring products, jet fuel, and tea are included in this category.

Possible carcinogens include occupation as a firefighter, coffee, and pickled vegetables, in addition to magnetic fields. Exposures identified as probable carcinogens include high temperature frying and occupation as a hairdresser. Finally, known carcinogens include benzene, asbestos, solar radiation, use of tanning beds, and tobacco smoking. There is much uncertainty about whether certain agents will lead to cancer, and possible and probable carcinogens include substances to which we are commonly exposed or are common exposure circumstances.

	Epidemiology Studies				Animal Studies			
	Sufficient evidence	Limited evidence	Inadequate evidence	Evidence suggesting lack of carcinogenicity	Sufficient evidence	Limited evidence	Inadequate evidence	Evidence suggesting lack of carcinogenicity
Known Carcinogen	✔							
Probable Carcinogen		✔			✔			
Possible Carcinogen		✔				✔	✔	
Not Classifiable			✔			✔	✔	
Probably not a Carcinogen				✔				✔

Sufficient evidence in epidemiology studies—A positive association is observed between the exposure and cancer in studies, in which chance, bias and confounding were ruled out with "reasonable confidence."

Limited evidence in epidemiology studies—A positive association has been observed between the exposure and cancer for which a causal interpretation is considered to be credible, but chance, bias or confounding could not be ruled out with "reasonable confidence."

Inadequate evidence in epidemiology studies—The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.

Evidence suggesting a lack of carcinogenicity in epidemiology studies—There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. The results from these studies alone or combined should have narrow confidence intervals with an upper limit close to the null value (e.g. a relative risk of 1.0). Bias and confounding should be ruled out with reasonable confidence, and the studies should have an adequate length of follow-up.

Sufficient evidence in animal studies—An increased incidence of malignant neoplasms is observed in (a) two or more species of animals or (b) two or more independent studies in one species carried out at different times or indifferent laboratories or under different protocols. An increased incidence of tumors in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide sufficient evidence.

Limited evidence in animal studies—The data suggest a carcinogenic effect but are limited for making a definitive evaluation, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; etc.

Inadequate evidence in animal studies—The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available

Evidence suggesting a lack of carcinogenicity in animal studies—Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic.

Figure 4. Basic IARC method for classifying exposures based on potential carcinogenicity

2 Human Health Research

The following sections provide an overview of peer-reviewed research published between October 1, 2010, and April 1, 2015. A literature review was conducted to identify new epidemiologic and *in vivo* research published on 50 or 60-Hz ELF EMF. A large number of search strings referencing the exposure and diseases of interest, as well as authors who regularly publish in this area, were included as search terms in the PubMed database, a service of the U.S. National Library of Medicine that includes over 17 million citations from MEDLINE and other life science journals for biomedical articles dating to the 1950s.[6] Scientists with experience in this area reviewed the search results to identify relevant studies.

This report focuses on the diseases that have received the most attention—cancer, reproductive effects, developmental effects, and neurodegenerative diseases. Other health effects have been studied (i.e., rare cancer types, suicide, depression, electrical hypersensitivity, and cardiovascular effects), but because research on these topics evolves slowly, these topics are not separately summarized here. The WHO review provides a good resource for the status of research on these additional health effects.

This update focuses on identifying and summarizing new epidemiologic and major *in vivo* research, since these study types are the most informative for risk assessment in this field.

Cancer

Childhood leukemia

What was previously known about childhood leukemia?

While authoritative scientific panels have not concluded that the overall evidence confirms the existence of any adverse health effects, these panels consistently recognized the limited evidence from childhood leukemia epidemiologic studies, which provided the basis for the "possibly carcinogenic to humans" classification of ELF magnetic fields. Since 1979, several dozen epidemiologic studies have been conducted in the United States, Canada, Europe, New

[6] PubMed includes links to full-text articles and other related resources (http://www.ncbi.nlm.nih.gov/PubMed/).

Zealand, and Asia that evaluated the relationship between childhood leukemia and magnetic fields using various methods to estimate exposure. These methods have included long-term (48-hour) personal monitoring; spot or long-term (24- or 48-hour) measurements indoors and outdoors; calculations using loading, line configuration, and distance of nearby power installations to estimate historical, residential exposure; and wire code categories.[7] As a group of independent studies, they did not show a clear or consistent association between magnetic fields and childhood leukemia. The largest and most methodologically sound case-control studies to estimate personal magnetic field exposure directly did not report a consistent relationship (Linet et al., 1997; McBride et al., 1999; UKCCS, 2000). When two independent pooled analyses combined the data from these case-control studies, however, a statistically significant association was observed between rare average magnetic-field exposure above 3-4 mG and childhood leukemia (Ahlbom et al., 2000; Greenland et al., 2000). Both pooled analyses indicated that children with leukemia were about two times more likely to have had estimated magnetic-field exposures above 3-4 mG. Average exposures at this level are uncommon; according to the WHO, results from several extensive surveys showed that approximately 0.5–7.0% of children had time-averaged exposures in excess of 3 mG and 0.4–3.3% had time-averaged exposures in excess of 4 mG (WHO, 2007a). While these analyses provide a valuable quantitative summary of the data, pooled analyses are limited by the disparate methods used to collect the underlying data in the individual studies included in the pooled analyses. Questions have been raised as to whether the original studies, particularly those that are large and estimated exposure directly, provide a more valid estimate of the association than the pooled analyses (Elwood, 2006).

Despite the association observed in these pooled analyses, health agencies have not concluded that magnetic fields are a known or probable cause of childhood leukemia. The studies are of insufficient strength to rule out with "reasonable confidence" the role that chance, bias, and confounding may have played in the observed statistical association. In other words, researchers do not have enough confidence in the way these studies were conducted to conclude that the measured statistical association represents a true relationship between magnetic fields and childhood leukemia. Furthermore, experimental data do not provide evidence for a risk in

[7] Wire code categories are categories used to classify the potential magnetic field exposures at residences based on the characteristics of and distance to nearby power installations.

the more highly-controlled *in vivo* studies, and *in vitro* studies do not provide evidence of a plausible biological mechanism whereby magnetic fields lead to carcinogenesis.

Since chance, bias, and confounding could not be ruled out as an explanation for the association, the IARC concluded in 2002 that the data on childhood leukemia provided limited evidence of carcinogenicity (IARC, 2002). In 2007, the WHO reviewed studies on childhood leukemia and magnetic-field exposure published since the 2002 IARC review (WHO, 2007a). They concluded that the new epidemiologic studies were consistent with previous results and they did not provide new evidence to alter the classification of limited epidemiologic evidence in support of carcinogenicity. Taken together with the largely negative *in vivo* and *in vitro* research, the WHO confirmed the previous IARC classification of magnetic fields as a possible carcinogen based upon IARC criteria (Figure 4).[8]

Since it is unclear whether the association is real, the WHO review evaluated other factors that might be partially, or fully, responsible for the association, including chance, control selection bias, confounding from hypothesized or unknown risk factors, and misclassification of magnetic field exposure (Figure 5). The following is a summary of their evaluation:

- ✓ The WHO review concluded that **chance** is an unlikely explanation since the pooled analyses had a large sample size and decreased variability.
- ✓ **Control selection bias** occurs when the controls that are selected from the population and decide to participate in the study do not represent the true exposure experience of the entire non-diseased population. In the case of magnetic fields, the WHO speculates that controls with a higher socioeconomic status (SES) may participate in studies more often than controls with a lower SES. Since persons with a higher SES may have lower magnetic-field exposures or tend to live farther from transmission lines, the control group's magnetic-field exposure may be artificially low. Thus, when the exposure experience of the control group is compared to the case group, there may be a difference in exposure distribution between the case and control groups in the study that does not

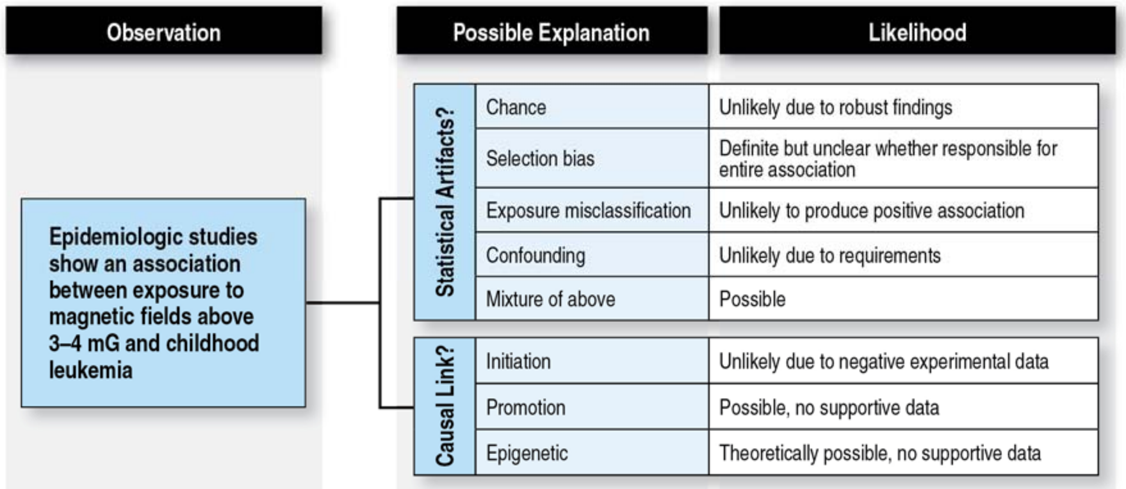
8 The WHO concluded the following: "Consistent epidemiological evidence suggests that chronic low intensity ELF magnetic field exposure is associated with an increased risk of childhood leukaemia. However, the evidence for a causal relationship is limited, therefore exposure limits based upon epidemiological evidence are not recommended, but some precautionary measures are warranted" (WHO, 2007a, pp. 355-356).

exist in the general population. The WHO concluded that **control selection bias** is probably occurring in these studies and would result in an overestimate of the true association, but may not explain the entire observed statistical association

- ✓ The WHO panel concluded that **confounding** is less likely to be causing the observed association than other factors, although the possibility that some yet-to-be identified confounder is responsible for the association cannot be excluded completely. Suggested risk factors that may be confounding the relationship include SES, residential mobility, contact currents, and traffic density.[9]

- ✓ The WHO stated that the possible effects of **exposure misclassification** are the most difficult to predict. EMF presents unique challenges in exposure assessment because it is ubiquitous, imperceptible, and has many sources (Kheifets and Oksuzyan, 2008). No target exposure or exposure window has been identified, and the numerous methods of estimating exposure likely result in a different degree of error within and between studies. Most reviews have concluded that exposure misclassification would likely result in an underestimate of the true association, meaning the association we observe is lower than the true value; however, the extent to which this might occur varies widely and is difficult to assess (Greenland et al., 2000). The WHO concluded that **exposure misclassification** is likely present in these studies, but is unlikely to entirely explain the observed association.

[9] For example, if dwellings near power lines encounter higher traffic density and pollution from traffic density causes childhood leukemia, traffic density may cause an association between magnetic-field exposure and childhood leukemia, where a relationship does not truly exist.



Source: Adapted from Schüz and Ahlbom (2008)

Figure 5. Possible explanations for the observed association between magnetic-field exposure and childhood leukemia

The WHO review stated that reconciling the epidemiologic data on childhood leukemia and the negative (i.e., no hazard or risk observed) experimental findings through innovative research is currently the highest priority in the field of ELF EMF research. Given that few children are expected to have average magnetic-field exposures greater than 3-4 mG, however, the WHO stated that the public health impact of magnetic fields on childhood leukemia would be low if the association was determined to be causal.

As discussed in the previous update by Exponent (2011), the results of epidemiologic studies of childhood leukemia conducted and published following the WHO review up to 2010 were consistent with previous results. While some of the studies reported a statistical association, due to methodological limitations in these studies, chance, confounding, and bias could not be ruled out as a potential explanation for the observed associations. Overall, these studies provided no new evidence or insight that would alter the conclusions about limited epidemiologic evidence from childhood leukemia studies.

Recent studies (October 2010 – April 2015)

In spite of the opinion by some researchers that epidemiology has reached its limits in this area and any future research must demonstrate a significant methodological advancement to be justified (Schmiedel and Blettner, 2010), childhood leukemia has continued to be the main focus of ELF EMF epidemiologic research due to the previously reported and unexplained associations. A number of studies investigating childhood leukemia and magnetic fields have been published since the previous Exponent report that provided an update of the literature up to October 2010 (Table 1). While some of the recent studies continue to support a weak association between elevated magnetic-field levels and childhood leukemia, some recently published large and methodologically advanced studies showed no association. The previously reported association, however, remains unexplained. Overall, the results of the new studies published since 2010 have not resulted in a change of the overall evidence that would alter the classification of the epidemiologic data as limited. Similar conclusions were expressed in the most recent SCENIHR report (SCENIHR, 2015).

A review of the EMF and childhood leukemia literature by Calvente et al. (2010) that included studies related to both ELF and radiofrequency exposures concluded that "*studies to date have not convincingly confirmed or ruled out an association between non-ionizing radiation and the risk of childhood leukemia.*" The authors also note that inconsistencies between studies may be explained by the influence of confounding factors, selection bias, and misclassification. A general review of childhood leukemia etiology highlighted genetic factors and ionizing radiation as factors known to contribute to leukemia development among children (Eden, 2010). While the review also mentioned the potential for EMF to be a contributor, the author notes that if EMF has any effect, it "*would account for only a small percentage of cases,*" and that a plausible biological mechanism has not been identified to explain any potential carcinogenic effects. Two recent papers have also evaluated the potential impact of EMF (Teepen and van Dijck, 2012; Grellier et al., 2014). Both reviews emphasize the lack of biological support for a potential carcinogenic effect and the importance that various sources of bias may play in the studies that report the association. They conclude that even if the association with EMF was causal, it would have limited public health impact. The authors also continue to emphasize that further improvement in our understanding may only be gained by studies with improved methodology and reduced potential for bias such as can be achieved by international and interdisciplinary collaborations (Ziegelberger et al., 2011; Teepen and van Dijck, 2012).

A case-control study of childhood leukemia from Brazil (Wünsch-Filho et al., 2011) that included 162 cases recruited between 2003 and 2009 and 565 matched controls identified through the regional birth registry utilized two approaches for exposure assessment; the researchers conducted spot and 24-hour measurements in the children's homes and also determined the distance of the homes to the closest power line with voltages of 88 kV, 138 kV, 230 kV, 345 kV, and 440 kV. The authors reported no statistically significant associations between leukemia and magnetic-field exposure >3 mG (OR, 1.09; CI, 0.33-3.61) or living within 100 meters of a transmission line (OR, 1.54; CI, 0.26-9.12). The authors also discussed several sources of potential bias, most notably selection bias, which in their assessment may have potentially influenced the results. A small case-control study from the Czech Republic (Jirik et al., 2012) included 79 cases of childhood leukemia and 79 controls and reported no statistically significant association between leukemia and measured magnetic-field exposure in the children's homes (OR for >0.4mG, 0.90; CI, 0.37-2.22).

A case-control study reported from Northern California included 245 children under the age of 8 years diagnosed with leukemia between 2000 and 2007 and 269 matched control children without leukemia. The researchers assessed the potential for exposure to magnetic fields and contact currents in the homes of the participating children. No associations were reported for any of the investigated exposure metrics (Does et al., 2011).

In recent years, several large case-control studies on EMF and childhood leukemia were published from France, Denmark, the United Kingdom, and Italy (Sermage-Faure et al., 2013; Bunch et al., 2014; Pedersen et al., 2014; Magnani et al., 2014; Salvan et al., 2015). Sermage-Faure et al. (2013) collected geocoded information on residential addresses and power line locations in France to examine the risk of childhood leukemia in association with distance to power lines. The study included 2,779 cases of childhood leukemia, diagnosed between 2002 and 2007, and 30,000 control children. Overall, the authors reported no statistically significant increase in leukemia risk with distance to power lines. The authors, however, noted a statistically non-significant association of distance with childhood leukemia in a sub-analysis within 50 meters of 225-kV – 400-kV lines. This estimate was based on only nine leukemia cases, rendering the association imprecise.

Pedersen et al. (2014) reported results of a similar study from Denmark. The Danish study included 1,698 cases of childhood leukemia and 3,396 healthy control children. The authors reported no risk increases for childhood leukemia with residential distance to power lines (living <200 meters from a transmission line, OR, 0.76; CI, 0.40-1.45). Exposure prevalence, however, was very low in the study; less than 1% of the cases (n=13) lived within 200 meters of a transmission line. Bunch et al. (2014) updated and extended an earlier study by Draper et al. (2005) in the United Kingdom. The update extended the study period by 13 years, included Scotland in addition to England and Wales, and included 132-kV lines in addition to 275-kV and 400-kV transmission lines.

The Bunch et al. study, which included over 53,000 childhood cancer cases diagnosed between 1962 and 2008, and over 66,000 healthy children as controls, is the largest study to date conducted on this subject. The authors reported no statistically significant association with residential distance to power lines with any of the voltage categories. The statistical association reported in the earlier study (Draper et al., 2005) was no longer apparent in the updated analysis by Bunch et al. (2014). According to an analysis by calendar time, the association was only present in the earlier decades (1960s and 1970s) but not in the later decades starting from the 1980s (Bunch et al., 2014). This pattern of diminishing association with calendar time weakens the argument that the associations observed in the earlier decades are due to magnetic-fields.

The strengths of the French, Danish, and British studies include their large size and their population-based design that minimized the potential for selection bias. These studies, however, relied on a poor proxy of the actual residential magnetic-field exposure and relied on distance to the nearest transmission lines as their main exposure metric. The limitations of distance as an exposure proxy have been discussed in the scientific literature by several observers in the context of the French study (Bonnet-Belfais et al., 2013; Clavel et al., 2013). Chang et al. (2014) recently provided a detailed discussion of the limitations of exposure assessment methods based on geographical information systems.

Italian researchers have also published the methods and results of a large childhood leukemia case-control study (Magnani et al., 2014; Salvan et al., 2015). The investigators included 412 leukemia cases under the age of 10 years diagnosed in Italy between 1998 and 2001 along with

587 controls in their study of leukemia and residential exposure to 50-Hz magnetic fields. Long term (24 – 48-hr) measurements in the children's bedroom were conducted to assess exposure. Conditional logistic regression was used to calculate RR and adjust for potentially confounding variables. The researchers evaluated the influence of various exposure metrics used in the analyses (measures of central tendency or peak-exposure measures, continuous or categorical exposures), the influence of time of measurements (nighttime, weekend, entire measurements), and the effect of residential mobility on the observed associations. No consistent exposure-response patterns were observed in any of the analyses. Restrictions on study subject eligibility, potential for participation bias, and low prevalence of highly-exposed subjects (particularly exposure above 3 mG), as also discussed by the authors, represent shortcomings in the studies that limit their potential interpretation.

British researchers examined the relationships between the fathers' occupational exposures to 33 various factors (including potential exposure to EMF on the job) and the likelihood of exposure of their offspring with childhood leukemia to EMF (Keegan et al., 2012). The authors studied a total of 15,785 childhood leukemia cases that were diagnosed between 1962 and 2006 and a similar number of matched controls. Paternal exposure to EMF in relation to leukemia in their children was not statistically significant when all types of leukemia or the two most common subtypes, lymphoid leukemia and myeloid leukemia, were considered. The authors reported a statistically significant increase for leukemia classified as "other types," which included only 7% of the leukemia cases. This observed association may be attributable to the small number of cases in this sub-analysis or the large number comparisons made in the overall analyses, which could falsely identify associations as statistically significant.

The potential association between exposure to magnetic fields and survival of children following a leukemia diagnosis has also been investigated by a recent pooled analysis (Schüz et al., 2012), which aimed to follow up on earlier observations. Two previous studies, based on very small number of cases, reported poorer survival among childhood leukemia cases with increased average exposure to magnetic fields, suggesting the magnetic fields may play a role in the progression in the disease following diagnosis (Foliart et al., 2006; Svendsen et al., 2007). The Schüz et al. (2012) study included exposure and clinical data on more than 3,000 cases of childhood leukemia from Canada, Denmark, Germany, Japan, the United Kingdom, and the

United States. The authors reported no association between magnetic-field exposure and overall survival or relapse of disease after diagnosis in children with leukemia.

Chinese scientists (Zhao et al., 2014) summarized the data from nine EMF-childhood leukemia epidemiologic studies published between 1997 and 2013 in a meta-analysis. The authors reported a statistically significant association between average exposure above 4 mG and all types of childhood leukemia (OR, 1.57, 95% CI, 1.03-2.4). The studies included in the meta-analysis largely overlapped with studies included in previous pooled analyses, thus they provided little new insight.

The potential role corona ions near power lines may play in childhood cancer development was investigated in a large childhood cancer epidemiologic study in the United Kingdom (Swanson et al., 2014). Corona ion distribution around power lines was modeled with consideration of meteorological data on wind conditions, in addition to power line characteristics and proximity to residential address. The results, in the authors' assessment, provided no empirical support for the corona ion hypothesis.

Potential non-causal, alternative explanations for the observed epidemiologic association between magnetic fields and childhood leukemia were examined in several methodological studies. Swanson and Kheifets (2012) hypothesized that if free radicals are involved in the biological mechanism that explains the epidemiologic association then, due to the small timescale of the reactions, the effects of ELF EMF and the earth's geomagnetic fields would be similar. The authors evaluated whether the magnitude of the earth's geomagnetic field modifies the effects reported by ELF EMF childhood leukemia studies from various parts of the world. The results were not fully supportive of the hypothesis. In another study, Swanson (2013) examined whether differences in residential mobility among residents who lived at varying distances from power lines may explain the statistical association of leukemia with residential proximity to power lines. The study reported some variations in residential mobility, "but only small ones, and not such as to support the hypothesis."

As part of the Northern California Childhood Leukemia study, researchers evaluated the role selection bias may play in the association between childhood leukemia and residential magnetic-field exposure (Slusky et al., 2014). Wire code categories were used to assess exposure among participant and nonparticipant subjects in the study. While systematic differences between participant and nonparticipant subjects were reported in both wire code categories and SES, these differences did not appreciably influence the association between childhood leukemia and magnetic-field exposure estimates. Wire code categories are poor surrogates of actual magnetic-field exposure, and the study showed no association between magnetic fields and childhood leukemia among the participant subjects, thus the study findings warrant cautious interpretation.

In addition to continued interest in EMF exposure distribution in the general population (Karipidis, 2015), a number of exposure assessment studies have evaluated various exposure scenarios, where highly exposed populations can reliably be identified without requiring participation of the study subjects (e.g., Okokon et al., 2014; Hareuveny et al., 2010; Zaryabova et al., 2013). Such exposure scenarios without the need for subject participation would enable a more accurate assessment of the importance of selection bias, which remains a key limitation of most epidemiologic studies.

In summary, while a number of new studies have been published since 2010, recent epidemiologic studies on childhood leukemia have not provided new evidence that would alter the overall conclusion; the epidemiologic evidence continues to be limited and remains unsupported by laboratory animal studies and by the lack of known biological mechanisms that could explain a carcinogenic effect.

Table 1. Relevant studies of childhood leukemia, October 2010 – April 2015

Author	Year	Study Title
Bunch et al.	2014	Residential distance at birth from overhead high-voltage powerlines: childhood cancer risk in Britain 1962-2008.
Calvente et al.	2010	Exposure to electromagnetic fields (non-ionizing radiation) and its relationship with childhood leukemia: a systematic review
Does et al.	2011	Exposure to electrical contact currents and the risk of childhood leukemia
Grellier et al.	2014	Potential health impacts of residential exposures to extremely low frequency magnetic fields in Europe
Jirik et al.	2012	Association between childhood leukaemia and exposure to power-frequency magnetic fields in middle Europe
Keegan et al.	2012	Case–control study of paternal occupation and childhood leukaemia in Great Britain, 1962–2006
Magnani et al.	2014	SETIL: Italian multicentric epidemiological case-control study on risk factors for childhood leukaemia, non hodgkin lymphoma and neuroblastoma: study population and prevalence of risk factors in Italy
Pedersen et al.	2014	Distance from residence to power line and risk of childhood leukemia: a population-based case-control study in Denmark
Pedersen et al.	2014	Distance to high-voltage power lines and risk of childhood leukemia - an analysis of confounding by and interaction with other potential risk factors.
Salvan et al.	2015	Childhood leukemia and 50 Hz magnetic fields: findings from the Italian SETIL case-control study
Schmiedel and Blettner	2010	The association between extremely low-frequency electromagnetic fields and childhood leukaemia in epidemiology: enough is enough?
Schüz et al.	2012	Extremely low-frequency magnetic fields and survival from childhood acute lymphoblastic leukemia: an international follow-up study
Sermage-Faure et al.*	2013	Childhood leukaemia close to high-voltage power lines – the Geocap study, 2002–2007
Slusky et al.	2014	Potential role of selection bias in the association between childhood leukemia and residential magnetic fields exposure: a population-based assessment
Swanson et al.	2014	Childhood cancer and exposure to corona ions from power lines: an epidemiological test
Swanson	2013	Residential mobility of populations near UK power lines and implications for childhood leukaemia
Swanson and Kheifets	2012	Could the geomagnetic field be an effect modifier for studies of power-frequency magnetic fields and childhood leukaemia?
Teepen and van Dijck	2012	Impact of high electromagnetic field levels on childhood leukemia incidence

Childhood brain cancer

What was previously known about childhood brain cancer?

The research related to magnetic fields and childhood brain cancer has been less consistent than that observed for childhood leukemia and the WHO review concluded that the evidence was inadequate to support a carcinogenic effect. In order to provide a more definitive answer, the WHO review recommended a combined analysis of childhood brain cancer studies similar to those completed for childhood leukemia:

> As with childhood leukaemia, a pooled analysis of childhood brain cancer studies should be very informative and is therefore recommended. A pooled analysis of this kind can inexpensively provide a greater and improved insight into the existing data, including the possibility of selection bias and, if the studies are sufficiently homogeneous, can offer the best estimate of risk (WHO 2007a, p. 18).

In response to the WHO recommendation above, a meta-analysis (Mezei et al., 2008) and a pooled analysis (Kheifets et al., 2010) of studies on childhood brain tumors and residential magnetic-field exposure were conducted. In the meta-analysis, 13 epidemiologic studies were identified that used various proxies of magnetic-field exposure (distance, wire codes, calculated magnetic fields, and measured magnetic fields). The combined effect estimate was close to 1.0 and not statistically significant, indicating no association between magnetic-field exposure and childhood brain tumors. A sub-group of five studies, however, with information on childhood brain tumors and calculated or measured magnetic fields greater than 3 – 4 mG reported a combined OR that was elevated but not statistically significant (OR, 1.68, 95% CI, 0.83-3.43). The authors suggested two explanations for this elevated OR. First, they suggested that an increased risk of childhood brain tumors could not be excluded at high exposure levels (i.e., >3 – 4 mG). Second, they stated that the similarity of this result to the findings of the pooled analyses of childhood leukemia suggests that control selection bias is operating in both analyses. Similar to the meta-analysis, some categories of high exposure in the pooled analysis of studies with measured or calculated magnetic-field levels had an OR $\geq$1.0, but none of the findings were statistically significant and enhanced calculations showed inconsistency in the results of subgroup analyses and no dose-response pattern (Kheifets et al., 2010b). The main analysis reported no association between childhood brain cancer and magnetic-field exposure >4 mG, compared to magnetic-field exposure <1 mG (OR=1.14, 95% CI=0.61-2.13). Both the authors of the meta-analysis and the pooled analysis concluded that their results provide little evidence for an association between magnetic fields and childhood brain tumors.

The pooled analysis included two case-control studies published after the WHO 2007 review (Kroll et al., 2010; Saito et al., 2010). In their study of 55 cases of childhood brain cancer, Saito et al. (2010) reported that children with brain cancer were more likely to have average magnetic-field exposure levels greater than 4 mG, compared to children without brain cancer.[10] The association was based on three cases and one control; interpretations of the data were, therefore, limited by small numbers in the upper exposure category. The strength of this study is the exposure assessment; measurements were taken continuously over a weeklong period in the child's bedroom approximately 1 year after diagnosis. An important limitation, however, is the very poor participation rates among study subjects; poor participation rates introduce the possibility of selection bias, among other biases. As described above, Kroll et al. (2010) included 6,584 cases of brain cancer diagnosed over a 33-year period in the United Kingdom. No associations were reported in any analysis of brain cancer, including calculated magnetic fields ≥1 – 2 mG, 2 – 4 mG, and 4 mG.

Thus, the combined analyses of childhood brain cancer epidemiologic studies provided no support for an association.

Recent studies (October 2010 – April 2015)

Given the observed general absence in the epidemiologic literature of associations between ELF EMF exposure and childhood brain cancer, there has been only limited interest in this area for further studies. Hug et al. (2010) investigated the potential relationship between estimated parental exposure to ELF EMF and cancer in their offspring in Germany. The study included 444 children with cancer of the central nervous system diagnosed between 1992 and 1997. Potential exposure to ELF EMF of the parents was estimated from their job titles, the industry in

[10] The unpublished results of this study were included in Mezei et al. (2008).

which they worked, and the time period, as reported in their occupational history. Neither paternal nor maternal exposure to ELF EMF was associated with the occurrence of brain cancer in the offspring. The updated and extended British study by Bunch et al. (2014), discussed in the childhood leukemia section, also included 11,968 cases of childhood brain cancer diagnosed in the United Kingdom between 1962 and 2008. Similar to previous results reported from the earlier stud (Draper et al., 2005; Kroll et al., 2010), no association was observed between estimates of residential exposure to EMF from high-voltage power lines and childhood brain cancer.

In summary, the recent data do not alter the classification of the epidemiologic data in this field as inadequate.

Table 2. Relevant studies of childhood brain cancer, October 2010 – April 2015

Authors	Year	Study
Bunch et al.*	2014	Residential distance at birth from overhead high-voltage powerlines: childhood cancer risk in Britain 1962-2008.
Hug et al.	2010	Parental occupational exposure to extremely low frequency magnetic fields and childhood cancer: a German case-control study

Breast cancer

What was previously known about breast cancer?

The 2007 WHO report reviewed studies of breast cancer and residential magnetic-field exposure, electric blanket usage, and occupational magnetic-field exposure. These studies did not report consistent associations between magnetic-field exposure and breast cancer, and the WHO concluded that, since the recent body of research was higher in quality compared with previous studies, it provided strong support to previous consensus statements that magnetic-field exposure does not influence the risk of breast cancer.[11] The WHO recommended no further research with respect to breast cancer and magnetic-field exposure.

[11] The WHO concluded, "Subsequent to the IARC monograph a number of reports have been published concerning the risk of female breast cancer in adults associated with ELF magnetic field exposure. These studies are larger than the previous ones and less susceptible to bias, and overall are negative. With these studies, the evidence for an association between ELF exposure and the risk of breast cancer is weakened considerably and does not support an association of this kind" (WHO 2007a, p. 307).

Recent studies (October 2010 – April 2015)

A case-control study from Brazil investigated environmental exposures as potential risk factors for breast cancer including 110 cases of breast cancer diagnosed between 1999 and 2002 among women aged 20-35 years (Ortega Jacome et al., 2010). Information on environmental exposures, including residential proximity to electrical power transformers, was collected with the use of questionnaires. No statistically significant association was reported between breast cancer and residence within 20 meters of a power transformer; however, very limited, if any, inference can be drawn from the study as the study was small with limited statistical power, the exposure assessment was severely limited for EMF exposure, and no description of control selection was provided.

A large case-control study in the United Kingdom investigated estimated exposure to ELF EMF due to residential proximity to high-voltage transmission lines and cancers among adults (Elliott et al., 2013). Among other cancer outcomes, the study included 29,202 newly diagnosed female breast cancer cases from England and Wales diagnosed between 1974 and 2008, and a total of over 79,000 controls between the age of 15 and 74 years. Data from geographical information systems were used to identify location of power lines and residential addresses for cases and controls. Magnetic-field exposure was calculated for each control address and for each case address for the year of and 5 years prior to diagnosis. Breast cancer risk among women showed no association with residential distance to power lines or with estimated magnetic-field exposure. The study was criticized by several researchers following publication with respect to its exposure assessment, exposure categorization, and the potential for confounding (de Vocht, 2013; Philips et al., 2013; Schüz, 2013).

Three large cohort epidemiologic studies from the United Kingdom, China, and the Netherlands reported on occupational exposure to ELF EMF and breast cancer development. Close to 80,000 British workers from electricity generation and transmission facilities were included in a study by Sorahan (2012). Cancer incidence within the cohort was studied between 1973 and 2008. Standardized registration rates were calculated among the workers and compared to rates observed in the general population. Based on these comparisons, no statistically significant increases were reported for breast cancer among either male or female workers. There was no trend for breast cancer incidence with year of hire, years of being employed, or years since leaving employment. The longitudinal follow up of the cohort and its large size are among the main strengths of the study. The study, however, is limited in its exposure assessment; cancer risk was not calculated by magnetic-field exposure levels, and incidence rates were compared to an external reference group.

Breast cancer incidence was studied among more than 267,000 female textile workers in Shanghai (Li et al., 2013). Between 1989 and 2000, a total of 1,687 incidence breast cancer cases were identified in the cohort. The authors conducted a case-cohort analysis, in which they compared the estimated exposure to ELF EMF among the cases to that among 4,702 non-cases selected from the cohort. Exposure assessment was based on complete work history and a job-exposure matrix was developed specifically for the cohort. No association was observed between cumulative exposure and breast cancer regardless of age, histological type, and whether lag period was used or not. According to an editorial that accompanied the paper, the study added additional evidence against a link between ELF EMF and breast cancer and is consistent with the previous "consistently negative" literature in this area (Feychting, 2013). The editorial also suggested that further studies on breast cancer "have little new knowledge to add," considering the substantial improvement in study quality over time in breast cancer epidemiologic research.

In a cohort of about 120,000 men and women in the Netherlands Cohort study, the relationship between occupational exposure to ELF magnetic fields and cancer incidence was investigated (Koeman et al., 2014). A case-cohort approach was used to analyze the data. A total of 2,077 breast cancer cases among women and no breast cancer cases among men were identified. Exposure to ELF magnetic fields was assigned based on job title using a job-exposure matrix. Breast cancer showed no association with the level of estimated ELF magnetic-field exposure, or the length of employment, or cumulative exposure in the exposed jobs.

Several meta-analyses of breast cancer studies were conducted by Chinese investigators for both female and male breast cancers (Chen et al., 2013; Sun et al., 2013; Zhao et al., 2014). For female breast cancer, 23 case-control studies, published between 1991 and 2007 (Chen et al., 2013), and 16 studies, published between 2000 and 2007 (Zhao et al., 2014), were combined.

Overall, the authors of the two studies reported weak, but statistically significant associations between breast cancer and ELF magnetic-field exposure (OR, 1.07; 95% CI, 1.02-1.01; and OR, 1.10; 95% CI, 1.01-1.20). The authors' conclusions that ELF magnetic fields might be related to breast cancer are contrary to the conclusion of the WHO and other risk assessment panels. This might be explained by the reliance of the authors on mostly earlier and methodologically more limited studies. Sun et al (2013) included 7 case-control and 11 cohort studies of male breast cancer in their meta-analysis. The authors reported a moderate, but statistically significant association between male breast cancer and exposure to ELF EMF (OR, 1.32; 95% CI, 1.14-1.52). Methodological limitations, the small number of cases in the individual studies, and the potential for publication bias may contribute to these findings.

Overall, results from recent large case-control and cohort studies reporting no associations between female breast cancer and residential or occupational exposure to ELF EMF added to the growing support against a causal role for magnetic fields in breast cancer development. This is consistent with the conclusion by the SCENIHR that, overall, studies on adult cancer show no consistent associations (SCENIHR, 2015).

Table 3. Relevant studies of breast cancer, October 2010 – April 2015

Authors	Year	Study
Chen et al.	2013	A meta-analysis on the relationship between exposure to ELF-EMFs and the risk of female breast cancer
Elliott et al.*	2013	Adult cancers near high-voltage overhead power lines
Feytching	2013	Invited commentary: extremely low-frequency magnetic fields and breast cancer--now it is enough!
Koeman et al.	2014	Occupational extremely low-frequency magnetic field exposure and selected cancer outcomes in a prospective Dutch cohort
Li et al	2013	Occupational exposure to magnetic fields and breast cancer among women textile workers in Shanghai, China
Ortega Jacome	2010	
Sorahan et al.	2012	Cancer incidence in UK electricity generation and transmission workers, 1973–2008
Sun et al.	2013	Electromagnetic field exposure and male breast cancer risk: a meta-analysis of 18 studies
Zhao et al.	2014b	Relationship between exposure to extremely low-frequency electromagnetic fields and breast cancer risk: a meta-analysis.
*Comment and Replies on Elliot et al.		
Philips et al.	2013	Letter to the Editor: Adult cancers near high-voltage power lines
De Vocht	2013	Letter to the Editor: Adult cancers near high-voltage power lines
Schüz	2013	Commentary: power lines and cancer in adults: settling a long-standing debate?

Other adult cancers

What was previously known about adult cancers (other than breast cancer)?

In general, scientific panels have concluded that there is not a strong or consistent relationship between other types of cancers that occur in adults (primarily, leukemia, lymphoma, and brain cancer was the focus of epidemiologic studies) and exposure to magnetic fields; however, the possibility cannot be entirely ruled out because the findings have been inconsistent (IARC, 2002; WHO, 2007a). Stronger findings have not been observed in studies with better exposure assessment methods, which have led scientific panels to conclude that the evidence for an association is weak. The IARC classified the epidemiologic data with regard to adult leukemia, lymphoma, and brain cancer as "inadequate" in 2002, and the WHO confirmed this classification in 2007, with much of the remaining uncertainty attributed to limitations in exposure assessment methods.

Much of the research on EMF and adult cancers is related to occupational exposures, given the higher range of exposures encountered in the occupational environment. The main limitation of these studies, however, has been the methods used to assess exposure, with early studies relying simply on a person's occupational title (often taken from a death certificate) and later studies linking a person's full or partial occupational history to representative average exposures for each occupation (i.e., a job-exposure matrix). The latter method, while advanced, still has some important limitations, as highlighted in a review summarizing an expert panel's findings by Kheifets et al. (2009).[12] While a person's occupation may provide some indication of the overall magnitude of their occupational magnetic-field exposure, it does not take into account the possible variation in exposure due to different job tasks within occupational titles, the frequency and intensity of contact to relevant exposure sources, or variation by calendar time. Furthermore, since scientists do not know any mechanism by which magnetic fields could lead to cancer, an appropriate exposure metric is unknown.

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[12] Kheifets et al. (2009) reports on the conclusions of an independent panel organized by the Energy Networks Association in the United Kingdom in 2006 to review the current status of the science on occupational EMF exposure and identify the highest priority research needs.

In order to reduce the remaining uncertainty about whether there is an association between magnetic fields and these cancers, researchers have recommended (1) meta-analyses to clarify inconsistencies and (2) better exposure assessment methods that incorporate a greater level of detail on tasks and exposure characteristics such as spark discharge, contact current, and harmonics (WHO, 2007a; Kheifets et al., 2009). As described in a previous Exponent report (2011), a meta-analysis of occupational epidemiologic studies on adult brain cancer and leukemia has been conducted and published in 2008, partially in response to the WHO's recommendation (Kheifets et al., 2008). Based on all relevant publications of occupational EMF exposure and adult leukemia or brain cancer, summary estimates of association were calculated using various schemes to weight and categorize the study data. The authors reported a small and statistically significant association between leukemia and brain cancer in relation to the highest estimate of magnetic-field exposure in the individual studies. Several findings, however, led the authors to conclude that magnetic-field exposure is not responsible for the observed associations, including the lack of a consistent pattern among leukemia subtypes when the past and new meta-analyses were compared. In addition, for brain cancer, the recent meta-analysis reported a weaker association than the previous meta-analysis, whereas a stronger association would be expected since the quality of studies has increased over time. The authors concluded "the lack of a clear pattern of EMF exposure and outcome risk does not support a hypothesis that these exposures are responsible for the observed excess risk" (Kheifets et al., 2008, p. 677).

Adult brain cancer

What was previously known about adult brain cancer?

As described above, the IARC (2002) and the WHO (2007) reviews classified the epidemiologic evidence on adult brain cancer as inadequate. Results of studies published following these reviews, up to October 2010, as reviewed in the 2011 Exponent report, did not provide evidence that would alter the conclusions of IARC and WHO. While the potential for exposure misclassification were reduced by improved exposure assessment methods in some more recent studies and combined analyses have attempted to clarify inconsistencies, the epidemiologic literature, overall, provided no consistent support for an association between EMF exposure and adult brain cancer. The then most recent report by the SCENIHR described the data on brain cancers as "uncertain" (SCENIHR, 2009, p. 43).

Recent studies (October 2010 – April 2015)

Gomes et al. (2011) conducted a systematic review of the scientific literature on occupational and environmental risk factors and primary adult brain cancer. Among other risk factors, the review also included exposure to EMF. Based on their review, the authors concluded that the "[s]tudies on electromagnetic field exposures and the risk of brain neoplasm are inconsistent," any potential link is "inconclusive," and the "biological plausibility is not strong" (Gomes et al., 2011, p. 95). The authors made recommendations that future studies should concurrently evaluate the effects of multiple potential risk factors, improve exposure assessment to include lifetime exposure, and consider genetic and other potentially confounding factors.

Case-control epidemiologic studies from Brazil (Marcilio et al., 2011) and the United Kingdom (Elliott et al., 2013) have investigated EMF exposure due to residential proximity to high-voltage transmission lines and adult brain cancer. The Brazilian study included 2,357 cases of adult brain cancer deaths and 4,706 controls from the Metropolitan Region of São Paulo, Brazil. The authors reported no association between brain cancer mortality and living near a transmission line at death or calculated magnetic-field levels from these transmission lines at the last residential address (Marcilio et al., 2011).

Elliott et al. (2013), in their case-control epidemiologic study of adult cancers and residential proximity to power lines in the United Kingdom, discussed above, also included 6,781 brain cancer cases. The authors reported no statistically significant elevation in brain cancer risk in association with either distance to the nearest power line from the subjects' homes or estimated magnetic-field levels due to the nearest transmission lines.

In addition to studies of residential EMF exposure, a number of epidemiologic studies have been published since 2010 that investigated the potential relationship between occupational exposure to EMF and brain cancer. Baldi et al. (2011) conducted a case-control study in southwestern France to study the association between brain cancer and estimates of both residential and occupational exposure to EMF. They included 221 brain cancer cases diagnosed between 1999 and 2001 and 442 matched controls from the general population. The authors reported statistically non-significant associations for occupational exposure to ELF EMF based on a crude job-exposure matrix and residential distance within 100 meters of a high-voltage power line. The association with occupational exposure, but not with distance to power lines, became statistically significant when restricted to a subset of brain tumors (meningiomas) (Baldi et al., 2011). Meningiomas, however, constituted only less than one third of brain tumors in the study and the association may have been identified only by *post hoc* analyses.

In the study of cancer incidence among about 80,000 electricity generation and transmission workers in the United Kingdom (discussed earlier), no risk increases for brain cancer was reported either among male or female workers (Sorahan, 2012). Results of a more in-depth analysis focusing on brain cancers in the same population were reported in a separate paper (Sorahan, 2014a). Neither of the two main subtypes of brain tumors (gliomas and meningiomas) showed statistically significant increases with estimated occupational exposure to EMF, even when overall exposure, or exposure during either the more recent time period (within the last 10 years) or earlier time period (more than 10 years ago) was considered. An overall comparison of the cohort with the general population showed no risk increases for brain cancer within the cohort either.

In the Netherlands Cohort Study of about 120,000 adults, 160 and 84 cases of brain cancer were identified among men and women, respectively, during a 17-year period between 1986 and 2003 (Koeman et al., 2014). No statistically significant risk increase or trend was observed for cumulative occupational exposure to ELF EMF either among men or women.

An occupational historical cohort study of 201,784 jet engine manufacturing workers, employed between 1952 and 2001, has examined the development of central nervous system neoplasms in relation to individual level estimates of exposure to 11 physical and chemical agents during work (Marsh et al., 2013). Exposure to EMF, dichotomized as exposed vs. unexposed, was among the investigated occupational exposures. The authors analyzed the data using several statistical approaches: a nested case-control analysis, and a cohort analysis with both internal and external comparisons. None of the investigated occupational exposures, including EMF, showed an association with brain cancer in any of the analyses conducted by the authors.

As part of an international case-control study of brain cancer, occupational exposure to ELF EMF was also analyzed as a potential risk factor (Turner et al., 2014). A total of 3,761 cases of brain cancer diagnosed between 2000 and 2004 and 5,404 controls without brain cancer were included from Australia, Canada, France, Germany, New Zealand, the United Kingdom, and Israel. Assessment of occupational exposure to ELF EMF was based on individual job history and a job-exposure matrix. The authors reported no association with lifetime cumulative exposure, average exposure, or maximum exposure and glioma or meningioma. Although the authors reported an association for both brain cancer types with exposure in the 1 – 4 year time-window prior to diagnosis, a statistically significant decrease in risk for glioma was also reported in the highest maximum exposure category. This observed pattern may correspond to random variation or to exposure misclassification.

In summary, recent studies have not reported consistent increases for brain cancer overall or for specific subtypes with either occupational or residential exposure to ELF EMF. Thus, recent epidemiologic results provide no basis to change the previous conclusion that the evidence is inadequate to support the role of EMF in brain cancer development. Conclusions of recent evaluations by EHFRAN (2012) and SCENIHR (2015) are consistent with this assessment.

Table 4. Relevant studies of adult brain cancer, October 2010 – April 2015

Authors	Year	Study
Baldi et al.	2011	Occupational and residential exposure to electromagnetic fields and risk of brain tumors in adults: A case-control study in Gironde, France
Elliott et al.	2013	Adult cancers near high-voltage overhead power lines
Gomes et al	2011	Occupational and environmental risk factors of adult primary brain cancers: a systematic review
Koeman et al.	2014	Occupational extremely low-frequency magnetic field exposure and selected cancer outcomes in a prospective Dutch cohort
Marcilio et al.	2011	Adult mortality from leukemia, brain cancer, amyotrophic lateral sclerosis and magnetic fields from power lines: a case-control study in Brazil
Marsh et al.	2013	Long-term health experience of jet engine manufacturing workers: VI: incidence of malignant central nervous system neoplasms in relation to estimated workplace exposures
Sorahan et al.	2012	Cancer incidence in UK electricity generation and transmission workers, 1973–2008
Sorahan	2014a	Magnetic fields and brain tumour risks in UK electricity supply workers
Turner et al.	2014	Occupational exposure to extremely low frequency magnetic fields and brain tumour risks in the INTEROCC study

Adult leukemia and lymphoma

What was previously known about adult leukemia/lymphoma?

The same issues discussed above with regard to adult brain cancer are relevant to research on adult leukemia and lymphoma. The WHO classified the epidemiologic evidence as "inadequate" for all adult cancers (WHO 2007a). Studies that were published up to October 2010 and were reviewed in the previous report (Exponent 2011) did not materially change the overall evidence following the WHO report.

Recent studies (October 2010 – April 2015)

The case-control epidemiologic studies of residential proximity to transmission lines in Brazil and the United Kingdom also investigated leukemia (Marcilio et al., 2011; Elliott et al., 2013). The Brazilian study included 1,857 cases of adult leukemia deaths and 4,706 controls. The authors reported a statistically non-significant association with leukemia mortality for subjects' who resided within 50 meters of a transmission line at the time of death. The interpretation of this finding remains unclear because this association was reported to be stronger for lower voltage transmission lines (under 200 kV), where the magnetic-field levels are anticipated to be lower. A slightly elevated, but statistically non-significant, association was reported in the Marcilio et al. study between calculated magnetic fields and mortality due to leukemia, as well. Elliott et al (2013) included 7,823 cases of adult leukemia diagnosed in the United Kingdom between 1974 and 2008 along with close to 80,000 controls. The authors reported no elevated risk or trend for leukemia incidence to diminish with distance or lower estimated magnetic-field exposure from high-voltage power lines.

In a Spanish epidemiologic study of hematologic cancers (Rodriguez-Garcia and Ramos, 2012), the authors reported inverse correlations between acute myeloid leukemia, acute lymphoblastic leukemia (ALL), and distance to thermoelectric power plants and high-density power line networks. No firm conclusion can be drawn from the study, however, because it was severely limited due to the use of ecologic data and rudimentary exposure assessment methods and also lacked an appropriate comparison group.

In the cohort of electricity power plant and transmission workers in the United Kingdom, Sorahan (2012) reported no increase in risk for leukemia either among men or women, and no increasing trend was observed with length of employment. In a more in-depth analysis that focused on leukemia in the same electricity worker cohort, Sorahan (2014b) reported that neither estimated exposure to EMF in the more recent period nor in or more distant periods is related to leukemia development. Although there was a statistical association reported in a sub-analysis for acute lymphocytic leukemia, the author opined that this was most likely due to chance based on the inconsistent overall pattern. In the Netherlands Cohort Study discussed earlier, Koeman et al. (2014) identified 761 and 467 hematopoietic malignancies among men and women, respectively. No increases in risk or trend were observed in association with cumulative exposure to ELF magnetic fields among either men or women.

Results of recent epidemiologic studies did not provide consistent evidence in support of an association of adult leukemia and other lymphohematopoietic malignancies with exposure to EMF either in occupational or residential environments. Therefore, the earlier conclusions as expressed by IARC and WHO, with respect to the evidence being inadequate for adult cancers, remain unchanged. This is consistent with the assessment recently conducted by EFHRAN (2012) and SCENIHR (2015).

Table 5. Relevant studies of adult leukemia/lymphoma, October 2010 – April 2015

Authors	Year	Study
Elliott et al.	2013	Adult cancers near high-voltage overhead power lines
Koeman et al.	2014	Occupational extremely low-frequency magnetic field exposure and selected cancer outcomes in a prospective Dutch cohort
Marcilio et al.	2011	Adult mortality from leukemia, brain cancer, amyotrophic lateral sclerosis and magnetic fields from power lines: a case-control study in Brazil
Rodriguez-Garcia and Ramos	2012	High incidence of acute leukemia in the proximity of some industrial facilities in El Bierzo, northwestern Spain
Sorahan et al.	2012	Cancer incidence in UK electricity generation and transmission workers, 1973–2008
Sorahan	2014b	Magnetic fields and leukaemia risks in UK electricity supply workers

In vivo studies of carcinogenesis

What was previously known from *in vivo* studies of carcinogenesis?

It is standard procedure to conduct studies on laboratory animals to determine whether exposure to a specific agent leads to the development of cancer (USEPA, 2005). This approach is used because all known human carcinogens that were adequately tested also cause cancer in laboratory animals (IARC, 2006). In the field of ELF EMF research, a number of research laboratories have exposed rodents, including those with a particular genetic susceptibility to cancer, to high levels of magnetic fields over the course of the animals' lifetime and performed tissue evaluations to assess the incidence of cancer in many organs. In these studies, magnetic-field exposure has been administered alone (to test for the ability of magnetic fields to act as a complete carcinogen), in combination with a known carcinogen (to test for a promotional or co-carcinogenetic effect), or in combination with a known carcinogen and a known promoter (to test for a co-promotional effect).

Numerous whole animal studies published prior to the WHO review and shortly afterward found that magnetic-field exposure alone does not increase the occurrence of cancer or promote the effects of other known carcinogens (Bernard et al., 2008; Boorman et al., 1999a, 1999b; Chung et al., 2008, 2010; Harris et al., 1998; Mandeville et al., 1997; McCormick et al., 1999; Negishi et al., 2008; Sommer and Lerchel, 2004, 2006; Yasui et al., 1997).

A series of studies, however, from a single German research group reported that the incidence of 7, 12-dimethylbenz[a]anthracene (DMBA)-induced mammary tumors was increased in rats with magnetic field exposure (Löscher et al., 1993, 1994, 1997; Baum et l., 1995; Löscher and Mevissen, 1995; Mevissen et al., 1993a, 1993b, 1996a, 1996b, 1998). Others were unable to replicate these findings (Anderson et al., 1999; Boorman et al., 1999a, 1999b) and further research has suggested that the Fischer 344 (F344) rat used in the German studies is a sensitive sub-strain, while other strains are not (Fedrowitz et al., 2004).

Overall, the WHO concluded the following with respect to *in vivo* research: "There is no evidence that ELF exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate" (WHO 2007a, p. 322). Recommendations for future research included the development of a rodent model for childhood ALL and the continued investigation of whether magnetic fields can act as a promoter or co-carcinogen. Studies published following the WHO review and discussed in the previous Exponent report (2011), overall, provided further evidence against a role for magnetic fields as a co-carcinogenic agent, and strengthened the conclusion that there is inadequate evidence of carcinogenicity from *in vivo* research.

Recent studies (October 2010 – April 2015)

Since 2010, no new animal studies have been published that examine the potential of magnetic-field exposure—alone or in combination with known carcinogens—to have an adverse effect on tumor growth and development.

To further investigate the sensitivity of the F344 rat to the promotional effect of magnetic field exposure in DMBA-induced mammary tumors, however, Fedrowitz and Löscher (2012) examined gene expression in the mammary gland tissues of female F344 rats and female Lewis rats that had been continuously exposed short-term to 1,000 mG, 50-Hz magnetic fields for 14 days. Controls were sham-exposed. All analyses were done in a blinded manner and a 2.5-fold change in expression was selected *a priori* as the cut-off for a response. Of 31,100 genes examined, magnetic-field exposure increased expression of nine genes in the Lewis rat; in contrast, eight genes were increased in expression and six were decreased in the F344 rat. Only one of these genes was affected in both rat sub-strains, but in opposite directions. The gene for α-amylase showed the greatest response to magnetic-field exposure in the F344 rats. In a follow-up study, the same researchers further examined the response of mammary tissue α-amylase to magnetic-field exposure using tissues collected from previous experiments (Fedrowitz et al., 2012). Again, controls were sham-exposed and analyses conducted in a blinded fashion. Both rat sub-strains showed increased α-amylase expression in either the caudal or the cranial mammary tissue in response to magnetic-field exposure, depending on the experiment. Control α-amylase activity, however, was found to vary considerably from one experiment to the next and the authors cautioned that α-amylase activity is highly stress-sensitive, limiting the conclusions that can be drawn.

Five animal studies were recently published that addressed the ability of ELF EMF to damage genetic material (i.e., DNA) (Alcaraz et al., 2014; Borhani et al., 2011; Miyakoshi et al., 2012; Saha et al., 2014; Wilson et al., 2015). Genotoxicity is conceptually linked to carcinogenesis as gene mutation is considered one of the initiating steps in the process by which a cell becomes cancerous. Alcaraz et al. (2014) exposed male mice to 2,000 mG, 50-Hz magnetic fields for 7, 14, 21, or 28 days. Controls were not sham-exposed; however, additional mice were exposed to 50 centi-Gray of X-rays as positive controls and all analyses were conducted in a blinded manner. Although the study investigators reported an increase in micronuclei (i.e., small nucleus-like structures containing DNA indicative of a chromosomal break) in bone marrow erythrocytes 24 hours after magnetic-field exposure, the increase was not duration-dependent and was substantially lower than that induced with X-irradiation. In a similar study, Wilson et al. (2015) examined the effect of exposure to 100 mG, 1,000 mG, or 3,000 mG, 50-Hz magnetic fields for 2 or 15 hours on the gene mutation frequency in sperm and blood cells. Negative controls were sham-exposed; positive controls were exposed to 1 Gray of X-irradiation. Twelve weeks after exposure (the necessary latency to ensure that the sperm had been exposed at the time of DNA synthesis and cell division), the blood mutation frequency after magnetic-field exposure was similar to that of the sham-treated controls; the sperm mutation frequency was slightly, but significantly, increased although the finding was not dose-dependent. In contrast, X-irradiation significantly increased the mutation frequency in both cell types. Borhani et al. (2011) reported increased DNA damage (i.e., fragmentation) in 4-day old mouse embryos of female mice exposed to 5,000 mG, 50-Hz magnetic fields for 4 hours per day, 6 days per week for 2 weeks prior to mating. Controls were sham exposed, but analyses were not conducted in a blinded manner. In contrast, Saha et al. (2014) did not find increased DNA double-strand breaks in the embryonic neuronal stem cell compartment of mouse embryos exposed to 1,000 mG, 50-Hz magnetic fields for 2 hours on gestational day (GD) 13.5 or with continuous or intermittent (5 minutes on, 10 minutes off) exposure to a 3,000 mG magnetic field for 15 hours starting on GD 12.5. This study included a sham-exposed control as well as multiple positive control groups exposed to 10-200 milli-Gray of X-irradiation on GD 13.5. Additionally, appropriate statistical methods were used to account for litter effects. Because of these methodological strengths, greater weight should be given to the Saha et al. study. Finally, Miyakoshi et al. (2012) examined the effect of co-exposure to bleomycin and a 100,000 mG, 50-Hz magnetic field for 3 days on DNA damage in newborn male rats. Controls were sham-exposed, but analyses were not reported to have been conducted in a blinded manner. In the absence of bleomycin treatment or with 5 milligrams per kilogram (mg/kg) of bleomycin, magnetic-field exposure had no effect on the observed frequency of micronuclei, a marker of

DNA double strand breaks. Magnetic-field exposure, however, appeared to increase the micronuclei frequency observed in conjunction with exposure to 10 mg/kg bleomycin.

Three recent studies examined the potential therapeutic use of 50-Hz electromagnetic-field exposure to treat tumors (Berg et al., 2010; El-Bialy and Rageh, 2013; Mahna et al., 2014). In Berg et al. (2010), male SCID-mice were transplanted with 5 x 10^5 MX-1 tumor cells, then treated with 0.1 milligram (mg) of bleomycin injected directly into the tumor, exposed to 200,000 mG, 50-Hz magnetic fields for 8 days (3 hour per day), or both. A thermostat was used during the exposure to ensure a constant temperature of 22 degrees Celsius. Controls were not sham exposed and analyses were not blinded. Compared to untreated controls, all three treatments reduced relative tumor volume and tumor weight; the combination treatment was most effective. Other experiments reported in this study looked at the effect of magnetic-field exposure on tumor cells and lymphocytes *in vitro*. In a similar study (El-Bialy and Rageh, 2013), female Balb mice were injected with Ehrlich ascites carcinoma cells, then treated with the anti-tumor agent, cisplatin, for 3 days, exposed to 100,000 mG, 50-Hz magnetic fields for 2 weeks (1 hour per day), or both. Again, controls were not sham exposed and the analyses were not blinded. All three treatments were reported to increase DNA fragmentation, an early indicator of apoptosis. Cell proliferation and subsequent tumor volume were also reduced. Again, the greatest response came with the combined treatment. Finally, Mahna et al. (2014) injected female Balb/c mice with spontaneous mouse mammary tumor cells, and then exposed them to 150,000 mG, 50-Hz magnetic fields for 10 minutes per day for 12 days. Other groups were exposed to the magnetic field and also treated to electrochemotherapy with bleomycin, electroporation, or bleomycin injection. A sham-exposed control group was included, but analyses were not reported to have been conducted in a blinded manner. As in the other studies, magnetic-field exposure alone or in combination with the other treatments was reported to reduce tumor volume. These studies, although limited, suggest that high magnetic-field exposure may have therapeutic potential in the treatment of tumors.

Overall, the results of these *in vivo* studies are difficult to interpret with regard to carcinogenesis as the animal models, magnetic-field strengths, and exposure durations used vary considerably across the body of studies. Further, none specifically assessed tumor development, although a few looked at the therapeutic potential of high magnetic-field strengths for tumor treatment.

The results of the recent *in vivo* studies on genotoxicity are mixed, with some suggesting slight increases in DNA damage with magnetic-field exposure and others suggesting no effect or finding a response that is not dose or duration dependent. Studies at high magnetic-field strengths suggest that ELF-EMF exposure may be useful in in the treatment of tumors, particularly in combination with other therapies. In summary, the results of these recent studies do not alter the conclusions of the WHO that "[t]here is no evidence that ELF exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate" (WHO 2007a, p. 322).

Table 6. Relevant *in vivo* studies of carcinogenesis, October 2010 – April 2015

Authors	Year	Study
Alcaraz et al.	2014	Effect of long-term 50 Hz magnetic field exposure on the micronucleated polychromatic erythrocytes of mice
Berg et al.	2010	Bioelectromagnetic field effects on cancer cells and mice tumors
Borhani et al.	2011	Analysis of DNA fragmentation in mouse embryos exposed to an extremely low-frequency electromagnetic field
El-Bialy and Rageh	2013	Extremely low-frequency magnetic field enhances the therapeutic efficacy of low-dose cisplatin in the treatment of Ehrlich carcinoma
Fedrowitz and Löscher	2012	Gene expression in the mammary gland tissue of female Fischer 344 and Lewis rats after magnetic field exposure (50 Hz, 100 μT) for 2 weeks
Fedrowitz et al.	2012	Effects of 50 Hz magnetic field exposure on the stress marker α-amylase in the rat mammary gland
Mahna et al.	2014	The effect of ELF magnetic field on tumor growth after electrochemotherapy
Miyakoshi et al.	2012	Tempol suppresses micronuclei formation in astrocytes of newborn rats exposed to 50-Hz, 10-mT electromagnetic fields under bleomycin administration
Saha et al.	2014	Increased apoptosis and DNA double-strand breaks in the embryonic mouse brain in response to very low-dose X-rays but not 50 Hz magnetic fields
Wilson et al.	2015	The effects of extremely low frequency magnetic fields on the mutation induction in mice

In vitro studies of carcinogenesis

In vitro studies are widely used to investigate the mechanisms for effects that are observed in humans and animals. The relative value of *in vitro* tests to human health risk assessment, however, is far less than that of *in vivo* and epidemiologic studies. Responses of cells and tissues outside the body may not always reflect the response of those same cells if maintained in a living system, so the relevance of *in vitro* studies cannot be assumed (IARC, 1992). The IARC and other scientific review panels that systematically evaluated *in vitro* studies of magnetic field exposure concluded that there is no clear evidence indicating a mechanism by which ELF magnetic fields could adversely affect biological processes in cells (IARC, 2002; ICNIRP, 2003; NRPB, 2004). The WHO panel reviewed the *in vitro* research published since the time of those reviews and reached the same conclusion. The WHO noted that previous studies have not indicated a genotoxic effect of ELF magnetic fields on mammalian cells; however, a series of experiments reported DNA damage in human fibroblasts exposed intermittently to 50-Hz magnetic fields (Ivancsits et al., 2002a, 2002b; Ivancsits et al., 2003a, 2003b). These findings were not replicated by other laboratories (Scarfi et al., 2005; Burdak-Rothkamm et al., 2009), and the WHO recommended continued research in this area (WHO, 2007a).

Additional *in vitro* studies investigating the potential of ELF EMF to damage DNA have been conducted in recent years (Buldak et al., 2012; Cho et al., 2014; Duan et al., 2015; Focke et al., 2010; Jin et al., 2012, 2014, 2015; Kim et al., 2010, 2012; Luukkonen et al., 2011, 2014; Mizuno et al., 2014; Yoon et al., 2014). Most of these studies exposed human- or mouse-derived cells to 10,000 or 20,000 mG (50-60 Hz) magnetic fields, although some used fields as low as 100 mG or as high as 70,000 mG. The exposure durations ranged from 10 minutes to 72 hours. Some of these studies found an association between magnetic-field exposure and DNA damage, primarily DNA double strand breaks (Buldak et al., 2012; Duan et al., 2015; Focke et al., 2010; Kim et al., 2010, 2012; Luukkonon et al., 2011, 2014; Yoon et al., 2014). In some cases, this damage was only observed after repeated exposures (Kim et al., 2010) or with intermittent, but not continuous, exposures (Focke et al., 2010) and at higher, rather than lower, magnetic-field strengths (Duan et al., 2015; Yoon et al., 2014). Other studies, however, found no effect of magnetic-field exposure on the observed frequency of DNA damage (Jin et al., 2012, 2014, 2015; Mizuno et al., 2014). Recent studies were also contradictory with regard to the ability of magnetic fields to alter the cellular response to known genotoxicants, with some reporting increased DNA damage with co-exposure (Luukkonen et al., 2011, 2014; Yoon et al., 2014) and others reporting no effect (Jin et al., 2012, 2014, 2015) or a reduction in DNA damage with co-exposure (Buldak et al., 2012). Many of these *in vitro* studies also examined the effects of magnetic-field exposure on other biological mechanisms, including oxidative stress and apoptosis, the results of which are not reported here. Overall, the results of these studies with regard to genotoxicity are conflicting and many suffer from significant design flaws. None of these studies reported genotyping the cells lines used in order to verify their lineage. While the majority of studies incorporated positive DNA damage controls and sham exposure of negative controls, some did not. Also, few studies examined more than one magnetic-field level or exposure duration, making it impossible to look at dose-response relationships. Further, study investigators were blinded to the exposure status of the samples for the analysis in only a few cases. Finally, in the case of Focke et al. (2010), the statistical methods applied in the study have been criticized (Lerchl, 2010). In summary, the results of these recent studies do not alter the conclusions of IARC, the WHO, and other scientific review panels that there is no clear evidence indicating that ELF magnetic fields exert a genotoxic effect on mammalian cells, especially at exposure levels that occur in everyday environments

Table 7. Relevant *in vitro* studies of carcinogenesis, October 2010 – April 2015

Authors	Year	Study
Buldak et al.	2012	Short-term exposure to 50 Hz ELF-EMF alters the cisplatin-induced oxidative response in AT478 murine Squamous cell carcinoma cells
Cho et al.	2014	Enhanced cytotoxic and genotoxic effects of gadolinium following ELF-EMF irradiation in human lymphocytes
Duan et al.	2015	Comparison of the genotoxic effects induced by 50 Hz extremely low-frequency electromagnetic fields and 1800 MHz radiofrequency electromagnetic fields in GC-2 cells
Focke et al.	2010	DNA fragmentation in human fibroblasts under extremely low frequency electromagnetic field exposure
Jin et al.	2012	Effects on micronuclei formation of 60-Hz electromagnetic field exposure with ionizing radiation, hydrogen peroxide, or c-Myc overexpression
Jin et al.	2014	Absence of DNA damage after 60-Hz electromagnetic field exposure combined with ionizing radiation, hydrogen peroxide, or c-Myc overexpression
Jin et al.	2015	Effects on G2/M phase cell cycle distribution and aneuploidy formation of exposure to a 60 Hz electromagnetic field in combination with ionizing radiation or hydrogen peroxide in L132 nontumorigenic human lung epithelial cells
Kim et al.	2010	Repetitive exposure to a 60-Hz time-varying magnetic field induced DNA double-strand breaks and apoptosis in human cells
Kim et al.	2012	Time-varying magnetic fields of 60 Hz at 7 mT induce DNA double-strand breaks and activate DNA damage checkpoints without apoptosis
Luukkonen et al.	2011	Pre-exposure to 50 Hz magnetic fields modifies menadione-induced genotoxic effects in human SH-SY5Y neuroblastoma cells
Luukkonen et al.	2014	Induction of genomic instability, oxidative processes, and mitochondrial activity by 50 Hz magnetic fields in human SH-SY5Y neuroblastoma cells
Mizuno et al.	2014	ELF magnetic fields do not affect cell survival and DNA damage induced by ultraviolet B
Yoon et al.	2014	Increased γ-H2AX by exposure to a 60-Hz magnetic fields combined with ionizing radiation, but not hydrogen peroxide, in non-tumorigenic human cell lines

Reproductive and developmental effects

What was previously known about reproductive and developmental effects?

The epidemiologic literature on reproductive health outcomes and EMF provide no consistent evidence for an association. Two studies published in 2002 received considerable attention because of a reported association between peak magnetic-field exposure greater than approximately 16 mG and miscarriage (Li et al., 2002; Lee et al., 2002). While at the time these two studies relied on improved methodology for exposure assessment, using 24-hour personal magnetic-field measurements (early studies on miscarriage were limited because they used surrogate measures of exposure, including visual display terminal use, electric blanket use, or wire code data), limitations in design of the two studies precluded drawing firm conclusions. It has been proposed that the observed association may be the result of behavioral differences between women with "healthy" pregnancies that went to term (less physically active) and women who miscarried (more physically active) (Savitz, 2002). Furthermore, nearly half of the miscarriages reported in the cohort by Li et al. had magnetic-field measurements taken after miscarriage occurred, when changes in physical activity may have already occurred, and all measurements in Lee et al. occurred post-miscarriage; thus there was high potential for exposure misclassification in the study.

Later exposure assessment studies supported an association between physical activity and peak exposure to EMF (Savitz et al., 2006; Mezei et al., 2006; Lewis et al., 2015).

The scientific panels that have considered these two studies concluded that the possibility of these biases preclude making any conclusions about the effect of magnetic fields on miscarriage (NRPB, 2004; FPTRPC, 2005; WHO, 2007a). The WHO concluded, "There is some evidence for increased risk of miscarriage associated with measured maternal magnetic field exposure, but this evidence is inadequate" (WHO 2007a, p. 254). The WHO stated that, given the potentially high public health impact of such an association, further epidemiologic research is recommended.

Epidemiologic research published following the WHO report and up to 2010, as summarized in the previous report (Exponent, 2011) did not provide sufficient evidence to alter the conclusion that the evidence for reproductive or developmental effects is inadequate. Similarly, studies of animals *in vivo* did not provide evidence to change the conclusions expressed by the WHO.

Recent studies (October 2010 – April 2015)

There is a great variability in the quality in the epidemiologic research that has continued to focus on reproductive and developmental outcomes. Using data from an earlier cohort study of pregnant women and their offspring (Li et al., 2002), researchers studied the association between EMF exposure experienced in the mother's womb during pregnancy and various health outcomes, such as asthma (Li et al., 2011) and obesity(Li et al., 2012), during childhood. The first of these studies (Li et al., 2011) analyzed data on children from 626 pregnancies and reported that that asthmatic children were more likely to have mothers with median magnetic-field exposures >2 mG during pregnancy, compared to children without asthma. The reported association was statistically significant and consistent with an exposure-response pattern. The paper triggered criticism in the scientific literature and it was suggested that unmeasured confounders may be responsible for the observed association (e.g., SES and other indoor and ambient environmental exposures), as many known risk factors for asthma were not controlled for in the analysis and no mechanism is known to explain the association between EMF and asthma (Villeneuve, 2012; Brain et al., 2012). This study, being the first of this kind, requires independent confirmation in studies with more detailed information on and control for known risk factors for childhood asthma.

Li et al. (2012) also published results on childhood obesity and exposure during pregnancy of the mothers using the same data set. The mothers' EMF exposure during pregnancy was related to the weight of their children. The children of mothers with average magnetic-field exposures >1.5 mG were significantly more likely to be over the 97.5 percentile of age-specific weight than children of mothers with exposures ≤ 1.5 mG. A statistical trend between weight and EMF exposure was also reported. Methodological concerns related to the underlying cohort study of pregnant women pertain to all the analyses using the resulting data set. These concerns include the potential for selection bias, a low compliance rate, and the apparent selection of exposure categories after inspection of the data (NRPB, 2002). Because analysis related to asthma and obesity was not part of the original study, and these analyses were conducted on a *post-hoc* basis, it raises potential concerns with multiple comparisons and chance findings.

Canadian researchers investigated the relationship between residential proximity to high-voltage transmission lines and adverse birth outcomes and stillbirth (Auger et al., 2011; Auger et al., 2012). In the first study, the authors identified over 700,000 singleton live births occurring between 1990 and 2004 through provincial birth files. The relative occurrence of adverse birth outcomes, including preterm birth, low birth weight, and being small for gestational age, was investigated in relation to residential distance to transmission lines. The distance of the birth residence to transmission lines was categorized using cut-points at 50, 75, 100, 150, and 400 meters. No voltage information was reported for the transmission lines and no EMF levels were estimated in the study. No associations were observed with residential distance of the mothers for any of the investigated outcomes.

The second study included more than half a million live births along with 2,033 stillbirths in Québec (Auger et al., 2012) occurring between 1998 and 2007. The authors reported that residential proximity to transmission lines was not associated with the likelihood of stillbirth overall and stratified by early preterm (<28 weeks) and late preterm (28-36 weeks) births. No exposure-response pattern was observed overall and by term of stillbirth, although an association was reported for residences within 25 meters of power transmission lines in a sub-analysis. Considering their results, the authors concluded that "residential proximity is unlikely to be associated with stillbirth." The use of distance as a proxy for ELF EMF exposure without information on the level of EMF exposure from the lines is a main limitation of this study, and potential bias may also result due to in- and out-migration from the study area.

The risk of birth defects in relation to residential exposure magnetic fields from high-voltage power lines was investigated in a population-based case-control study in Northern Italy (Malagoli et al., 2012). The authors identified 228 cases of congenital malformations diagnosed in live births, stillbirths, and induced abortions during the period between 1998 and 2006. The authors reported no associations between birth defects and estimated exposure, and concluded that their results do not support the hypothesis that *in utero* exposure of the fetus to EMF is related to birth defects. We note, however, that the study had low statistical power to detect an association because of small number of cases and controls in the study who lived close to transmission lines.

Mahram and Ghazavi (2013) studied the fetal growth and development of children in Iran born to 222 women who lived in close proximity to high-voltage lines during pregnancy (defined as exposed) and 158 women with no exposure during pregnancy. The authors reported no significant differences between the exposed and unexposed groups for any of the investigated outcomes, including pregnancy duration, birth weight, birth length, head circumference, and congenital malformation. The study was, however, severely limited in its exposure assessment and in its control of potential confounding variables. Another study from Iran was a hospital-based case-control study (Shamsi Mahmoudabadi et al., 2013) that included 58 women with spontaneous abortion and 58 pregnant women. The measured magnetic-field levels were reported to be higher among the cases than among controls. The study, however, provides very limited information on major study characteristics, such as subject recruitment, exposure assessment, exposure metric used, and assessment of potential confounders. Thus no firm conclusions can be drawn from the study and it contributes little weight, if any, to an overall assessment of EMF effects on adverse pregnancy outcomes.

Wang et al. (2013) identified 413 pregnant women in China at 8 weeks of gestation between 2010 and 2012. The researchers reported no statistically significant associations between miscarriage and still birth and magnetic-field levels measured at the front door of the participants' homes. The authors reported an association, however, with maximum fields measured in the alleys in front of the homes. Because magnetic-field levels measured at the front door or in the alley in front of the residences are very poor predictors of personal exposure, the study provides a very limited contribution, if any, to our understanding of associations of EMF and birth outcomes.

Residential proximity to power lines during pregnancy and birth outcomes were investigated in Northwest England between 2004 and 2008 (de Vocht et al., 2014a). Hospital records for over 140,000 births were scrutinized and distance to the nearest power lines for the homes during pregnancy were determined using geographical information systems by the researchers. The authors reported moderately lower birth weight within 50 meters of power lines, but observed no statistically significant increase in risk of any adverse clinical birth outcomes (such as preterm birth, small for gestational age, or low birth weight). The limitations of the study include its reliance on distance for exposure assessment and the potential for confounding by SES, as also discussed by the authors. A follow-up investigation to the study indicated that minimizing residual confounding due to missing data for most potentially confounding variables by using multiple imputations and the use of propensity scores reduced the estimated effect size (de Vocht and Lee, 2014).

Bellieni et al. (2012) estimated the effect of ELF EMF present in incubators on the blood melatonin levels on newborns. The authors reported a statistically significant increase of blood melatonin levels among 28 newborns 48 hours after being taken out of the incubators with assumed elevated ELF EMF exposure, but not among 28 control newborns who were not in incubators. Neither the before nor the after values, however, were statistically different from each other in the two groups (incubator vs. control), thus the clinical significance of the findings, if any, is unclear.

The potential influence of magnetic-field exposure on male fertility measures, such as semen quality and abnormalities, was evaluated in a population-based case-control study of healthy semen donors in China (Li et al., 2010). A statistically significant association was reported between a measure of peak magnetic-field levels and poor sperm quality. Personal magnetic-field exposures were measured during a 24-hour period for the included subjects, which could be considered a strength of the study. The authors, however, were not able to control for potential exposure to chemicals and other factors that are known to have a major influence on sperm quality.

Overall, recent epidemiologic research on reproductive and developmental effects has not changed the conclusion that the evidence is inadequate to support an association for any of the investigated adverse reproductive or developmental outcomes. The most recent review by SCENIHR (2015) concluded that "recent results do not show an effect of ELF MF [magnetic field] exposure on reproductive function in humans."

Table 8. Relevant studies of reproductive and developmental effects, October 2010 – April 2015

Authors	Year	Study
Auger et al.	2011	The relationship between residential proximity to extremely low frequency power transmission lines and adverse birth outcomes.
Auger et al.	2012	Stillbirth and residential proximity to extremely low frequency power transmission lines: a retrospective cohort study
Bellieni et al.	2012	Is newborn melatonin production influenced by magnetic fields produced by incubators?
Brain et al	2012	Observations of power-line magnetic fields associated with asthma in children
de Vocht et al.	2014a	Maternal residential proximity to sources of extremely low frequency electromagnetic fields and adverse birth outcomes in a UK cohort
de Vocht and Lee	2014	
Li et al.	2010	Exposure to magnetic fields and the risk of poor sperm quality
Li et al.	2011	Maternal exposure to magnetic fields during pregnancy in relation to the risk of asthma in offspring
Li et al.	2012	A prospective study of in-utero exposure to magnetic fields and the risk of childhood obesity
Mahram and Ghazavi	2013	The effect of extremely low frequency electromagnetic fields on pregnancy and fetal growth, and development
Malagoli et al.	2012	Maternal exposure to magnetic fields from high-voltage power lines and the risk of birth defects
Shamsi Mahmoudabadi et al.	2013	Exposure to Extremely Low Frequency Electromagnetic Fields during Pregnancy and the Risk of Spontaneous Abortion: A Case-Control Study
Villeneuve	2012	Exposure to magnetic fields during pregnancy and asthma in offspring
Wang et al.	2013	Residential exposure to 50 Hz magnetic fields and the association with miscarriage risk: a 2-year prospective cohort study

In vivo reproductive studies (October 2010 – April 2015)

No studies that specifically evaluated the effect of ELF EMF on the female reproductive system were found. Seven studies were conducted that examined the effects of ELF EMF on male reproductive organs and sex hormone concentrations (Akdag et al., 2013; Duan et al., 2014; Hajhosseini et al., 2013; Kim et al., 2014; Tenorio et al., 2010, 2011, 2014). These studies varied considerably in their exposure regimens and reported conflicting findings. While the majority of studies involved sham exposure of controls, only two (Akdag et al., 2013; Duan et al., 2014) incorporated blinding to minimize bias. Kim et al. (2014) found that exposure of mice to 1,000 mG, 50-Hz magnetic fields for 6 weeks or to 200, 1000, or 2,000 mG magnetic fields for 8 weeks did not affect testes weights, but was associated with reduced epididymal sperm counts and increased apoptosis of the spermatogonia. Increased apoptosis in the testes was also reported by Akdag et al. (2013) after exposure of rats to 5,000 mg, 50-Hz magnetic fields (but not 1,000 mG) for 2 hours per day for 10 months, but the specific cell type affected was not identified. Epididymal sperm counts, however, were unaffected. Hajhosseini et al. (2013) reported increased apoptosis after 6 weeks exposure to 80,000 mG, 50-Hz magnetic fields; in this case, however, the apoptotic cells were identified as Sertoli cells, which help to support development of sperm in the seminiferous tubules. These investigators also found that exposure was associated with reduced serum testosterone levels. In contrast, Duan et al. (2014) found no effects of exposure to 5,000 mG magnetic fields for 4 hours per day for 4 or 8 weeks on multiple parameters related to spermatogenesis in the rat, including testes and epididymal weights, epididymal sperm count, serum testosterone, testicular histology, and the various stages of spermatogenesis. They also saw no effect of exposure on the rate of apoptosis in the testes.

Two studies by the same group of investigators (Tenorio et al., 2010, 2011) examined the effects of ELF EMF exposure during late gestation and the early postnatal period on testicular development in rats. Exposures to 10,000 mG, 60-Hz magnetic fields for three 30-minute sessions per day began on GD 13 and continued until postnatal day (PND) 21 or PND 90. Plasma testosterone levels were unaffected by exposure. Although the investigators reported alterations in a number of testicular morphometric measures with exposure on PND 21 (Tenorio et al., 2010), these measures seemed to recover somewhat by PND 90 (Tenorio et al., 2011). Testicular degeneration was highly variable but evident in some rats from both exposure groups. Because littermates are known to be more similar than offspring derived from separate litters, the litter should be used as the statistical unit for analysis, but this was not done in these studies. Finally, Tenorio et al. (2014) conducted another study of adult rats involving similar exposures for 15, 30, or 60 days after thermal heating of the testes. In this case, the authors reported that magnetic-field exposure interfered with recovery from the reversible testicular damageproduced by heating. Overall, many of the studies of ELF EMF exposure in male rats suggest possible reproductive system alterations. The results are highly variable, however, and conflicting across the body of studies. Further, it is not evident if any of the reported changes translate to decrements in reproductive capacity or health.

Three studies examined the effects of ELF EMF exposure during prenatal development (Lahijani et al., 2011; Roshanger et al., 2014; Vallejo and Hidalgo, 2011). Lahijani et al. (2011) reported that a 24-hour exposure of chicken embryos to a 73,200 mG, 50-Hz magnetic field resulted in embryonic deaths, malformations, and extensive tissue hemorrhaging. Both an unexposed control and a sham-exposed control were included in the study; however, control of confounding variables related to exposure and blinded analyses were not described and the data reporting for the study was fairly limited. Further, chicken embryos are not an appropriate model for mammalian embryonic development in that it occurs outside of the maternal animal.

In another study, Roshanger et al. (2014) found that oocyte differentiation and follicular development were adversely affected in the female offspring of mice exposed to 30,000 mG, 50-Hz magnetic fields throughout pregnancy for 4 hours per day. The findings observed in neonatal animals were still apparent in adult offspring, suggesting an irreversible change. It should be noted, however, that this study suffers from significant limitations. Specifically, the controls were not sham exposed, the exposure methods and control of confounding variables were not reported, analyses were not blinded, and appropriate statistical methods to control for potential litter effects were not described. Finally, Vallejo and Hidalgo (2011) reported that continuous exposure to a 150 mG, 50-Hz magnetic field from 98 days premating through 220 days after birth had no effect on the fertility, reproduction, maternal body weight, litter size, or offspring birth weight of mice. Exposure was associated, however, with slight shifts in the growth kinetics of the offspring into adulthood. The control group in this study was not sham exposed and the investigators were not blinded as to the exposure status of the animals. Overall, due to the limitations of these studies, no firm conclusions can be drawn from these studies.

Table 9. Relevant *in vivo* studies of reproductive and developmental effects, October 2010 – April 2015

Authors	Year	Study
Akdag et al.	2013	Can safe and long-term exposure to extremely low frequency (50 Hz) magnetic fields affect apoptosis, reproduction, and oxidative stress?
Duan et al.	2014	Effects of exposure to extremely low frequency magnetic field on spermatogenesis in adult rats
Hajhosseini et al.	2013	Effect of Rosmarinic acid on Sertoli cells apoptosis and serum antioxidant levels in rats after exposure to electromagnetic fields
Kim et al.	2014	Continuous exposure to 60 Hz magnetic fields induces duration- and dose-dependent apoptosis of testicular germ cells
Lahijani et al.	2011	Effects of 50 Hz electromagnetic fields on the histology, apoptosis, and expression of c-Fos and β-Catenin on the livers of preincubated white leghorn chicken embryos
Roshanger et al.	2013	Effect of low-frequency electromagnetic field exposure on oocyte differentiation and follicular development
Tenorio et al.	2010	Testicular development evaluation in rats exposed to 60 Hz and 1 mT electromagnetic field

Authors	Year	Study
Tenorio et al.	2011	Evaluation of testicular degeneration induced by low-frequency electromagnetic fields
Tenorio et al.	2014	Extremely low-frequency magnetic fields can impair spermatogenesis recovery after reversible testicular damage induced by heat
Vallejo and Hidalgo	2011	Growth variations of OF1 mice following chronic exposure of parental and filial generations to a 15 μT, 50 Hz magnetic field

Neurodegenerative disease

What was previously known about neurodegenerative diseases?

Research into the possible effect of magnetic fields on the development of neurodegenerative diseases began in 1995, and the majority of research since then has focused on Alzheimer's disease and a specific type of motor neuron disease called amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. The inconsistency of early Alzheimer's disease studies prompted the NRPB to conclude that there is "only weak evidence to suggest that it [ELF magnetic fields] could cause Alzheimer's disease" (NRPB, 2001b, p. 20). Although early studies on ALS reported an association between ALS mortality and certain electrical occupations, the review panels were hesitant to conclude that the associations provided strong support for a causal relationship. Rather, they felt that an alternative explanation (i.e., electric shocks received at work) may be the source of the observed association.

The majority of the more recent studies reviewed by the WHO reported statistically significant associations between occupational magnetic-field exposure and mortality from Alzheimer's disease and ALS, although the design and methods of these studies were relatively weak (e.g., disease status was based on death certificate data, exposure was based on incomplete occupational information from census data, and there was no control for confounding factors). Furthermore, there was no biological data to support an association between magnetic fields and neurodegenerative diseases. The WHO panel concluded that there is "inadequate" data in support of an association between magnetic fields and Alzheimer's disease or ALS.[13] The panel recommended more research in this area using better methods; in particular, studies that

[13] After considering the entire body of literature and its limitations, the WHO report concluded, "When evaluated across all the studies, there is only very limited evidence of an association between estimated ELF exposure and [Alzheimer's] disease risk" (WHO 2007a, p. 194).

enrolled incident Alzheimer's disease cases (rather than ascertaining cases from death certificates) and studies that estimated electrical shock history in ALS cases were recommended.

Some of the studies published following the WHO review and until 2010, as summarized in the previous report (Exponent, 2011), had indicated an association for Alzheimer disease and ALS, but the study results overall indicated no consistent pattern. The main limitations of these studies include the reliance on death certificates for case identification and diagnosis; the difficulty of identifying a relevant exposure window given the long and nebulous course of this disease; the difficulty of estimating magnetic-field exposure prior to the appearance of the disease; the under-reporting of Alzheimer's disease on death certificates; crude exposure evaluations that are often based on the recollection of occupational histories by friends and family given the cognitive impairment of the study participants; and the lack of consideration of both residential and occupational exposures or confounding variables. Thus, overall, epidemiologic studies published until 2010 did not alter the conclusion that there is inadequate data on Alzheimer's disease or ALS. There was no body of *in vivo* research to suggest an effect and two studies reported no effect of magnetic fields on ALS progression (Seyhan and Canseven, 2006; Poulletier de Gannes et al., 2009). These conclusions were consistent with the then most recent review by the SCENIHR (SCENIHR, 2009).

Recent studies (October 2010 – April 2015)

Occupational exposure estimates remained the focus of the majority of epidemiologic research related to ELF EMF. As part of the previously described occupational cohort study of British electricity supply workers, mortality due to Alzheimer disease, motor neuron disease, and Parkinson's disease were also investigated (Sorahan and Mohammed, 2014). The authors included over 73,000 workers in their analyses, for which the follow-up period included almost 40 years between 1973 and 2010. Exposure to power-frequency magnetic fields were calculated for all workers throughout their working years. Relative risks for the neurodegenerative diseases studied were calculated using Poisson regression. Various exposure categories were considered in the analyses based on cumulative lifetime exposures, and also by considering only the recent or more distant time periods of exposure. The authors reported no statistically significant trends in any of their analyses that would indicate an association between estimated magnetic-field exposure and neurodegenerative disease development.

Mortality due to motor neuron disease in relation to occupational exposure to magnetic fields was evaluated using data from the National Longitudinal Mortality Study in the United States (Parlett et al., 2011). The study included more than 300,000 participants, who provided information on their job at the time of the interview. An EMF job-exposure matrix was used to estimate magnetic-field exposure levels in the participants' jobs. Mortality within the cohort was observed using the National Death Index and cause of death was determined based on death certificates. Over the 2.7 million years of follow-up time, 40 deaths due to motor neuron diseases were observed in the cohort. After adjustment for age, sex, and education, the authors reported no increase in the risk of motor neuron disease in relation to magnetic-field exposure.

From the previously described Netherlands Cohort Study that included about 120,000 male and female study subjects and a follow-up time of about 17 years, analyses on occupational exposures and mortality due to Parkinson's disease have also been reported (Brouwer et al., 2015). In total, 402 deaths among males and 207 deaths among females, due to Parkinson's disease, were observed. The study reported an association between Parkinson's disease mortality and work exposure to EMF categorized as "ever exposed to high EMF," in one analysis. No association, however, was observed for EMF exposure or electric shocks when cumulative exposure was evaluated. Similarly, no statistical trends were observed between any of these two exposures. The authors concluded that their study "does not support the hypothesis that the investigated occupational exposures increase PD [Parkinson's disease] mortality, although we cannot exclude that small risks may exist."

Davanipour et al. (2014) conducted a study of severe cognitive dysfunction and occupational ELF magnetic-field exposure among "3,050 Mexican Americans, aged 65+, enrolled in Phase I of the Hispanic Established Population for the Epidemiologic Study of the Elderly (H-EPESE) study." In-home personal interviews were used to obtain information on occupational history, and socio-demographic variables. Occupational exposure to magnetic fields was classified as low, medium, and high. Cognitive function was evaluated with the use of the mini-mental state exam and cognitive dysfunction was defined as an exam score below 10. Although the authors describe their study as a population-based case-control study, the study is a cross-sectional survey. The authors report a statistically significant association between estimated occupational magnetic-field exposure and severe cognitive dysfunction. The reported association is, however, difficult to interpret due to the number of severe limitations of the study; including the cross-sectional design, the lack of clear clinical diagnosis for case-definition, and the rudimentary assessment of exposure to occupational EMF.

A hospital-based case-control study was conducted by Dutch researchers to evaluate the association between Parkinson's disease and occupational exposure to electric shocks and ELF magnetic fields (van der Mark et al., 2014). The authors included 444 cases of Parkinson's disease and 876 matched controls in their study. Occupational history was determined based on telephone interviews. JEMs were used to categorize jobs for exposure to both electric shocks and magnetic fields. The authors reported no risk increases with any of the estimated exposure metrics for electric shocks or magnetic fields and concluded that their results suggest no association with Parkinson's disease.

Other studies also have addressed the issue of whether electric shocks may explain the observed association reported for neurodegenerative diseases. A few earlier studies, although limited in size and methodology, provided no overall support for an association (Das et al., 2012; Grell et al., 2012). More recent and larger studies have also failed to observe an association with electric shocks. Researchers in the United States conducted a mortality case-control study analyzing death certificates between 1991 and 1999 (Vergara et al., 2015). In total 5,886 ALS deaths were identified during the study period and their exposure experience was compared to 10-times as many matched control deaths. Exposure to electric shocks and ELF magnetic fields was classified based on job titles reported on the death certificates and using corresponding job-exposure matrices. Similar to previous results, a statistically significant association was reported for "electrical occupations," but no consistent associations were observed for either magnetic fields or electric shocks. The main limitation of the study is the use of death certificates for case ascertainment and exposure assessment potentially resulting in disease and exposure misclassifications.

Data from the Swiss National Cohort between 2000 and 2008 was used to assess the relationship between occupational electric shock and magnetic-field exposures and ALS mortality. A total of 2.2 million workers were included in the cohort. Job-exposure matrices for magnetic fields and shocks were used to classify to workers' exposure as high, medium, or low for both exposures based on their occupations reported during the 1990 and 2000 censuses. The authors reported a statistically significant association of ALS mortality with estimated medium or high occupational magnetic-field exposure based at both censuses, but not with estimates of electric shock exposure. The main limitations of the study include the use of mortality data, which may result in disease misclassification, and the use of census data for exposure assessment, which may result in exposure misclassification.

Residential exposure to EMF due to residential proximity to high-voltage transmission lines and neurodegenerative diseases were also examined in epidemiologic studies in Brazil, Switzerland, and the Netherlands. Researchers in Brazil (Marcilio et al., 2011) identified 367 deaths due to ALS between 2001 and 2005 in the city of Sao Paulo and compared their residential proximity to transmission lines to that of 4,706 controls. The authors reported no associations between ALS and either distance from transmission lines or calculated magnetic-field levels.

A Swiss population-based case-control study (Frei et al., 2013) identified cases of neurodegenerative diseases between 1994 and 2010 from hospital discharge records in the whole of Denmark. Six controls from the general population on Denmark were selected for each case. The authors determined the distance from the nearest power line to the residential address for all newly-reported cases and matched controls using geographical information systems. Overall, none of the investigated diseases, including Alzheimer disease and other types of dementia, ALS, Parkinson's disease, or multiple sclerosis was related to residential proximity to power lines. The inclusion of newly-diagnosed cases from hospital discharge records represents a significant methodological improvement over mortality studies. The study, however, was limited by the methods used for the exposure assessment that, as in previous studies, relied on distance to power lines.

A large population-based case-control study of ALS and residential proximity to high-voltage power lines was also conducted in the Netherlands (Seelen et al., 2014). The authors identified

1,139 ALS cases diagnosed between 2006 and 2013. A total of 2,864 controls from general practitioners' rosters were frequency matched to cases from the same time period. The Municipal Personal Records Database was used to determine lifetime residential history for all cases and controls. Addresses were geocoded and the shortest distance to a high-voltage power lines (50 – 380 kV) was determined for each address. No statistically significant association was reported between residential proximity to power lines of any voltage, and ALS. The authors combined their results with the two previously mentioned studies (Marcilio et al., 2011; Frei et al., 2013) and reported no overall associations for living within 200 meters of a high voltage power line (OR 0.9; 95% CI 0.7-1.1). As in other power-line studies, the main limitation of the Dutch study is the use of distance to power lines as an estimate for magnetic-field exposure. By reconstructing lifetime residential history, however, the authors achieved a methodological improvement compared to previous studies.

Two meta-analyses were published that assessed the relationship between occupational exposure to ELF EMF and ALS (Zhou et al., 2012) or neurodegenerative diseases (Vergara et al., 2013). Both of these reported weak to no associations with the investigated outcomes. Vergara et al. (2013) reported evidence for publication bias, and both analyses reported consistent variation in results by study characteristics. Thus, the authors of both analyses concluded that potential within-study biases, evidence of publication bias, and uncertainties in the various exposure assessments greatly limit the ability to infer an association, if any, between occupational exposure to magnetic fields and neurodegenerative disease. In conclusion, the results presented by the two meta-analyses provided no convincing evidence of a relationship between ELF EMF and neurodegenerative disease.

Overall, results from recent epidemiologic literature does not provide sufficient new insight or evidence that would alter the conclusion that the evidence is currently inadequate to support a causal link between exposure to ELF magnetic fields and any of the neurodegenerative diseases. Most of the recent studies provided no support for a potential association. The potential etiologic role of electric shocks in the development of neurodegenerative diseases has also been investigated in several recent studies (Das et al., 2012; Grell et al., 2012; Vergara et al., 2013; van der Mark et al., 2014), but none of these studies reported associations that would support such a hypothesis. The main limitations of most of the recent studies are similar to those in previous studies. These limitations include the potential for exposure misclassification, reliance on mortality data (e.g., under-reporting of Alzheimer's disease on death certificates), the lack of known biophysical mechanism to explain a potential effect, and the resulting difficulty of identifying a relevant exposure window. The most recent scientific review and assessment conducted by SCENIHR (2015) concluded that newly published studies "do not provide convincing evidence of an increased risk of neurodegenerative diseases, including dementia, related to ELF MF [magnetic field] exposure" (SCENIHR, 2015, p.186). Consideration of more recent studies in 2014 and 2015, presented in this review, does not change this conclusion.

Table 10. Relevant studies of neurodegenerative diseases, October 2010 – April 2015

Authors	Year	Study
Das et al.	2012	Familial, environmental, and occupational risk factors in development of amyotrophic lateral sclerosis
Davanipour et al	2014	Severe Cognitive Dysfunction and Occupational Extremely Low Frequency Magnetic Field Exposure among Elderly Mexican Americans
Frei et al.	2013	Residential distance to high-voltage power lines and risk of neurodegenerative diseases: a Danish population-based case-control study
Grell et al.	2012	Risk of neurological diseases among survivors of electric shocks: a nationwide cohort study, Denmark, 1968-2008
Marcilio et al.	2011	Adult mortality from leukemia, brain cancer, amyotrophic lateral sclerosis and magnetic fields from power lines: a case-control study in Brazil
Parlett et al.	2011	Evaluation of occupational exposure to magnetic fields and motor neuron disease mortality in a population-based cohort
Seelen et al.	2014	Residential exposure to extremely low frequency electromagnetic fields and the risk of ALS
Sorahan and Mohammed	2014	Neurodegenerative disease and magnetic field exposure in UK electricity supply workers
van der Mark et al.	2014	Extremely low-frequency magnetic field exposure, electrical shocks and risk of Parkinson's disease
Vergara et al.	2013	Occupational exposure to extremely low-frequency magnetic fields and neurodegenerative disease: A meta-analysis
Vergara et al.	2015	Case-control study of occupational exposure to electric shocks and magnetic fields and mortality from amyotrophic lateral sclerosis in the US 1991-1999
Zhou et al.	2012	Association between extremely low-frequency electromagnetic fields occupations and amyotrophic lateral sclerosis: A meta-analysis

3 Other Areas of Research

Pacemakers and implanted cardiac devices

The sensing system of pacemakers and other implanted cardiac devices (ICD) is designed to be responsive to the heart's electrical signal. For this reason, other electrical signals potentially can interfere with the normal functioning of pacemakers and ICDs, a phenomenon called electromagnetic interference (EMI). Most sources of EMF are too weak to affect a pacemaker or ICD; however, EMF from certain sources (e.g., some appliances and industrial equipment), may cause interference. This section considers potential EMI with implanted cardiac devices such as pacemakers and defibrillators.

In the presence of electromagnetic fields, pacemakers and ICDs can respond in different ways, defined as modes. The probability of interference occurring and the mode of the response depend on the strength and nature of the interference signal, the patient's orientation in the electromagnetic field, the exact location of the device, and the variable parameters of the device that are specific to a patient.

There are a number of experimental studies dating back to the 1990s that were conducted to assess whether interference may occur when currents are induced in the patient's body by ELF electric or magnetic fields (e.g., Toivonen et al., 1991; Astridge et al., 1993; Scholten and Silny, 2001). In general, pacing abnormalities in these tests occurred at magnetic-field levels that are much higher than the levels a person would encounter on a daily basis. Electric fields did produce interference at levels that can be produced by certain electrical sources, but most pacemakers were not affected by high levels of electric fields (up to 20 kV/m) and did not exhibit any pacing abnormalities. Unipolar (single lead) pacemakers tended to be more sensitive to electric fields compared to bipolar (two lead) devices, which are designed specifically to reduce the effects of EMI.

A recent study by Joosten et al. (2009) confirmed earlier work by Scholten and Silny (2001). Both studies found that the performance of a pacemaker in the presence of external ELF electric fields varied considerably based on anatomical and physiological conditions. The 15 study subjects in Joosten et al., (2009) experienced a variance of up to 200% when the interference voltage was applied at the input of their cardiac pacemakers. This variance was due to personal factors such as state of respiration, systole and diastole of the heart, filling of the stomach, and muscle activity. The authors' analyses further suggested that for a 50-Hz electric field to affect the function of the most sensitive unipolar pacemaker, the field levels would have to be greater than 4.3 kV/m and 6.2 kV/m during inhalation and exhalation, respectively. Unipolar pacemakers are less and less common today; the study authors found that in Germany, only 6% of the pacemakers in use have a unipolar sensing system.

In the absence of specific recommendations from medical device manufacturers, two organizations, the American Conference of Governmental Industrial Hygienists (ACGIH) and the Electric Power Research Institute (EPRI), have suggested exposure levels to prevent pacemaker EMI. Both organizations suggest that exposures be kept below 1.5-2 kV/m for electric fields and the ACGIH recommends an exposure level not to exceed 1 Gauss (G) for magnetic fields (ACGIH 2001, EPRI 2004). These recommendations are general in nature and do not address that classes of pacemakers from some manufacturers are quite immune to interference even at levels much greater than these recommended guidelines. Both the ACGIH and EPRI recommend that patients consult their physicians and the respective pacemaker manufacturers before following these organizations' guidelines.

The Food and Drug Administration's Center for Devices and Radiological Health has also issued guidelines for both the development of pacemakers and the design of new electrical devices to minimize susceptibility to electrical interference from any source. Pacemakers are designed to filter out electrical stimuli from sources other than the heart (e.g., the muscles of the chest, currents encountered from touching household appliances, or currents induced by external electric or magnetic fields). Used in both temporary and permanent pacemakers, these electrical filters increase the pacemaker's ability to distinguish extraneous signals from legitimate cardiac signals (Toivonen et al., 1991). Furthermore, most circuitry of modern pacemakers is encapsulated by titanium metal, which insulates the device by shielding the pacemaker's pulse generator from electric fields. Some pacemakers also may be programmed to pace the heart automatically if interference from electric or magnetic fields is detected (fixed pacing mode).

This supports cardiac function and allows the subject to feel the pacing and move away from the source.

Many pacemakers currently in use would not be susceptible to electric fields typically encountered in the daily environment electric fields due to recent design improvements. There remains a very small possibility that some pacemakers, particularly those of older design and with single-lead electrodes, may sense potentials induced on the electrodes and leads of the pacemaker and provide unnecessary stimulation to the heart.

In the past 5 years, scientific research to evaluate potential interference with pacemakers and other implanted cardiac devices has continued. Much of the published literature, however, focused on possible interference from dental, medical, surgical, diagnostic, and therapeutic equipment (e.g., Zaphiratos et al., 2013; Stoopler et al., 2011; Maheshwari et al., 2015; Magnani et al., 2012; Magnani et al., 2014; Yoshida et al., 2014) or personal electronic devices (e.g., Misiri et al., 2012; Tiikkaja et al., 2012a; Kozik et al., 2014). While some of these reports indicate the possibility of interference in certain scenarios with these equipment devices, these interference scenarios are not relevant to transmission line environments due to differences in many factors, including, most importantly, the proximity of the interfering signal sources and the intensity and frequency of the interfering electromagnetic fields.

Several recent studies tested the functioning of cardiac pacemakers and ICDs in high power-frequency (50-60 Hz) EMF. Korpinen and colleagues reported on testing 31 pacemakers placed in human-shaped phantoms directly under a 400-kV transmission line (Korpinen et al., 2012). The results showed no interference with bipolar sensing and interference with only one unipolar pacemaker. The electric-field level was 6.7 – 7.5 kV/m at the time of this interference. The same research team reported on testing 10 different ICD devices placed in a human-shaped phantom in a similar experimental setting under a 400-kV transmission line (Korpinen et al., 2014). Anomalous behavior in one ICD device was reported when the electric-field level exceeded 5.1 kV/m; in a subsequent test, however, the same ICD exhibited no disturbances at an electric field level of 7.5 kV/m.

Souques et al. (2011) investigated electric utility workers with ICDs at electric substations in France. No interference with ICDs was observed with a magnetic field as high as 650 microtesla (µT) [6,500 mG] and electric fields as high as 12.2 kV/m. Tiikkaja et al. (2013) tested 11 volunteers with pacemakers and 13 volunteers with ICDs in an experimental setting at ELF magnetic-field levels up to 300 µT (3,000 mG). Frequencies tested in the experimental setting ranged from 2 to 200 Hz. No interference was observed with ICDs or pacemakers with bipolar sensing, while three pacemakers with unipolar sensing experienced some form of interference. The authors note that magnetic-field intensities used in their study are rare even in industrial environments, and the public is unlikely to encounter such high magnetic fields. Similar findings were reported in earlier reports by the same research group (Tiikkaja et al., 2012b; Tiikkaja et al., 2012c).

French researchers developed an exposure system for testing ICD devices at high power-frequency magnetic fields up to 4,000 µT [40,000 mG] at 50 Hz and up to 3,900 µT at 60 Hz. Four ICDs were tested in these settings and no dysfunctions were reported (Katrib et al., 2013). Numerical modeling performed by the same researchers indicated that exposure to magnetic field levels above 5,000 µT [50,000 mG] or 1,400 µT [14,000 mG] are required for potential interference inhomogeneous or anatomical models, respectively (Katrib et al., 2011).

Napp et al. (2014) evaluated interference thresholds for 110 patients with ICDs in an experimental setting. Patients were exposed to single and combined 50-Hz electric fields and magnetic fields with strength of up 30 kV/m and 2.55 millitesla (mT) [25,500 mG], respectively. Tests were conducted with ICD devices set to maximum and normal sensitivities. No interference was detected for either electric or magnetic fields below European Union (1999/519/EC) exposure limits for the general public (5 kV/m and 100 µT [1,000 mG]). With normal sensitivity, no interference was detected with any of the ICD devices in fields up to about 0.5 mT [5,000 mG] and about 9 – 10 kV/m. The authors concluded that ELF EMF fields typically encountered in daily life do no not interfere with ICDs. High fields that may be present in some occupational environments, however, may cause inappropriate sensing in some ICD devices.

French scientists conducted a survey of almost 1,000 physicians who dealt with patients with active implanted medical devices in France (Hours et al., 2014). About 16% of the physicians reported that they were aware of at least one incident of electromagnetic interference between the implanted device and an EMF source. The main sources for interference were electronic security systems (anti-theft gate of 21% and airport security gate 10%) and medical electromagnetic devices (14%) and in only two instances (<1%) were power lines suspected as the source of the underlying issue. However, no detail was provided on what types of implanted device (e.g., cardiac, urologic, neurologic, or ENF devices) were involved in the latter two instances.

Recent searches of the Manufacturer and User Facility Device Experience database maintained by the United States Food and Drug Administration, the Recalls and Safety Alerts Database of Health Canada's MedEffect™, and the Medicines and Healthcare Products Regulatory Agency, the relevant regulatory body in the United Kingdom, have not identified any reports in these databases as of 2014, that would suggest episodes where EMI occurred with ICDs due to exposure to electric fields or magnetic fields from power lines.

In summary, interference with the functioning of pacemakers or ICDs from strong electric and magnetic fields is theoretically possible under certain circumstances. The likelihood of interference occurring is low, however, particularly with modern devices and sources that produce low levels of EMF. Transmission-line magnetic fields are too weak to affect pacemakers, and electric-field strength decreases with distance and is shielded by trees, buildings, vehicles, fences, and other objects. Most modern ICDs are now designed and constructed with features that make these devices more immune to extraneous electrical signals and significantly reduce the potential for interference. It is recommended that concerned patients contact their doctors to discuss the make and model of their implanted device, their clinical condition, and any lifestyle factors that put them in close contact with strong electric or magnetic fields.

Flora

Electric currents are involved in cell to cell communication in plants (Framm and Lautner, 2007). For this reason, numerous laboratory and on-site studies over the past 35 years have been conducted to assess the possible effects of exposure to ELF EMF from transmission lines on flora—including agricultural crops, trees, and forest and woodland vegetation (e.g., Hodges et al., 1975; Bankoske et al., 1976; McKee et al., 1978; Miller et al., 1979; Rogers et al., 1980; Lee and Clark, 1981; Warren et al., 1981; Rogers et al., 1982; Greene 1983; Hilson et al., 1983; Hodges and Mitchell, 1984; Brulfert et al., 1985; Parsch and Norman, 1986; Conti et al., 1989; Krizaj and Valencic 1989; Ruzic et al., 1992; Reed et al., 1993; Smith et al., 1993; Mihai et al., 1994; Davies 1996; Zapotosky et al., 1996). Researchers have found no adverse effects on plant responses from exposure to EMF levels comparable to that produced by high-voltage transmission lines, including seed germination, seedling emergence and growth, leaf area per plant, flowering, seed production, longevity, and biomass production. The one confirmed adverse effect was damage to the tops of trees growing under or within 40 feet of an *experimental* transmission line operating at a voltage of 1,200 kV, attributable to corona-induced damage to branch tips. The right-of-way (ROW) clearance on *operational* transmission lines is typically a 100 to 200 foot clearance on each side of the line; this area would be cleared of trees or the branches trimmed back sufficiently to prevent flashover and other interference. This effect is not relevant to trees growing at greater distances from the ROW clearance area.

Experimental studies of plants have suggested that magnetic fields increased plant size and weight for radish and barley but not mustard plants (Davies, 1996). A group of studies evaluated the influence of ELF EMF on germination, seedling growth, and subsequent yield. Huang and Wang (2008) evaluated the effects of magnetic fields on the early seed germination of mung beans. The exposures from an inverter system were applied at six different frequencies between 10 Hz and 60 Hz, producing magnetic-field levels from 6 mG to 20 mG. The authors found that magnetic-field exposure at frequencies of 20 and 60 Hz enhanced early mung bean growth, while magnetic fields induced by 10, 30, 40, and 50 Hz frequencies had an inhibitory effect on early mung bean growth. Costanzo (2008) performed a similar study of soy beans exposed *in vitro* to 50-Hz electric fields at strengths of 1.3 kV/m and 2.5 kV/m (root mean square). The author found that this exposure increased soy bean growth in length. In addition, this same study reported that direct current (DC) electric fields of the same peak to peak value had no effect (Costanzo, 2008). A later study by the same investigator reported both increases and decreases in growths of mung beans at varying levels of exposure to ELF electric fields (Costanzo, 2011). A study of 60 Hz magnetic-field treatments of 80,000-200,000 mG on tomato seeds found exposure significantly improved seed performance *in vitro* and plant yield in the soil (De Souza et al., 2010). Researchers in Russia reported that exposure to 50 Hz magnetic field levels at 5,000 mG had a stimulating effect on lipid synthesis in the chloroplast, mitochondrial and cell membranes of radish seedlings (Novitskii et al., 2014). A study of 60-Hz magnetic field exposure at 20,000 mG reported that exposed coffee plants showed significant increase in photosynthesis compared to unexposed plants (Isaac Aleman et al., 2014).

Thus, researchers have found no adverse effects on plant responses at the levels of EMF produced by typical high- or low-voltage transmission lines.

Fauna

Since the 1970s, research has been conducted on the possible effect of EMF on wild and domestic animals in response to concerns about the effects of high-voltage and ultra-high-voltage transmission lines in the vicinity of farms and the natural habitat of wild animals. National agencies and universities have conducted research on an assortment of fauna using a variety of study designs including observational studies of animals in their natural habitats and highly-controlled experimental studies. The research to date does not suggest that AC magnetic or electric fields (or any other aspect of high-voltage transmission lines, such as audible noise) result in adverse effects on the health, behavior, or productivity of fauna, including livestock (e.g., dairy cows, sheep, and pigs) and a variety of other species (e.g., small mammals, deer, elk, birds, and bees).

Dairy cattle and deer

Burchard et al. (2007) is the most recent publication in a long-term series of controlled studies conducted at McGill University (e.g., Rodriquez et al., 2002, 2003, 2004; Burchard et al., 2003; 2004) on the possible effects of strong and continuous EMF exposure on the health, behavior, and productivity of dairy cattle. The broad goal of this research program was to assess whether EMF exposure could mimic the effect of days with long periods of light and increase milk production and feed intake through a hormonal pathway involving melatonin. In previous studies, some differences were reported between EMF-exposed and unexposed cows; however, they were not reported consistently between studies, the changes were still within the range of what is considered normal, and it did not appear that the changes were adverse in nature.

The study by Burchard et al. in 2007 differed from previous studies in that the exposure was restricted to magnetic fields; the outcomes evaluated included the hormones progesterone, melatonin, prolactin, and insulin-like growth factor 1 (IGF-1), as well as feed consumption. No significant differences in melatonin levels, progesterone levels, or feed intake were reported. Significant decreases in prolactin and IGF-1 levels were reported. Thus, similar to the previous studies by this group of investigators, Burchard et al. (2007) did not report findings that suggest magnetic fields cause changes in the melatonin pathway that could result in effects on reproduction or milk production.

The research does indicate that some species of animals are able to detect and orient to DC magnetic fields at levels associated with the earth's static geomagnetic field (~ 500 mG), and this detection may be important for navigational purposes (in particular for species such as birds). Based upon the characteristics of the major hypothesized detection mechanisms and testing in some species, it seems unlikely that a weak 60-Hz magnetic field would be detected or that it would perturb navigational functions.

Along these lines, two studies, both of which received considerable press attention, published analyses of the orientation of cattle and deer using satellite images and field observations that identify a possible geomagnetic component influencing the animals' behavior. A report by Begall et al. (2008) found that domestic cattle and red and roe deer tend to orient their bodies pointing in a northerly direction. The authors' hypothesize that this body orientation is related to the earth's static geomagnetic field because in areas where the earth's magnetic North Pole can be distinguished more easily from the geographic North Pole's high magnetic declination, body orientation appeared to point more towards the magnetic north rather than the geographic north. This northerly body orientation was not correlated with time of day or the position of the sun, and although the authors speculated that the orientation of the animals was not influenced by wind, no analyses were presented. Based on these limited and indirect data the authors raised the possibility that these species can detect the earth's geomagnetic field.

In the second study, Burda et al. (2009) also explored the possible magnetic basis for the northerly orientation of cattle and deer by analyzing their behavior in the vicinity of high-voltage power lines. They report that cattle within 150 m and deer within 50 m of high-voltage power lines exhibit a random body orientation with respect to magnetic north. Some of the effect might be attributed to the deflection of the geomagnetic field by steel towers close to the line, but the authors did not test this possibility. Other analyses indicated that the orientation of cattle differed around power lines running in an east-west or north-south direction, which suggests that neither sun nor wind cues explain the orientation of these animals with respect to magnetic north. If the observed orientations of cattle and deer are attributable to the earth's geomagnetic field, the biological significance is not clear and the authors suggest additional experimental study. With respect to deer, the authors commented that deer prefer to locate near power lines, perhaps because of the browse or shelter afforded.

These observational studies were later criticized by researchers who performed similar analyses but were unable to replicate the initial findings (Hert et al., 2011). Hert et el. (2011) pointed out several methodological limitations in the original studies, including the limited quality of the publicly available satellite images, the un-blinded nature of herd and animal selection and evaluation, and that potential alternative explanations to magnetoreception were ignored. As Hert et al. (2011) concluded these limitations "could easily have led to an unsubstantiated positive conclusion about the existence of magnetoreception" (Hert et al., p. 677). In their response to these criticisms, the authors of the original studies disputed the conclusions of Hert et al., and pointed to potential differences in the analyses conducted by the two groups (Begall et al., 2011). Another recently published study aimed at replicating the original findings reported mixed results (Slaby et al., 2013). They concluded that while solitary cows or cows in small groups showed a tendency for north-south alignment, cows in larger herds did not.

Wild bees and honey bees

Wild bees have an important role in natural plant and forest ecosystems. Research on wild bees was conducted at a site near a United States Navy communications system in Northern Michigan where two species of honeybees were observed living in the vicinity of this facility. The researchers studied the bees' exposure to 76-Hz electric and magnetic fields produced by the facility's communications system and compared the mortality, foraging behavior, and nest architecture to a group of honeybees living at a distance from the facility. A few differences were found in nesting parameters, although the effects were small, inconsistent, and likely due to other factors. Although a small increase in the overwinter mortality was reported in one of the two species studied, the researchers concluded that since the reported differences were small and inconsistent between experiments, there were no findings that raised concern about ELF EMF exposures to wild bees (Zapotosky et al., 1996). This conclusion was confirmed in a review by the United States National Academy of Sciences (NAS, 1997).

More research has focused on commercial honeybees since farmers often place hives on fields near transmission lines. Greenberg et al. (1981) studied the effect of a 765-kV transmission line on honeybee colonies placed at varying distances from the transmission line's centerline, with some hives exposed to EMF from the line and some shielded. Differences between the shielded and unshielded hives were reported at exposures above 4.1 kV/m, including decreases in hive weight, abnormal amounts of propolis at hive entrances, increased mortality and irritability, loss of the queen in some hives, and a decrease in the hive's overwinter survival.

These adverse effects were reported only in the unshielded group. Since the shielding only prevented exposure to electric fields, not magnetic fields, the results indicate that these adverse effects are attributable to electric field exposure. These results have been replicated by other investigators (Rogers et al., 1980, 1981, 1982). Further studies indicated that the effects were indirect, i.e., the electric fields were not affecting the bees directly, and that field levels greater than 200 kV/m were required to affect the behavior of free-flying bees. Thus, heating of the hive by induced currents caused some of the adverse effects and the rest were attributed to shocks within the hive (Bindokas et al., 1988a, 1988b, 1989). Prevention is easily accomplished by placing a grounded metal cover on top of the hive.

Since the nests of wild bees in the ground or in trees contain no metal or highly conductive materials, there appears to be little relevance of such effects to wild bees. At these locations, wild bees also are naturally shielded from electric fields. Laboratory studies indicate that bees are unable to discriminate 60-Hz magnetic fields reliably at intensities less than 4,300 mG, although they can detect fluctuations in the earth's static geomagnetic field as weak as 0.26 mG (Kirschvink et al., 1997). The difference in the sensitivity of honey bees is an illustration that a sensory mechanism has developed to detect static magnetic fields that effectively rejects extraneous signals, in this case AC (60-Hz) magnetic fields.

More recent research on bees and magnetoreception continues to focus on the role that static magnetic fields, like the geomagnetic field of the earth, may play in orientation of various bee species (e.g., Wajnberg et al., 2010; Dovey et al., 2013; Dittmar et al., 2014; Esquivel et al., 2014). The role of static electric fields in communication of bees has also been investigated (e.g., Greggers et al., 2013). Given the varying sensitivity of bees to static and time-varying fields, this large body of literature is not directly relevant to AC transmission lines.

The use of right-of-way corridors under transmission lines has been proposed to play a role in pollinator conservation. A recent review of studies in this area concluded that vegetation in these corridors provides habitat for pollinating species, and when managed properly, it may exert a strong positive effect of native pollinator diversity and local abundance (Wojcik and Buchmann, 2012). These beneficial effects were similar to those reported near edges of cultivated fields (Sydenham et al., 2014). Similar to bee findings, power-line corridors have also been reported to provide alternative habitat for butterflies (Lensu et al., 2011).

A recent study examined bees in power-line corridors in Maryland, Wisconsin, and Oregon (Russell, 2013). The authors reported that integrated vegetation management and planting of native vegetation significantly increased the number of native bee species. The authors also reported that measured EMF levels did not have a demonstrable effect on bee abundance, diversity or behavior.

Birds

A recent study by Dell'omo et al. (2009) analyzed the effects of exposure to magnetic fields from high-voltage power lines during the embryonic and post-hatching period of kestrel nestling. The authors found that exposure does not have any significant short-term physiological effects on these birds.

The ability of birds to detect and use of the earth's geomagnetic field during migration does not translate to a capability to detect 60-Hz magnetic fields. Scientists have hypothesized that the mechanism for detection of the earth's geomagnetic field by birds (and bees), for which there is the most evidence, indicates they would be far less sensitive to 60-Hz magnetic fields. The WHO suggested that power frequency fields at intensities much less than the earth's geomagnetic field of around 500 mG are unlikely to be of much biological significance in relation to birds' navigational abilities because the changes produced by ELF magnetic fields and static magnetic fields are similar (WHO, 2007).

Finally, in a study by Elmusharaf et al. (2007), veterinarians in the Netherlands noted the beneficial effects of AC magnetic fields in poultry. The researchers infected broiler chickens with coccidiosis and reported that exposure to a 50 mG AC magnetic field for 30 minutes each day for a course of 15 days prior to infection provided significant protection against intestinal lesions and reduced growth characteristic of this disease.

Overall, the research over the course of the past 35 to 40 years does not suggest that electric or magnetic fields result in any adverse effects on the health, behavior, or productivity of fauna, including livestock, small mammals, deer, elk, birds, and bees.

Marine life

Although transmission lines mostly traverse the land they also frequently cross water bodies as well. Therefore, the potential for effects on certain marine ecological systems are evaluated regarding the potential impact of EMF on aquatic species in rivers and creeks. To date, there is little or no evidence that fish, mammals, or birds exhibit any harmful effects when exposed to EMF of frequencies close to or at power frequencies (50-60 Hz) at levels found under transmission lines, even for a prolonged period of time (e.g., NRC, 1997a, 1997b; NIEHS 1998; WHO, 2007a). Thus, there is no concern that EMF would have any direct toxic effects on the marine biota.

A number of fish species, however, are reported to make use of the earth's geomagnetic field in navigation and migration, including Pacific salmon (*Oncorhynchus spp.*); the chinook salmon (*O. tschawytscha*) and the steelhead (*O. mykiss*) species particularly spend their adult lives in estuarine or oceanic environments and are well known for their annual spawning runs into freshwater, returning to the home streams and rivers where they were spawned and spent the first few months of their lives (Groot and Margolis, 1998). Pacific salmon are an important part of the history, ecology, and economy of the Pacific Northwest region.

Transmission lines will be a source of potential exposure to 60-Hz magnetic fields in rivers and streams below the conductors, but not electric field exposure because the water shields the fish from electric fields. Since the level of EMF decreases with distance from the source, maximum magnetic-field exposures of fish will occur when they are directly under the lines. The magnetic field levels in rivers and streams below transmission lines would be expected to be significantly lower than for spans on land because clearances for river and stream crossings are usually much higher. Additionally, prolonged exposure is not a critical issue as the fish species of most interest are migratory by nature and will only be exposed to magnetic fields during the relatively short time they take to spawn or travel down or up the river during their life cycle.

The Pacific salmon have been thought to navigate by several mechanisms: detecting and orienting to the earth's geomagnetic field, using a celestial compass (i.e., based on the position of the sun in the sky), and using their innate ability to imprint on their home stream by odor (Groot and Margolis, 1998, Quinn et al, 1981).

Generally, scientific studies have reported that, along with other cues or biological mechanisms, certain species of birds, bees, and fish may have magnetite in certain organs in their bodies, and use magnetite crystals as an aid in navigation (Bullock, 1977; Wiltschko and Wiltschko, 1991, Kirschvink et al, 1993, Walker et al. 1988). Crystals of magnetite have been found in Pacific salmon (Mann et al, 1998; Walker et al, 1998). These magnetite crystals are believed to serve as a compass that orients to the earth's magnetic field. Other studies, however, have not found magnetite in sockeye salmon (*Oncorhynchus nerka*) fry (Quinn et al., 1981). While salmon can apparently detect the geomagnetic field, their behavior is governed by multiple stimuli as demonstrated by the ineffectiveness of magnetic field stimuli in the daytime (Quinn et al., 1982) and the inability of strong magnetic fields from permanent magnets attached to sockeye salmon (Ueda et al., 1998) or other salmon (Yano et al., 1997) to alter their migration behavior. A review of the relevant research on potential effects of marine renewable energy facilities, which also included potential exposure to EMF from associated cables, concluded that although the available evidence is limited, it currently does not indicate that there are biologically significant effects as a result of exposure to EMF (Gill et al., 2012). This conclusion is consistent with a review of magnetic fields from submarine cable and research on interactions of magnetic fields with marine species (BOEMRE, 2011).

An important consideration is that the earth's geomagnetic field is static (0 Hz), in contrast to the oscillating magnetic field created by AC transmission lines, which produce currents that change direction and intensity 60 times per second. Static magnetic fields have fixed polarity, i.e. the earth's magnetic north and south poles. AC transmission lines produce magnetic fields that do not have fixed polarity.

No studies have been conducted to date that specifically examine the effects of AC magnetic fields on the salmon's ability to orient to the earth's geomagnetic field. Theoretical calculations do not suggest that 60-Hz magnetic fields could affect magnetite at levels less than 50 mG (Adair 1994). Studies on the response of other organisms that also use magnetite crystals as one means of navigation can, however, provide useful insight regarding salmon. Kirschvink et al. (1993) reports studies of the effects of AC magnetic fields on honey bees, which use magnetite crystals to navigate. In this study, the honey bees only oriented to an AC magnetic field when it was one million times greater in intensity than the DC field needed to elicit the same orientation response. This difference in intensity indicates that the AC magnetic field is less influential than the DC magnetic field in the navigation of honey bees and potentially other organisms that orient to the earth's geomagnetic field using magnetite crystals (Kirschvink et al., 1993). The level of AC magnetic fields under transmission lines are well below the levels reported in that study.

The scientific literature does not support the conclusion that the EMF associated with the proposed transmission line will have an adverse impact on the survival, growth, and reproduction of organisms in a marine ecosystem. There are no data on the effects of AC EMF on salmon navigation, but based on a study with honey bees, it appears that organisms that use magnetite crystals to orient to the earth's geomagnetic field would be affected only when the field levels are very much greater than the levels expected from a transmission line. Given this evidence and the salmon's ability to navigate using multiple sensory cues, overhead transmission lines are unlikely to have an adverse impact on these species of interest and the aquatic ecosystems of these creeks.

4 Standards and Guidelines

Scientific agencies develop exposure standards and guidelines to protect against known health effects following a thorough review of the relevant research. One of the main objectives of weight-of-evidence reviews is to identify the lowest exposure level below which no health hazards have been found (i.e., a threshold level). Exposure limits are then set *well below* the threshold level established by these reviews to take into account individual variability and sensitivity that may exist in susceptible populations.

The only effects known to be produced in humans by exposure to ELF EMF are seen at very high field levels to which the average person is not typically exposed. The effects are short-term, immediate, perceptible reactions to the electrical stimulation of the muscle and the nervous system. These effects are neither severe nor life-threatening.

Two international scientific organizations, ICNIRP and ICES, have published guidelines for limiting public exposure to ELF EMF to protect against these effects (ICNIRP, 1998, 2010; ICES, 2002). ICNIRP is an independent organization of scientists from various disciplines with expertise in the field of non-ionizing radiation assembled from around the world. It is the formally recognized, non-governmental organization that develops safety guidance for non-ionizing radiation for the WHO, the International Labour Organization, and the European Union.

The ICES is sponsored by the American National Standards Institute and IEEE. The mandate for ICES is the "[d]evelopment of standards for the safe use of electromagnetic energy in the range of 0 Hz to 300 GHz relative to the hazards of exposure to man … to such energy." [14] The ICES encourages a balanced international volunteer participation from several sectors: the interested general public; the scientific, health and engineering communities; agencies of governments; energy producers; and energy users.

[14] The ICES is a 50-year-old internationally recognized, EMF standard-setting organization, which is sponsored by the IEEE that itself was established in 1884. The ICES should not be confused with a group of scientists who have acted together as an advocacy group and banded together in 2003 under the similar name of the International Commission for Electromagnetic Safety.

Although both organizations have the same objectives and use similar methods, their recommended exposure limits to 60-Hz EMF for the general public differ (Table 11). The ICNIRP recommends screening values for magnetic fields of 2,000 mG for the general public and 10,000 mG for workers (ICNIRP, 2010). The ICES recommends maximum permissible exposure of 9,040 mG for magnetic fields (ICES, 2002). The ICNIRP's screening value for exposure to 60-Hz electric fields for the general public is 4.2 kV/m and the ICES screening value is 5 kV/m. Both organizations allow higher exposures if it can be demonstrated that exposures do not produce current densities or electric fields within tissues that exceed basic restrictions on internal current densities or electric fields.

Table 11. Reference levels for whole body exposure to 60-Hz fields: general public

Organization recommending limit	Magnetic fields	Electric fields
ICNIRP reference level	2,000 mG	4.2 kV/m
ICES maximum permissible exposure (MPE)	9,040 mG	5 kV/m 10 kV/m[a]

[a] This is an exception within transmission line ROWs because people do not spend a substantial amount of time in ROWs and very specific conditions are needed before a response is likely to occur (i.e., a person must be well insulated from ground and must contact a grounded conductor) (ICES, 2002, p. 27).

These guidelines were developed following a weight-of-evidence review of the literature by each organization, including epidemiologic and experimental evidence related to both short-term and long-term exposure. Both reviews concluded that the stimulation of nerves and the central nervous system could occur at very high exposure levels immediately upon exposure. While ICNIRP and ICES reference levels for electric fields are similar, the reference levels for magnetic fields in the ICES guideline are higher than those in the ICNIRP guideline. As explained by Reilly (2005), this difference results from the way the two guidelines have extrapolated responses of the retina of the eye to magnetic fields at around 20 Hz to higher frequencies and other tissues. The actual limits on magnetic field exposure, termed basic restrictions published by ICNIRP, however, are higher than those of ICES. Their reviews also concluded that there was not sufficient evidence to support a causal role for EMF in the development of cancer or other long-term adverse health effects. Therefore, neither organization found a basis to recommend quantitative exposure guidelines to prevent effects at lower exposure levels.

Following the publication of their 1998 guidelines, the ICNIRP published an evaluation of the epidemiologic literature (ICNIRP, 2001) and a full weight-of-evidence evaluation of health research on EMF (ICNIRP, 2003), concluding again that there is no basis for exposure restrictions for long-term health effects. In June 2009, the ICNIRP published an updated review of the scientific literature related to potential short- and long-term adverse effects, and *draft* guidelines to replace their 1998 ELF EMF exposure guidelines (ICNIRP, 2009). The final guideline was published in December 2010 and those screening vales are listed in Table 11.

There are no national or state standards in the United States limiting exposures to ELF EMF based on health effects. Two states, Florida and New York, have enacted standards to limit magnetic fields at the edge of transmission line ROWs (150 mG and 200 mG, respectively) (NYPSC, 1978, 1990; FDER, 1989; FDEP, 1996). The basis for limiting magnetic fields from transmission lines was to maintain the status quo so that fields from new transmission lines would be no higher than those produced by existing transmission lines.

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Appendix 1

World Health Organization International EMF Project Summary of ELF EMF Conclusions in EHC 238

Overview

The World Health Organization (WHO) is a scientific organization within the United Nations system whose mandate includes providing leadership on global health matters, shaping the health research agenda, and setting norms and standards. The WHO established the International EMF Project in 1996, in response to public concerns about exposure to electric and magnetic fields (EMF) and possible adverse health effects. The Project's membership includes 8 international organizations, 8 collaborating institutions, and over 54 national authorities. The overall purpose of the Project is to assess health and environmental effects of exposures in the EMF frequency range of 0 – 100 gigahertz (GHz): static fields (0 Hz); extremely low frequency (ELF) fields (up to 100 kilohertz [kHz]); and radiofrequency fields (100 kHz – 300 GHz). A key objective is to evaluate the scientific literature and make a status report on health effects, to be used as the basis for a coherent international response, including the identification of important research gaps and the development of internationally acceptable standards for EMF exposure, the results of which are published as part of the WHO's Environmental Health Criteria (EHC) Programme. Their Monograph on ELF EMF (EHC 238) was published in June 2007

The EHC 238 report used standard scientific procedures, as outlined in the Preamble, to conduct its weight-of-evidence review.[1] The Task Group responsible for the report's overall conclusions consisted of 21 scientists from around the world with expertise in a wide range of disciplines. The Task Group relied on the conclusions of previous weight-of-evidence reviews, where possible, and (with regard to cancer) mainly focused on evaluating studies published after the IARC review in 2002. Specific terms were used by the Task Group to describe the strength of the evidence in support of causality. *Limited evidence* describes a body of research where the findings are inconsistent or there are outstanding questions about study design or other methodological issues that preclude making strong conclusions. *Inadequate evidence* describes a body of research where it is unclear whether the data are supportive or unsupportive of causation because there is a lack of data or there are major quantitative or qualitative issues.

[1] The term weight-of-evidence review is used in this report to denote a systematic review process by a multidisciplinary, scientific panel involving experimental and epidemiologic research to arrive at conclusions about possible health risks, as described in Section 1 above. The WHO Monograph on EMF does not specifically describe their report as a weight-of-evidence review. Rather, they describe conducting a health risk assessment. Although the two terms are similar, a health risk assessment differs from a weight-of-evidence review in that it also incorporates an exposure assessment and an exposure-response assessment.

The following sections describe the conclusions of the WHO by health outcome (cancer, reproductive effects, and neurodegenerative diseases). The conclusions and perspectives of weight-of-evidence reviews conducted by other scientific organizations are discussed, where appropriate, to highlight consistencies and inconsistencies in conclusions.

Data Considered in EHC 238 and the WHO's Conclusions

Cancer

The overwhelming majority of health research related to ELF EMF has focused on the possibility of a relationship with cancer, including leukemia, lymphoma, breast cancer, and brain cancer. The vast majority of epidemiologic studies in this field enrolled persons with a specific cancer type (*cases*); selected a group of individuals similar to the cancer cases (*controls*); estimated past magnetic- or electric-field exposures, or both; and compared these exposures between the cases and controls to test for statistical differences. Some of these studies looked for statistical associations of these diseases with magnetic fields produced by nearby power lines (estimated through calculations or distance) or appliances, while other studies actually measured magnetic-field levels in homes or estimated personal magnetic-field exposures from all sources. In studies of adult cancers, occupational magnetic-field exposures were estimated in some studies as well. *In vivo* studies in this field exposed animals to high levels of magnetic fields (up to 50,000 milligauss [mG]) over the course of their entire lifetime to observe whether exposed animals had higher rates of cancer than unexposed animals. Some of these studies exposed animals to magnetic fields in tandem with a known carcinogen to test whether magnetic-field exposure promoted carcinogenesis. Since the energy level associated with ELF EMF is extremely low, researchers believe it is highly unlikely that electric or magnetic fields can directly damage DNA. Therefore, *in vitro* studies in this field have largely focused on investigating whether ELF EMF could promote damage from other known carcinogens or cause cancer through a pathway other than DNA damage (e.g., hormonal or immune effects or alterations in signal transduction).

The International Agency for Research on Cancer (IARC) is the division of the WHO with responsibility to coordinate and conduct research on the causes of human cancer and the mechanisms of carcinogenesis and to develop scientific strategies for cancer control. The IARC convened a scientific panel in 2001 to conduct an extensive review and arrive at conclusions about the possible carcinogenicity of EMF (IARC, 2002). The IARC has a standard method for classifying exposures based on the strength of the scientific research in support of carcinogenicity. Categories include (from highest to lowest risk): carcinogenic to humans, probably carcinogenic to humans, possibly carcinogenic to humans, unclassifiable, and probably not carcinogenic to humans. As a result of two pooled analyses reporting an association between high, average magnetic-field exposure and childhood leukemia, the epidemiologic data were classified as providing "limited evidence of carcinogenicity"[2] in relation to childhood leukemia. With regard to all other cancer types, the epidemiologic evidence was classified as inadequate. The IARC panel also reported that there was "inadequate evidence of carcinogenicity" in studies of experimental animals. Overall, magnetic fields were evaluated as "possibly carcinogenic to humans." The IARC usage of "*possibly*" denotes an exposure in which epidemiologic evidence points to a statistical association, but other explanations cannot be ruled out as the cause of that statistical association (e.g., bias and confounding)[3] and experimental evidence does not support a cause-and-effect relationship. Considering the published epidemiologic, *in vivo,* and *in vitro* research since the IARC review, the WHO concluded that the IARC's classification of possibly carcinogenic to humans remains accurate (WHO, 2007a).

Childhood Leukemia

The issue that has received the most attention is childhood leukemia. Research in this area was prompted by an epidemiologic study of children in the United States that reported a statistical association between childhood leukemia and a higher predicted magnetic-field level in the home based on characteristics of nearby distribution and transmission lines (Wertheimer and Leeper, 1979). Subsequently, some epidemiologic studies reported that children with leukemia were more likely to live closer to power lines or have higher estimates of magnetic-field exposure (compared to children without leukemia), while other epidemiologic studies did not report this statistical

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2 Each type of evidence is categorized based on the strength of the evidence in support of carcinogenicity. The categories include: sufficient evidence of carcinogenicity, limited evidence of carcinogenicity, inadequate evidence of carcinogenicity, and evidence suggesting lack of carcinogenicity. If a positive association between an exposure and cancer is found (although factors such as chance, bias and confounding cannot be ruled out with reasonable confidence), the epidemiologic evidence is rated as "limited evidence of carcinogenicity." If chance, bias and confounding can be ruled out with reasonable confidence, then the evidence is classified as "sufficient evidence of carcinogenicity." The *in vivo* studies are ranked using a similar system, and the totality of the evidence is then considered to reach a conclusion about a particular exposure's carcinogenicity.

3 Bias refers to any systematic error in the design, implementation, or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease. A confounder is something that is related to both the disease under study and the exposure of interest such that we cannot be sure what causes the observed association, the confounder or the exposure of interest.

association. Of note, the largest epidemiologic studies of childhood leukemia that actually measured personal magnetic field exposure (as opposed to estimating exposure through calculations or distance) did not report evidence to support a causal relationship, nor did they report a dose-response relationship with exposure to higher magnetic-field levels (Linet et al., 1997; McBride et al., 1999; UKCCS, 1999).

In 2000, researchers combined the data from previously published epidemiologic studies of magnetic fields and childhood leukemia that met specified criteria (Ahlbom et al., 2000; Greenland et al., 2000). The researchers pooled the data on the individuals from each of the studies, creating a study with a much larger number of subjects and, as a result, greater statistical power to detect an effect (should one exist) than any single study. In both pooled analyses, a weak association was reported between childhood leukemia and estimates of average magnetic-field exposures greater than 3-4 mG. The authors were appropriately cautious in the interpretation of their analyses, and noted the uncertainty related to pooling estimates of exposure obtained by different methods from studies of diverse design, as did other researchers (e.g., Elwood, 2006). Because of the inherent uncertainty associated with observational epidemiologic studies, the results of these pooled analyses were not considered to provide strong epidemiologic support for a causal relationship. Furthermore, *in vivo* studies have not found that magnetic fields induce or promote cancer in animals exposed under highly controlled conditions for their entire lifespan, nor have *in vitro* studies found a cellular mechanism by which magnetic fields could induce carcinogenesis. As discussed above, these findings resulted in the classification of magnetic fields as a possible carcinogen (IARC, 2002).

The WHO evaluated two subsequently-published studies related to childhood leukemia and magnetic fields (Draper et al, 2005; Kabuto et al., 2006). Draper et al. conducted a case-control study of childhood cancer, which included 9,700 children with leukemia (i.e., cases) and an equal number of children that did not have leukemia (i.e., controls). The study compared the distance of birth address to high-voltage transmission lines among cases and controls and reported a weak association between childhood leukemia and birth addresses within 600 feet of high-voltage transmission lines. Kabuto et al. conducted a smaller case-control study in Japan that measured the average weekly magnetic field in the bedrooms of 312 children with leukemia and 603 children without leukemia. The investigators reported that children with leukemia were more likely to have average magnetic-field levels >4 mG compared to children without leukemia.

The WHO did not assign a high weight or significance to these studies in their overall evaluation, stating that the low participation rate in Kabuto et al. and the use of distance as a proxy for magnetic-field exposure in Draper et al. were important limitations. Less weight should be placed on these studies relative to studies that used good exposure assessment techniques and had high participation rates. The WHO described the results of these two studies as consistent with the classification of limited epidemiologic evidence in support of carcinogenicity and, together with the largely negative *in vivo* and *in vitro* research, consistent with the classification of magnetic fields as a possible carcinogen.

The WHO concluded that several factors might be fully, or partially, responsible for the consistent association observed between high, average magnetic-fields and childhood leukemia, including misclassification of magnetic-field exposure due to poor exposure assessment methods, confounding from unknown risk factors, and selection bias.[4] The WHO concluded that reconciling the epidemiologic data on childhood leukemia and the negative (i.e., no hazard) experimental findings through innovative research is currently the highest priority in the field of ELF EMF research. Given that few children are expected to have average magnetic-field exposures greater than 3-4 mG, however, the WHO stated that the public health impact of magnetic fields on childhood leukemia would be low if the association were causal.

Breast Cancer

Research on breast cancer has examined the possible effects of ELF EMF from three sources: workplace exposures, residential exposure from power lines, and electric blankets. Some of the early epidemiologic studies in this field reported a weak association between breast cancer and higher magnetic-field exposures, while others did not; however, the conclusions that could be drawn from this initial body of research were limited because of study quality issues (e.g., poor exposure assessment, inadequate control for confounding variables, and small sample sizes within subgroups with reported associations). Review panels evaluating this initial body of research

4 Selection bias arises if there are differences in the persons who participate in a study compared to the persons who do not participate in a study that are related to the exposure and differential by case/control status. For example, if the parents of a child with leukemia were informed that the study was investigating magnetic-field exposure and they resided close to a transmission line, they may be more likely to participate than a family that lived far from a transmission line. As a result, children with leukemia that lived closer to transmission lines (and with a presumably higher magnetic-field exposure) would be over-represented in the study population compared to the source population. In this scenario, the study may report that children with leukemia are more likely to have higher magnetic-field exposure when, if the entire source population of leukemia cases were to be considered, there would be no difference in the exposure levels between leukemia cases and controls.

concluded that the evidence in support of an association was weak, but should be further evaluated with higher quality studies (NRPB, 2001a; IARC, 2002; ICNIRP, 2003).

A large number of studies on breast cancer and magnetic-field exposure have been conducted since the publication of the IARC review in 2002. These studies were systematically reviewed by the WHO and included seven studies that estimated residential magnetic-field exposure, four studies reporting associations with electric blanket usage, and nine studies that estimated occupational magnetic-field exposure. No consistent associations between magnetic-field exposure and breast cancer were reported in these studies. The WHO concluded that this recent body of research was higher in quality compared with previous studies, and, for that reason, provides strong support to previous consensus statements that magnetic-field exposure does not influence the risk of breast cancer. In summary, the WHO stated “With these [recent] studies, the evidence for an association between ELF magnetic field exposure and the risk of female breast cancer is weakened considerably and does not support an association of this kind” (WHO, 2007a, p. 9). The WHO recommended no further research with respect to breast cancer and magnetic-field exposure.

Breast cancer has received additional attention because of some initial epidemiologic and experimental findings suggesting that magnetic fields may depress levels of the hormone melatonin (which is believed to have anti-carcinogenetic effects), leading to the development of breast cancer. A comprehensive weight-of-evidence review by the Health Protection Agency of Great Britain (HPA) in 2006 concluded that the evidence to date did not support the hypothesis that exposure to magnetic fields affects melatonin levels, or the risk of breast cancer in general (HPA, 2006). The WHO also considered this body of research, concluding “Overall, these data do not indicate that ELF electric and/or magnetic fields affect the neuroendocrine system in a way that would have an adverse impact on human health and the evidence is thus considered inadequate” (WHO, 2007a, p. 186).

Adult leukemia and brain cancer

A large number of studies of variable quality and using a wide range of techniques have been conducted in both occupational and residential settings to explore the possible relationship between EMF exposure and adult brain cancer and leukemia. The scientific committees assembled by the IARC, the International Commission on Non-Ionizing Radiation Protection (ICNIRP), and the National Radiological Protection Board of Great Britain (NRPB) concluded that the evidence is weak and does not support a role for electric or magnetic fields in the etiology of brain cancer or leukemia among adults (NRPB, 2001a; IARC, 2002; ICNIRP, 2003). The WHO reviewed the body of research published since the time of these reviews, including three studies estimating residential exposure, four cohort studies estimating occupational exposure, and eight case-control studies reporting on occupation and brain cancer or leukemia risk. The WHO concluded, "[i]n the case of adult brain cancer and leukaemia, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF [EMF] and the risk of these diseases remains inadequate" (WHO, 2007a, p. 307). The WHO panel recommended updating the existing European cohorts of occupationally exposed individuals and then pooling the epidemiologic data on brain cancer and adult leukemia to confirm the absence of an association.

In vivo and *in vitro* research on carcinogenesis

It is standard procedure to conduct studies of laboratory animals to determine whether exposure to a specific agent leads to the development of cancer (USEPA, 2005). This approach is used because all known human carcinogens cause cancer in laboratory animals. In the field of ELF EMF research, a number of research laboratories have exposed rodents with a particular genetic susceptibility to cancer to high levels of magnetic fields over the course of their lifetime and performed tissue evaluations to assess the incidence of cancer in many organs. In these studies, magnetic-field exposure has been administered alone (to test for the ability of magnetic fields to act as a complete carcinogen), in combination with a known carcinogen (to test for a promotional or co-carcinogenetic effect), or in combination with a known carcinogen and a known promoter (to test for a co-promotional effect). The WHO described four large-scale, long-term studies of rodents exposed to magnetic fields over the course of their lifetime that did not report increases in any type of cancer (Mandeville et al., 1997; Yasui et al., 1997; Boorman et al., 1999a, 1999b; McCormick et al., 1999). No directly relevant animal model for childhood acute lymphoblastic leukemia (ALL) currently exists. Some animals, however, develop a type of lymphoma similar to childhood ALL and studies exposing transgenic mice predisposed to this lymphoma to power-frequency magnetic fields have not reported an increased incidence of lymphoma associated with exposure (Harris et al., 1998; McCormick et al., 1998; Sommer and Lerchel 2004). Based on this body of research, the WHO panel concluded that exposure to ELF magnetic fields, does not appear to cause cancer alone, although it is a high priority to identify and perform studies on an animal model that is more directly relevant to childhood ALL.

Studies investigating whether exposure to magnetic fields can promote cancer or act as a co-carcinogen used known cancer-causing agents, such as ionizing radiation, ultraviolet radiation, or other chemicals. No effects were observed for studies on chemically-induced preneoplastic liver lesions, leukemia/lymphoma, skin tumors, or brain tumors; however, the incidence of DMBA-induced mammary tumors was increased with magnetic-field exposure in a series of experiments (Löscher et al., 1993, 1994, 1997; Baum et al., 1995; Löscher and Mevissen, 1995; Mevissen et al., 1993a, 1993b, 1996a, 1996b, 1998), suggesting that magnetic-field exposure increased the proliferation of mammary tumor cells. These results were not replicated in a subsequent series of experiments in another laboratory (Anderson et al., 1999; Boorman et al.1999; NTP, 1999), possibly due to differences in experimental protocol and the species strain (Fedrowitz et al., 2004). Some studies have reported an increase in genotoxic effects among exposed animals (e.g., DNA strand breaks in the brains of mice [Lai and Singh, 2004]), although the results have not been replicated.

In summary, the WHO concluded with respect to *in vivo* research, "[t]here is no evidence that ELF exposure alone causes tumours. The evidence that ELF field exposure can enhance tumour development in combination with carcinogens is inadequate" (WHO, 2007, p. 322) Recommendations for future research include the development of a rodent model for childhood ALL and the continued investigation of whether magnetic fields can act as a co-carcinogen.

In vitro studies are widely used to investigate the mechanisms for effects that are observed in humans and animals. The relative value of *in vitro* tests to human health risk assessment, however, is much less than that of *in vivo* and epidemiologic studies. Responses of cells and tissues outside the body may not always reflect the response of those same cells if maintained in a living system, so the relevance of *in vitro* studies cannot be assumed (IARC, 1992).

The IARC and other scientific review panels that systematically evaluated *in vitro* studies concluded that there is no clear evidence indicating how ELF magnetic fields could adversely affect biological processes in cells (IARC, 2002; ICNIRP, 2003; NRPB, 2004). The WHO panel reviewed the *in vitro* research published since the time of these reviews and reached the same conclusion. The WHO noted that previous studies have not indicated a genotoxic effect of ELF magnetic fields on mammalian cells, however a series of experiments reported DNA damage in human fibroblasts exposed intermittently to 50-Hz magnetic fields (Ivancsits et al., 2002a, 2002b; Ivancsits et al., 2003a, 2003b). These findings have not been replicated by other laboratories (Scarfi et al., 2005), and the WHO recommended continued research in this area. Research in the field of *in vitro* genotoxicity of magnetic fields combined with known DNA-damaging agents is also recommended, following suggestive findings from several laboratories. As noted by the Swedish Radiation Protection Authority, the levels at which these effects were observed are much higher than the levels we are exposed to in our everyday environments and therefore are not directly relevant to questions about low-level, chronic exposures (SSI, 2007). *In vitro* studies investigating other possible mechanisms, including gene activation, cell proliferation, apoptosis, calcium signaling, intercellular communication, heat shock protein expression and malignant transformation, have produced "inconsistent and inconclusive" results (WHO, 2007a, p. 347).

Reproductive Effects

Epidemiologic studies have been conducted to observe whether maternal or paternal EMF exposures are associated with adverse reproductive effects, including effects on fertility, reproduction, miscarriage, and prenatal and postnatal growth and development. A body of *in vivo* literature is also available on this topic. Early studies on the potential effect of EMF exposures on reproductive outcomes were limited because the majority of the studies used surrogate measures of exposure (including visual display terminal use, electric blanket use, or wire code data) or assessed exposure retrospectively.

Two studies related to miscarriage improved exposure assessment by directly measuring magnetic-field exposure. These two studies reported a positive association between miscarriage and exposure to high maximum, or instantaneous, peak magnetic fields (Li et al., 2002; Lee et al., 2002). No consistent associations were reported, however, with high, average magnetic-field levels, the typical method for assessing magnetic-field exposure. The WHO noted several issues that have been raised by other investigators and scientific review panels concerning the validity of these associations (HCN, 2004; NRPB, 2004; Feychting et al., 2005; Mezei et al., 2005; Savitz et al., 2006). First, the studies had a low response rate, which means that the case and control groups may not be comparable because those who participated in the study may have differed from those who declined (i.e., selection bias). Second, in the study by Lee et al. (2002), magnetic-field measurements were taken 30 weeks after a woman's last menstrual period. Some of these women had already miscarried at 30 weeks when magnetic-field exposure was measured. This introduces the possibility for bias because pregnancy may alter physical activity levels and physical activity may be associated with magnetic-field exposure in pregnant women, as confirmed in a study by Savitz et al. (2006). It is possible that the women who miscarried prior to 30 weeks in the study by Lee et al. (2002) subsequently increased their physical activity levels (i.e., returned to work or their normal routine), which resulted in greater opportunities to encounter higher peak magnetic-field levels. Furthermore, there is no biological basis to indicate that EMF increases the risk of reproductive effects. *In vivo* studies exposed animals to high levels of EMF and reported no significant, adverse developmental effects. The WHO stated that *in vivo* studies on other reproductive outcomes are inadequate at this time.

The WHO concluded that, overall, the body of research does not suggest that maternal or paternal exposures to ELF EMF cause adverse reproductive outcomes. The evidence from epidemiologic studies on miscarriage is inadequate, and the WHO recommended further research on this possible association, although they gave it a low priority.

Neurodegenerative Diseases

Research into the possible effect of magnetic fields on the development of neurodegenerative diseases began in 1995, and the majority of research since then has focused on Alzheimer's disease and a specific type of motor neuron disease called amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease. The inconsistency of the Alzheimer's studies prompted the NRPB[5] to conclude that there is "only weak evidence to suggest that it [extremely low frequency magnetic fields] could cause Alzheimer's disease" (NRPB, 2001b, p. 20). Early studies on ALS, which had no obvious biases and were well conducted, reported an association between ALS mortality and estimated occupational magnetic-field exposure. The review panels, however, were hesitant to conclude that the associations provided strong support for a causal relationship between ALS and occupational magnetic-field exposure. The scientific panels felt that an alternative explanation (i.e., electric shocks received at work) may be the source of the observed association. The NRPB

[5] The NRPB merged with the Health Protection Agency in April 2005 to form its new Radiation Protection Division and subsequently became part of Public Health England in 2013.

concluded: "[i]n summary, the epidemiological evidence suggests that employment in electrical occupations may increase the risk of ALS, possibly, however, as a result of the increased risk of receiving an electric shock rather than from the increased exposure to electromagnetic fields" (NRPB, 2001b, p. 20).

Most recent studies reported associations between occupational magnetic-field exposure and mortality from Alzheimer's disease and ALS, although the design and methods of these studies were relatively weak (disease status based on death certificate data, exposure based on incomplete occupational information from census data, and no control for confounding factors). There is currently no biological data to support an association between magnetic fields and neurodegenerative diseases. The WHO concluded that there is inadequate data in support of an association between magnetic fields and Alzheimer's disease or ALS. The WHO highly recommended that further studies be conducted in this area, particularly studies where the association between magnetic fields and ALS is estimated while controlling for the possible confounding effect of electric shocks.

Appendix 2

WHO Fact Sheet

Fact sheet N°322
June 2007

Electromagnetic fields and public health
Exposure to extremely low frequency fields

The use of electricity has become an integral part of everyday life. Whenever electricity flows, both electric and magnetic fields exist close to the lines that carry electricity, and close to appliances. Since the late 1970s, questions have been raised whether exposure to these extremely low frequency (ELF) electric and magnetic fields (EMF) produces adverse health consequences. Since then, much research has been done, successfully resolving important issues and narrowing the focus of future research.

In 1996, the World Health Organization (WHO) established the International Electromagnetic Fields Project to investigate potential health risks associated with technologies emitting EMF. A WHO Task Group recently concluded a review of the health implications of ELF fields (WHO, 2007).

This Fact Sheet is based on the findings of that Task Group and updates recent reviews on the health effects of ELF EMF published in 2002 by the International Agency for Research on Cancer (IARC), established under the auspices of WHO, and by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) in 2003.

ELF field sources and residential exposures

Electric and magnetic fields exist wherever electric current flows - in power lines and cables, residential wiring and electrical appliances. **Electric** fields arise from electric charges, are measured in volts per metre (V/m) and are shielded by common materials, such as wood and metal. **Magnetic** fields arise from the motion of electric charges (i.e. a current), are expressed in tesla (T), or more commonly in millitesla (mT) or microtesla (µT). In some countries another unit called the gauss, (G), is commonly used (10,000 G = 1 T). These fields are not shielded by most common materials, and pass easily through them. Both types of fields are strongest close to the source and diminish with distance.

Most electric power operates at a frequency of 50 or 60 cycles per second, or hertz (Hz). Close to certain appliances, the magnetic field values can be of the order of a few hundred microtesla. Underneath power lines, magnetic fields can be about 20 µT and electric fields can be several thousand volts per metre. However, average residential power-frequency magnetic fields in homes are much lower - about 0.07 µT in Europe and 0.11 µT in North America. Mean values of the electric field in the home are up to several tens of volts per metre.

Task group evaluation

In October 2005, WHO convened a Task Group of scientific experts to assess any risks to health that might exist from exposure to ELF electric and magnetic fields in the frequency range >0 to 100,000 Hz (100 kHz). While IARC examined the evidence regarding cancer in 2002, this Task Group reviewed evidence for a number of health effects, and updated the evidence regarding cancer. The conclusions and recommendations of the Task Group are presented in a WHO Environmental Health Criteria (EHC) monograph (WHO, 2007).

Following a standard health risk assessment process, the Task Group concluded that there are no substantive health issues related to ELF electric fields at levels generally encountered by members of the public. Thus the remainder of this fact sheet addresses predominantly the effects of exposure to ELF magnetic fields.

Short-term effects

There are established biological effects from acute exposure at high levels (well above 100 µT) that are explained by recognized biophysical mechanisms. External ELF magnetic fields induce electric fields and currents in the body which, at very high field strengths, cause nerve and muscle stimulation and changes in nerve cell excitability in the central nervous system.

Potential long-term effects

Much of the scientific research examining long-term risks from ELF magnetic field exposure has focused on childhood leukaemia. In 2002, IARC published a monograph classifying ELF magnetic fields as "possibly carcinogenic to humans". This classification is used to denote an agent for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence for carcinogenicity in experimental animals (other examples include coffee and welding fumes). This classification was based on pooled analyses of epidemiological studies demonstrating a consistent pattern of a two-fold increase in childhood leukaemia associated with average exposure to residential power-frequency magnetic field above 0.3 to 0.4 µT. The Task Group concluded that additional studies since then do not alter the status of this classification.

However, the epidemiological evidence is weakened by methodological problems, such as potential selection bias. In addition, there are no accepted biophysical mechanisms that would suggest that low-level exposures are involved in cancer development. Thus, if there were any effects from exposures to these low-level fields, it would have to be through a biological mechanism that is as yet unknown. Additionally, animal studies have been largely negative. Thus, on balance, the evidence related to childhood leukaemia is not strong enough to be considered causal.

Childhood leukaemia is a comparatively rare disease with a total annual number of new cases estimated to be 49,000 worldwide in 2000. Average magnetic field exposures above 0.3 µT in homes are rare: it is estimated that only between 1% and 4% of children live in such conditions. If the association between magnetic fields and childhood leukaemia is causal, the number of cases worldwide that might be attributable to magnetic field exposure is estimated to range from 100 to 2400 cases per year, based on values for the year 2000, representing 0.2 to 4.95% of the total incidence for that year. Thus, if ELF magnetic fields actually do increase the risk of the disease, when considered in a global context, the impact on public health of ELF EMF exposure would be limited.

A number of other adverse health effects have been studied for possible association with ELF magnetic field exposure. These include other childhood cancers, cancers in adults, depression, suicide, cardiovascular disorders, reproductive dysfunction, developmental disorders, immunological modifications, neurobehavioural effects and neurodegenerative disease. The WHO Task Group concluded that scientific evidence supporting an association between ELF magnetic field exposure and all of these health effects is much weaker than for childhood leukaemia. In some instances (i.e. for cardiovascular disease or breast cancer) the evidence suggests that these fields do not cause them.

International exposure guidelines

Health effects related to short-term, high-level exposure have been established and form the basis of two international exposure limit guidelines (ICNIRP, 1998; IEEE, 2002). At present, these bodies consider the scientific evidence related to possible health effects from long-term, low-level exposure to ELF fields insufficient to justify lowering these quantitative exposure limits.

WHO's guidance

For high-level short-term exposures to EMF, adverse health effects have been scientifically established (ICNIRP, 2003). International exposure guidelines designed to protect workers and the public from these effects should be adopted by policy makers. EMF protection programs should include exposure measurements from sources where exposures might be expected to exceed limit values.

Regarding long-term effects, given the weakness of the evidence for a link between exposure to ELF magnetic fields and childhood leukaemia, the benefits of exposure reduction on health are unclear. In view of this situation, the following recommendations are given:

- Government and industry should monitor science and promote research programmes to further reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure. Through the ELF risk assessment process, gaps in knowledge have been identified and these form the basis of a new research agenda.
- Member States are encouraged to establish effective and open communication programmes with all stakeholders to enable informed decision-making. These may include improving coordination and consultation among industry, local government, and citizens in the planning process for ELF EMF-emitting facilities.
- When constructing new facilities and designing new equipment, including appliances, low-cost ways of reducing exposures may be explored. Appropriate exposure reduction measures will vary from one country to another. However, policies based on the adoption of arbitrary low exposure limits are not warranted.

Further reading

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Appendix 3

Comment on the BioInitiative Report

Background

In August 2007, an *ad hoc* group of 14 scientists and public health and policy consultants published an on-line report titled "*The BioInitiative Report: A Rationale for a Biologically-based Public Exposure Standard for Electromagnetic Fields (ELF and RF)*." The group's objective was to "assess scientific evidence on health impacts from electromagnetic radiation below current public exposure limits and evaluate what changes in these limits are warranted now to reduce possible public health risks in the future" (p. 4). The individuals who comprised this group did not represent any well-established regulatory agency, nor were they convened by a recognized scientific authority. The report is a collection of 17 sections on various topics each authored by 1 to 3 persons from the working group. The research on both ELF and radio frequency (RF) EMF was addressed, with major portions of the report focused largely or entirely on RF research. Epidemiologic literature related to ELF EMF and childhood cancers, Alzheimer's disease, and breast cancer was discussed, as well as experimental data for a number of mechanistic hypotheses.

In 2012 an updated version of the BioInitiative Report was posted on the internet. The updated report, along with the previously published reviews, also considered scientific research published on ELF and RF EMF in the 5 years since the first report. The 2012 BioInitiative Report (1,479 pages in total) is a compilation of 24 chapters written by an expanded group of 29 different authors. The 2012 BioInitiative Report includes chapters from the 2007 BioInitiative Report. The methods and approach the authors of the 2012 update employed were similar to those in the original report. The main conclusions of the 2012 BioInitiative Report are very similar to the conclusion expressed in the earlier version; namely, that existing standards that set exposure limits to ELF and RF EMF are insufficient.

Reviews of the BioInitiative Report by Scientific Organization

Following the publication of the BioInitiative Report in 2007, several scientific agencies commented on its methods and conclusions. These included the Health Council of the Netherlands (HCN), the Australian Centre for Radiofrequency Bioeffects Research (ACRBR), the EMF-NET Steering Committee of the European Commission, and the IEEE's Committee on Man and Radiation. The main comment and criticism of all of these agencies were that the BioInitiative Report did not follow the generally accepted methods of a standard weight-of-evidence review and, for this reason, its conclusions and recommendations were not convincing (EMF-NET, 2007; HCN, 2008; ACRBR, 2008; COMAR, 2009). The ACRBR wrote, "As it stands it [the BioInitiative Report] merely provides a set of views that are not consistent with the consensus of science, and it does not provide an analysis that is rigorous-enough to raise doubts about the scientific consensus" (ACRBR, 2008, p. 2).

EMF-NET, a committee funded by the European Commission, opined that the summary for the public is "written in an alarmist and emotive language and the arguments have no scientific support from well-conducted EMF research" and "There is a lack of balance in the report; no mention is made in fact of reports that do not concur with authors' statements and conclusions" (EMF-NET, 2007, p. 1).

The HCN also questioned the motives of the authors, asking why the BioInitiative report was written, in the first place, and they stated, "Upfront, therefore, the reason for writing the report was not to give an objective analysis of the current state of science, that would subsequently lead to recommendations. Instead, the aim was to present information to demonstrate why current standards are inadequate" (HCN, 2008, p. 3).

Conclusions and comments

The authors of the BioInitiative Report contended that the standard procedure for developing exposure guidelines—i.e., to set guidelines where adverse health effects have been established by using a weight-of-evidence approach—is not appropriate and should be replaced by a process that sets guidelines at exposure levels where biological effects have been reported in some studies, but not substantiated in a rigorous review of the science or linked to adverse health effects.

Based on this argument, the main conclusion of the BioInitiative Report was that existing standards for exposure to ELF EMF are insufficient because "effects are now widely reported to occur at exposure levels significantly below most current national and international limits" (Table 1-1). Specifically, the authors concluded that there was strong evidence to suggest that magnetic fields were a cause of childhood leukemia based on epidemiologic findings.

The report recommended the following:

> ELF limits should be set below those exposure levels that have been linked in childhood leukemia studies to increased risk of disease, plus an additional safety factor … While new ELF limits are being developed and implemented, a reasonable approach would be a 1 mG (0.1 μT) planning limit for habitable space adjacent to all new or upgraded power lines and a 2 mG (0.2 μT) limit for all other new construction. It is also recommended that a 1 mG (0.1 μT) limit be established for existing habitable space for children and/or women who are pregnant (WHO, 2007a, p. 22)

The recommendations made in the BioInitiative Report are not based on appropriate scientific methods and, therefore, do not warrant any changes to the conclusions from the numerous scientific agencies that have already considered this issue. These organizations are consistent in their conclusions that the research does not support the setting of exposure standards at these low levels of magnetic field exposure.

The World Health Organization (WHO) published the most recent weight-of-evidence review in June 2007 and concluded the following:

> Everyday, low-intensity ELF magnetic field exposure poses a possible increased risk of childhood leukaemia, but the evidence is not strong enough to be considered causal and therefore ELF magnetic fields remain classified as possibly carcinogenic (WHO 2007a, p. 357)

The report continued:

> Given the weakness of the evidence for a link between exposure to ELF magnetic fields and childhood leukaemia and the limited potential impact on public health, the benefits of exposure reduction on health are unclear and thus the cost of reducing exposure should be very low (WHO 2007a, p. 372)

The WHO made no recommendations for exposure standards at the magnetic field levels where an association has been reported in some epidemiologic studies of childhood leukemia. In a fact sheet created for the general public and published on their website, the WHO stated,

> When constructing new facilities and designing new equipment, including appliances, low-cost ways of reducing exposures may be explored…However, policies based on the adoption of arbitrary low exposure limits are not warranted (WHO 2007b).

As stated, the conclusions in the BioInitiative Report deviate substantially from those of reputable scientific organizations because they were not based on standard, scientific methods. Valid scientific conclusions are based on weight-of-evidence reviews, which entail a systematic evaluation of the entire body of scientific evidence in three areas of research (i.e., epidemiology, *in vivo* research, and *in vitro* research), by panels of experts in these relevant disciplines. The report by the BioInitiative working group does not represent a valid weight-of-evidence review for the following key reasons:

1. **Review panels should consist of a multidisciplinary team of experts that reach consensus statements by collaboratively contributing to and reviewing the final work product.** This process ensures that overall conclusions represent a valid and balanced view of each relevant area of research. The document released by the BioInitiative working group was a compilation of sections, with each authored by one to three members of the group. It does not appear that the report was developed collaboratively or reviewed in its entirety by each member.

2. **Valid conclusions about causality are based on systematic evaluations of three lines of evidence—epidemiology, *in vivo* research, and *in vitro* research.** The conclusions in the BioInitiative Report are not based on this multidisciplinary approach. In particular, little attention is provided to the results from *in vivo* studies on cancer and disproportionate weight is given to the results of *in vitro* studies reporting biological effects.

3. **The entire body of evidence to date should be considered when drawing conclusions regarding the strength of evidence in support of a hypothesis.** The BioInitiative Report is not a comprehensive review of the cumulative evidence. Rather, results from specific studies are cited, but no rationale is provided for their inclusion relative to the many other relevant, published studies.

4. **The evidence from each study must be evaluated critically to determine its validity and the degree to which it is relevant and able to support or refute the hypothesis under question.** The significance of the results reported in any study depends on the validity of the methods used in that study, so weight-of-evidence reviews must include an evaluation of the strengths and limitations of each study. In some discussions, the report claimed to use a weight-of-evidence approach, but the individual sections of the report provide little evidence that the strengths and limitations of individual studies (e.g., the quality of exposure assessment, sample size, biases, and confounding factors) were evaluated systematically.

5. **Support for a causal relationship is based on consistent findings from methodologically sound epidemiology studies that are coherent with the results reported from *in vivo* and *in vitro* studies**. The BioInitiative group often arrived at conclusions about causality by considering only a few studies from one discipline, with no consideration of the significance and validity of the study's results.

In summary, the authors of this report largely ignored basic scientific methods that should be followed in the review and evaluation of scientific evidence. These methods are fundamental to scientific inquiry and are not, as the BioInitiative Report states, "unreasonably high."

The policy responses proposed in the report are cast as consistent with the precautionary principle, i.e., taking action in situations of scientific uncertainty before there is strong proof of harm. A central tenet of the precautionary principle is that precautionary recommendations are proportional to the perceived level of risk and that this perception is founded largely on the weight of the available scientific evidence. The BioInitiative Report recommends precautionary measures on the basis of argument, rather than the basis of sound peer-reviewed scientific evidence.

Unlike the BioInitiative Report, the WHO review was the product of a multidisciplinary scientific panel assembled by an established public health agency that followed appropriate scientific methods, including the systematic and critical examination of all the relevant evidence. The recommendations from the WHO report (WHO, 2007a, pp. 372-373) are presented below:

- Policy-makers should establish guidelines for ELF field exposure for both the general public and workers. The best source of guidance for both exposure levels and the principles of scientific review are the international guidelines.

- Policy-makers should establish an ELF EMF protection programme that includes measurements of fields from all sources to ensure that the exposure limits are not exceeded either for the general public or workers.

- Provided that the health, social and economic benefits of electric power are not compromised, implementing very low-cost precautionary procedures to reduce exposures is reasonable and warranted.

- Policy-makers and community planners should implement very low-cost measures when constructing new facilities and designing new equipment including appliances.

- Changes to engineering practice to reduce ELF exposure from equipment or devices should be considered, provided that they yield other additional benefits, such as greater safety, or involve little or no cost.

- When changes to existing ELF sources are contemplated, ELF field reduction should be considered alongside safety, reliability and economic aspects.

- Local authorities should enforce wiring regulations to reduce unintentional ground currents when building new or rewiring existing facilities, while maintaining safety. Proactive measures to identify violations or existing problems in wiring would be expensive and unlikely to be justified.

- National authorities should implement an effective and open communication strategy to enable informed decision-making by all stakeholders; this should include information on how individuals can reduce their own exposure.

- Local authorities should improve planning of ELF EMF-emitting facilities, including better consultation between industry, local government, and citizens when siting major ELF EMF-emitting sources.

- Government and industry should promote research programmes to reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure.