Health Sciences Practice

Exponent®

EMF and Health: Comprehensive Review and Update of the Scientific Research January 15, 2010 through March 1, 2012

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Acronyms and Abbreviations

AC	Alternating current
ACGIH	American Conference of Governmental Industrial Hygienists
ALL	Acute lymphocytic leukemia
ALS	Amyotrophic lateral sclerosis
BCTC	British Columbia Transmission Corporation
BCUC	British Columbia Utilities Commission
CI	Confidence interval
E-field	Electric field
EC	European Commission
ELF	Extremely low frequency
EMF	Electric and magnetic fields
EMI	Electromagnetic interference
G	Gauss
GHz	Gigahertz
HPA	Health Protection Agency
Hz	Hertz
IARC	International Agency for Research on Cancer
ICD	Implantable cardiac defibrillator
ICES	International Committee for Electromagnetic Safety
ICNIRP	International Commission on Non-Ionizing Radiation Protection
ILM	Interior to Lower Mainland Project
kV/m	Kilovolts per meter
LPD	Lymphoproliferative disorder
µT	Microtesla
mG	Milligauss
MPD	Myeloproliferative disorder
MPE	Maximum permissible exposure
NHL	Non-Hodgkin's lymphoma
NRPB	National Radiological Protection Board of Great Britain
NTP	National Toxicology Program
OR	Odds ratio
RR	Relative risk
ROW	Right-of-way
SCENIHR	Scientific Committee of Emerging and Newly Identified Health Risks
SSI	Swedish Radiation Protection Authority
TWA	Time-weighted average
UK	United Kingdom
US	United States
USEPA	U.S. Environmental Protection Agency
V/m	Volts per meter
VITR	Vancouver Island Transmission Reinforcement Project
WHO	World Health Organization

Limitations

At the request of BC Hydro, Exponent prepared this summary report on the status of research related to power frequency EMF exposure and health. The findings presented herein are made to a reasonable degree of scientific certainty. Exponent reserves the right to supplement this report and to expand or modify opinions based on review of additional material as it becomes available, through any additional work, or review of additional work performed by others.

The scope of services performed during this investigation may not adequately address the needs of other users of this report, and any re-use of this report or its findings, conclusions, or recommendations presented herein are at the sole risk of the user. The opinions and comments formulated during this assessment are based on observations and information available at the time of the investigation. No guarantee or warranty as to future life or performance of any reviewed condition is expressed or implied.

Introduction

Exponent was requested by BC Hydro to prepare a summary of the current research related to extremely low frequency (ELF) electric and magnetic fields (EMF) and health. Exponent has prepared reports for the British Columbia Transmission Corporation (BCTC) to fulfill similar requests in the past.[1] The objective of this report is to fulfill the requirement of the British Columbia Utilities Commission (BCUC) Directive in its Vancouver Island Transmission Reinforcement (VITR) Decision that BCTC monitor and report on the science every two years to allow its customers to keep up to date with major developments in the field of EMF research.

This report updates Exponent's 2010 report, which evaluated the impact of research published between 2006 and 2010 on the conclusions of the World Health Organization's (WHO) comprehensive risk assessment that reviewed research through approximately December, 2005 (WHO, 2007). This report evaluates research published since the time of Exponent's 2010 report (i.e., January 15, 2010 through March 1, 2012) to determine if there are any new developments that justify changes to the conclusions of previous weight-of-evidence reviews. This report also fulfills the BCUC Directive to monitor and report on the science on a regular basis. During this period, approximately 63 relevant scientific studies were published and 3 scientific organizations prepared evaluations of the scientific evidence.

This report follows the same general structure and discusses the same scientific topics as the Exponent 2007 and 2010 reports. Sections 1 and 2 of this report follow the format of Sections 1 and 2 of Exponent's 2007 and 2010 reports. These sections provide the reader with a framework for understanding the discussion in later sections. Section 1 provides background information on EMF, and Section 2 outlines the standard scientific methods used to evaluate research. Section 3 summarizes the conclusions of recent weight-of-evidence reviews of ELF EMF prepared by scientific organizations. Section 4 provides an evaluation of relevant

[1] The reports include "VITR EMF Health Report Exhibit 1-37 - Response to Evidence Presented by Dr. Magda Havas" (Exponent, 2005); "EMF and Health: Review and Update of the Scientific Research" (Exponent, 2007); and "EMF and Health: Review and Update of the Scientific Research, September 2007 through January 2010" (Exponent, 2010). The 2005 and 2007 reports were filed with the British Columbia Utilities Commission in the Vancouver Island Transmission Reinforcement Project proceedings and the 2010 report was filed with BCUC in the Interior to Lower Mainland Project proceedings.

epidemiology and *in vivo* experimental studies published from January 15, 2010 through March 1, 2012 identified from a systematic review of the literature. These studies are organized within Section 4 by the health outcome of interest (leukemias and lymphomas, other cancers, reproductive and developmental outcomes, and neurodegenerative disease). Sections 5, 6, and 7 address additional topics relevant to a risk assessment of EMF: electromagnetic 'hypersensitivity,' electromagnetic interference, and possible effects on flora and fauna, respectively. A glossary of scientific terms is included at the end of the report to provide additional clarification.

1 Background: Electric and Magnetic Fields

Electric and magnetic fields are produced by both natural and man-made sources that surround us in our daily lives. Man-made EMF is found wherever electricity is generated, delivered, or used, including near power lines, wiring in homes, workplace equipment, electrical appliances, power tools, and electric motors. In North America, EMF from these sources changes direction and intensity 60 times, or cycles, per second—a frequency of 60 Hertz (Hz)—and are often referred to as power-frequency or ELF EMF.[2] The ELF range includes frequencies up to 300 Hz (ICNIRP, 1998). Natural sources of EMF include the earth's static magnetic field and the electrical fields created by the normal functioning of our nervous and cardiovascular system.

Electric fields occur as the result of the voltage applied to electrical conductors and equipment. Electric-field levels are expressed in measurement units of volts per meter (V/m) or kilovolts per meter (kV/m); 1 kV/m is equal to 1,000 V/m. Electric fields are easily blocked by most objects such as buildings, walls, trees, and fences. As a result, the major indoor sources of electric fields are the many appliances and equipment we use within our homes and workplaces. Electric-field levels increase in strength as voltage increases and are present even if an electrical device is turned off; field strength diminishes quickly, however, as one increases distance from the source.

Magnetic fields are produced by the movement of electric currents. Magnetic field levels are expressed as magnetic flux density in units called gauss (G), or in milligauss (mG), where 1 G equals 1,000 mG.[3] The magnetic-field level associated with a particular object (e.g., an appliance or power line) depends largely on various operating characteristics of the source and on the amount of current (i.e., electricity) flowing through the object. Unlike electric fields, magnetic fields are only present when an appliance or electrical device is turned on or a power line is energized. Similar to electric fields, magnetic fields diminish in strength quickly as

[2] Electrical facilities in most countries outside North America operate at a frequency of 50 Hz.

[3] Scientists also refer to magnetic flux density at these levels in units of microtesla (μT). Magnetic flux density in milligauss units can be converted to μT by dividing by 10, i.e., 1 milligauss = 0.1 μT.

distance increases from the source, but unlike electric fields they are not easily blocked by conductive objects.

ELF EMF is ubiquitous in modern society because of the abundance of electrical sources in our environments. Every person's "average" EMF exposure is defined by the environments where they spend time, the sources they encounter in those locations, and the duration of any exposure; any substantial changes to these variables may result in a change in average exposure. If someone worked as a welder or lived in a home with faulty wiring, for example, his or her average EMF exposure may be elevated during these periods. This ubiquitous and changing nature of EMF exposure makes it difficult to describe and quantify.

Electric fields in the home range up to approximately 0.010 kV/m in the center of rooms (away from appliances) and up to 0.25 kV/m near appliances (WHO, 1984). In most homes, the magnetic-field level measured in the center of rooms (away from appliances) is approximately 1 mG, resulting from wiring within the home, appliances, and any power lines just outside the home (Zaffanella, 1993). Based on a sample taken in the United States (US), the estimated daily average exposure to magnetic fields is approximately 1-2 mG for about 76% of the population (Zaffanella, 1997). In Canada, the average magnetic-field exposure of 382 children in five provinces, including British Columbia, was measured as 1.2 mG from individual recordings obtained from a wearable recording magnetic-field meter (Deadman et al., 1999). While higher magnetic-field levels are measured near distribution and transmission lines, the distance of most buildings from a power line's right-of-way (ROW) reduces the effect of these sources on magnetic-field levels measured inside a home or office, since the intensity of magnetic fields diminishes quickly with distance from the source. In fact, the strongest sources of magnetic fields encountered indoors are electrical appliances. For example, a study by the US Environmental Protection Agency (EPA) in 1992 reported the median magnetic field at 6 inches from a sampling of appliances was 6 mG (baby monitor), 7 mG (color televisions), 9 mG

(electric oven), 14 mG (computers), 90 mG (copier), 200 mG (microwave ovens), 300 mG (hair dryer), and 600 mG (can opener).[4]

The term of reference for this report is power-frequency EMF, i.e., the ELF fields produced by the generation, transmission and use of electricity.[5] This focus is scientifically critical. It is generally accepted in the scientific community that the frequency of electromagnetic energy is a key factor in its interaction with living things. ELF fields of 50- or 60-Hz, for example, have very long wavelengths and, as a result, impart very low energy when interacting with cells and living organisms. The interaction of ELF EMF with matter is very different than higher frequency fields in the electromagnetic spectrum such as microwaves (2 billion Hz) or solar energy, because of the interrelated nature of frequency, wavelength, energy, and biological response. Therefore, only studies of ELF EMF are relevant to assessing the potential biological and health effects of power-frequency fields.

[4] Mobile phones and their antennas, wireless communication networks, and radios of all types (AM, FM, police, and fire) operate using radio frequency (RF), which is a part of the electromagnetic spectrum.

[5] The major focus of the review is magnetic-field exposure. Research has focused on magnetic fields because, among other reasons, conductive objects shield electric fields, and so power lines have little effect on the potential long-term average electric-field exposure of nearby residents.

2 Methods for evaluating scientific research

2.1 Heath risk assessment approach

The standard process for evaluating a body of research to understand the potential health implications of exposure is a health risk assessment, which consists of several, sequential steps.[6] The process starts with systematically evaluating the body of research and identifying any possible risks associated with an exposure (hazard identification/weight-of-evidence review).[7] A follow-up question to hazard identification is, "if the exposure does cause any health risks, at what level do they occur?" (dose-response assessment). A risk assessment then characterizes the exposure circumstances of the situation under consideration (exposure assessment). Finally, using the findings from the hazard identification and dose-response assessment as a basis, a summary evaluation is provided (risk characterization).

2.2 Hazard identification/weight-of-evidence review

Science is more than a collection of facts; rather, it is a method of obtaining information and of reasoning to ensure that the information is accurate and correctly describes physical and biological phenomena. Many misconceptions in human reasoning occur when people casually observe and interpret their observations and experience (e.g., if a person develops a headache after eating a particular food, he or she may mistakenly ascribe the headache to the food). The proximity or co-occurrence of events or conditions, however, does not guarantee a causal relationship. Scientists use systematic methods to evaluate observations and assess the potential impact of a specific agent on human health.

The scientific process involves looking at *all* the evidence on a particular issue in a systematic and thorough manner (i.e., a weight-of-evidence review or hazard identification). This process

[6] Some of the scientific panels that have reviewed EMF research have described the risk assessment process in the introductory sections of their reviews or in separate publications (ICNIRP, 2002; IARC, 2006; SCENIHR, 2007; SSI, 2007; WHO, 2007; HCN, 2009; SSM, 2010; SCENIHR, 2012).

[7] The terms "weight-of-evidence review" and hazard identification are used interchangeably in this report to denote a systematic review process involving the review of experimental and epidemiologic research to arrive at conclusions about possible health risks.

is designed to ensure that more weight is given to studies of better quality and that studies with a given result are not selected out from the available evidence to advocate or suppress a preconceived idea of an adverse effect. Three broad steps define a weight-of-evidence review: a systematic review of the published literature to identify relevant studies, an evaluation of each study to determine its strengths and weaknesses, and an overall evaluation of the data, giving more weight to higher-quality data and study designs.

Data from several types of studies must be evaluated *together* in a weight-of-evidence review, including epidemiologic observations in people, experimental studies in animals (*in vivo*), and experimental studies in isolated cells and tissues (*in vitro*). Epidemiology and experimental studies complement one another because the inherent limitations of epidemiology studies are addressed in experimental studies and *vice versa*. Similar to puzzle pieces, the results of epidemiology and experimental studies are placed together to provide a picture of the possible relationship between exposure to a particular agent and disease.

Epidemiology is the discipline that studies the patterns of disease occurrence in human populations and the factors that influence those patterns. Epidemiology studies are critical for determining the causes of disease. Epidemiology studies are observational in nature, in that they examine and analyze people in their normal lives with little control over the many factors that affect disease. Such studies are designed to quantify and evaluate the association between exposures (e.g., a high fat diet) and health outcomes (e.g., coronary artery disease). An association is a statistical measure of how things vary together. Scientists may report, for example, that people with coronary artery disease eat a diet that is lower in fat compared to people without the disease (i.e., a negative association). Or, scientists may report that persons with coronary artery disease eat a diet that is higher in fat compared to persons without the disease (i.e., a positive association).

Epidemiology studies can help suggest factors that may contribute to the development of disease but, in the vast majority of situations, they cannot be used as the sole basis for drawing inferences about cause-and-effect relationships. Additional research needs to be considered. Continuing with our example from above, just because one epidemiology study finds a positive association between high fat diets and coronary artery disease, we cannot conclude that

consumption of fat (or any component of fat) causes coronary artery disease without further research. This additional research includes studies with experimental research designs, as well as additional epidemiology studies with improved designs.

In contrast to epidemiology studies, experimental studies are conducted under controlled laboratory conditions designed to test specific hypotheses. For example, *in vivo* studies can strictly control the exposure level in the exposed group as well as factors such as food, housing, and temperature so these variables are precisely measured in both the exposed and unexposed groups. Generally, experimental studies are required to establish cause-and-effect relationships, but the results of experimental studies by themselves may not always be directly extrapolated to predict effects in human populations. Therefore, it is both necessary and desirable that biological responses to agents that could present a potential health threat be explored by epidemiologic methods in human populations, as well as by experimental studies in the research laboratory.

A weight-of-evidence review is essential for arriving at a valid conclusion about causation because no individual study is capable of assessing causation independently. Rather, evaluating causation is an inferential process that is based on a comprehensive assessment of all the relevant scientific research. The final conclusion of a weight-of-evidence review is a conservative evaluation of the strength in support of a causal relationship. If a clear causal relationship is indicated by the data, the conclusion is that the exposure is a known cause of the disease. In most cases, however, because of limitations in study methods, the relationship is not clear and the exposure is characterized as probably related, possibly related, unclassifiable, or probably not related (IARC, 2006). Few exposures are categorized as known or unlikely causes (IARC, 2006).

2.3 Evaluating epidemiology studies

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

A case-control study (Figure 1) compares the characteristics of people who 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 to assess whether the cases have a higher exposure level than the controls, or *vice versa*.

In a case-control study, an odds ratio (OR) is used to estimate the association quantitatively. 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. If an OR is equal to 1.0, the general interpretation is there is no association between the exposure and disease in the study. If the OR is greater than 1.0, there is a positive association between the exposure and disease in the study and the inference is that the exposure may increase the risk of the disease (Figure 2). A negative association is indicated when the OR is less than 1.0.

Each OR is reported with a confidence interval (CI), which is a range of OR values that have a specified probability of occurring if the study is assumed to be repeated a large number of times. A 95% CI, for example, provides the range of values that are likely to occur in 95% of repeated experiments. In short, a CI tells one how confident we are about the OR calculated from the data; if the CI includes 1.0, one 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. If the CI does not include 1.0, the association is called statistically significant.

A cohort study is the reverse of a case-control study—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 (Figure 1). Cohort studies are evaluated statistically in a similar manner as case-control studies, although the risk estimate is referred to as a relative risk (RR). The RR is equal to the 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.

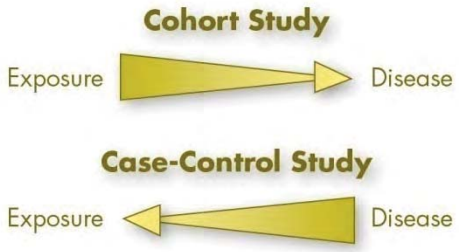


Figure 1. Basic design of cohort and case-control studies

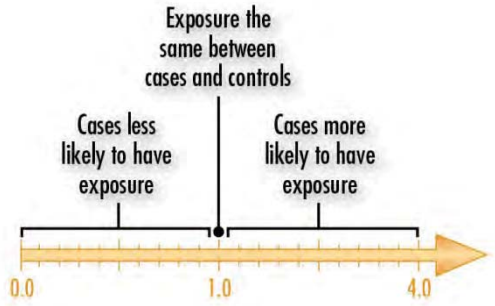


Figure 2. Interpretation of an odds ratio (OR) in a case-control study

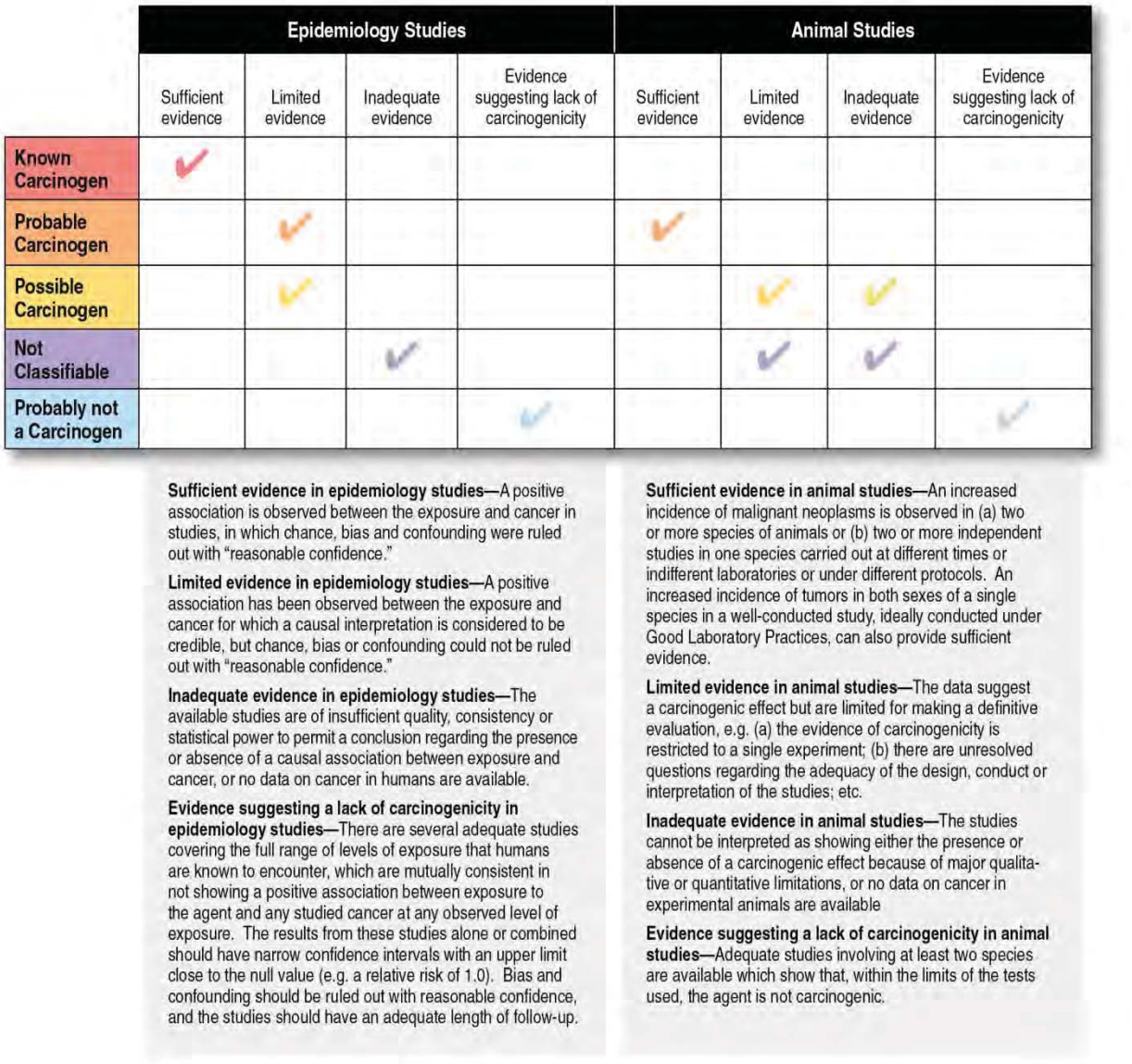
A RR or OR value is simply a measure of how often a disease and exposure occur together in a particular study population—it does not mean that there is a known or causal relationship. Before any conclusions can be drawn, all studies of the relationship between the exposure and disease must be identified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

- Chance refers to a random event, like a coincidence. An association can be observed between an exposure and disease that is simply the result of a chance occurrence. Statistics, such as the CI, are calculated to determine whether chance is a likely explanation for the findings.
- Bias refers to any error in the design, conduct, or analysis of a study resulting in 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 cases that participate in a study differ in a meaningful way from the characteristics of those subjects who do not participate (e.g., if cases who live near a power line are more likely to participate in the study than controls because they are concerned about a possible exposure, cases will tend to live closer to power lines than controls just because of this selection process).
- 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. Some women who drink coffee, however, 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 critically evaluated to determine if and how chance, bias, and confounding may have affected the results, and, as a result, the weight that should be placed on the study's findings.

A formal procedure for classifying scientific data has been developed by the International Agency for Research on Cancer (IARC). The IARC classifies epidemiology and *in vivo* studies as providing sufficient, limited, or inadequate evidence (Figure 3) in support of carcinogenicity, or evidence suggesting a lack of carcinogenicity. In epidemiology studies, the role of chance, bias, and confounding on the observed association must be ruled out with reasonable confidence to designate the evidence as "sufficient." If the role these factors may play in the calculated statistical association cannot be ruled out with reasonable confidence, then the data is classified as providing limited evidence. Inadequate evidence describes a data set that lacks quality, consistency, or power for conclusions to be drawn regarding causality. The categories on the left in Figure 3 (e.g., known, probable, etc.) are based on the combined evaluations of epidemiology and *in vivo* studies. Other biological data relevant to the evaluation of carcinogenicity and its mechanisms are considered, depending on the relevance to the agent under study.



	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 3. Basic IARC method for classifying exposures based on evidence for potential carcinogenicity

2.3.1 Association vs. causation

An association is a relationship between two events, a finding that they occur together more often than expected by chance. A reported association between a particular exposure and disease, however, is not sufficient evidence to conclude that the exposure is a cause of the

disease. Rather, an association is a finding from a particular study; evaluating causation is an inferential process that combines the totality of evidence (including epidemiology studies that have measured associations) in a weight-of-evidence review. For example, we may find in a particular study that children with respiratory infections are significantly more likely to have eaten ice cream than children without respiratory infections; in other words, there is a positive association between exposure to ice cream and respiratory infections that is not likely to be due to chance. We obviously could not conclude, however, that ice cream is a cause of respiratory infections based upon this information alone. While this example is simplistic, epidemiologic associations must always be evaluated with caution before determining that statistical results confirm cause and effect.

In order to support a cause-and-effect relationship, the overall data, or evidence, must present a logically coherent and consistent picture. Various guidelines have been used to assist in the evaluation of the plausibility of a cause-and-effect relationship between a particular exposure and disease. These guidelines, commonly referred to as *Hill's criteria* after the British physician who outlined them (Hill, 1965), typically form the foundation of causal inference (Rothman and Greenland, 1998). Since the publication of *Hill's criteria* in 1965, numerous revisions and updates have been suggested (e.g., Susser, 1991), although the basic tenets remain the same. As described in Table 1, *Hill's criteria* are used as an analytic framework in the weight-of-evidence review process (e.g., ICNIRP, 2002; USEPA, 2005).

Each criterion cannot be addressed with a simple "yes" or "no," nor are the criteria as a whole meant to be an inflexible set of rules; rather, they serve as guidance for weighing the evidence to reach a decision about the plausibility of a cause-and-effect relationship. The more firmly these criteria are met by the data, the more convincing the evidence. For example, the presence of a dose-response relationship provides weight in support of a cause-and-effect relationship, but by itself does not indicate a cause-and-effect relationship. Referring to the hypothetical example discussed above, the totality of the evidence would more strongly suggest that ice cream may be a cause of respiratory infections if: 1) strong associations were also found in other epidemiology studies and these associations showed a dose-response relationship, 2) animals with high ice

cream intake also had an increased incidence of respiratory infections, and 3) an organism was isolated from the ice cream that could cause the infection.

Table 1. Hill's guidelines for evaluating causation in epidemiologic data

Strength	The stronger the association between the disease and the exposure in question, the more persuasive the evidence. Some epidemiologists think that a relative risk of 3 or more (i.e., the risk of disease is at least 3 times higher in individuals with the exposure compared to individuals with no exposure) indicates a strong association. Smaller relative risks are more likely to be influenced by bias or confounding.
Consistency	Consistent results across different study populations and study designs are more convincing than isolated observations.
Specificity	The evidence for causation is stronger if the exposure produces a specific effect.
Dose-response	If the risk of disease increases as the exposure level increases (e.g., from low to high exposure), the exposure is more likely to be related to the disease.
Biological plausibility	Epidemiologic results are much more convincing if they are coherent with what is known about biology. That is, the evidence is stronger if scientists know of a biological mechanism that can explain the effect.
Temporality	The data must provide evidence of correct temporality. That is, the exposure must be documented to have occurred before the observed effect, with sufficient time for any induction period related to the disease.
Coherence	The association should be compatible with existing theory and knowledge.
Prevention of effect	Causation is likely if the disease has been shown to be prevented by the removal of the exposure through an intervention or prevention program.
Analogy	Established causal relationships observed with similar diseases and/or exposures provide more weight for a causal relationship.

This presentation of Hill's guidelines was adapted from the original source: Hill AB. The environment and disease: Association or causation. Proc R Soc Med. 58:295-300, 1965.

2.3.3 Meta- and pooled analyses

In epidemiologic research, the results of smaller studies are difficult to distinguish from the random variation that normally occurs in data. Meta-analysis is an analytic technique that combines the published results from a group of studies into one summary result. A pooled analysis, on the other hand, combines the raw, individual-level data from the original studies and analyzes the data from the studies together. These methods are valuable because they increase the number of individuals in the analysis, which allows for a more robust and stable estimate of association. Meta- and pooled analyses are also important tools for qualitatively synthesizing the results of a large group of studies.

The disadvantage of meta- and pooled analyses is that they can convey a false sense of consistency across studies if *only* the combined estimate of effect is considered (Rothman and Greenland, 1998). These analyses typically combine data from studies with different study populations, methods for measuring and defining exposure, and definitions of disease. This is particularly true for analyses that combine data from case-control studies, which often use very different methods for exposure assessment and the selection of cases and controls. Therefore, in addition to the synthesis or combination of data, meta- and pooled analyses should be used to understand what factors cause the results of the studies to vary, and how these factors affect the associations calculated from the data of all the studies (Rothman and Greenland, 1998). For example, in a meta-analysis of childhood leukemia and magnetic-field exposure, Greenland et al. (2000) performed analyses to assess how excluding particular studies from the group impacted the results of the meta-analysis. Meta- and pooled analyses are a valuable technique in epidemiology, but the quality of the underlying studies and the consistency and robustness of the results should always be taken into consideration.

2.3.4 Exposure estimation for electric and magnetic fields

One of the most crucial aspects in the review of any epidemiology study is an evaluation of how exposure was measured. A good exposure metric should measure the element that is believed to cause the disease at the appropriate time in the disease process. Estimating exposure to EMF is difficult since: 1) EMF is ubiquitous; 2) exposure is often estimated retrospectively; and 3) there is currently no accepted biological mechanism for carcinogenicity or any other disease process, so the appropriate exposure metric and timing is unknown. In the absence of substantive knowledge about a specific mechanism by which magnetic fields could affect normal cells, the focus on long-term exposure is based upon the standard assumption that exposure that affects the development of cancer requires repeated exposure at elevated levels, as does tobacco smoke, alcohol, sunlight, chemicals, and other agents in the environment that are known to cause cancer. Investigators have commonly used different types of magnetic-field measurements and calculations to estimate a person's long-term average exposure, i.e., their time-weighted average (TWA) exposure. One method of estimating a person's TWA exposure is to sum all magnetic-field exposure encountered during the day (e.g., while at work or school, at home, at a grocery

store, shopping, etc.), weight each estimate by the number of hours in that environment, and divide that value by the total number of hours.

Historical exposure to residential magnetic fields has been estimated in epidemiology studies using a variety of surrogates, including:

1) Ratings of potential magnetic-field exposure from nearby power lines based on the number and thickness of power line conductors and their distance to nearby residences (wire code categories);

2) Instantaneous, spot measurements in particular locations of a home;

3) Recordings of magnetic fields over 24- or 48-hour periods using measurements in a room where a person spends most of his or her time or using a measurement device that is carried by the person; and

4) Calculated field levels based on information on loading, height, configuration, etc. of nearby transmission lines.

In general, studies that estimate long-term exposure using personal magnetic-field measurements are preferred because they estimate exposure from all magnetic-field sources and directly estimate what a person is exposed to. The other methods only capture exposure from one type of source. Personal magnetic field measurements are obtained by wearing a personal exposure meter, which can take single readings each minute to estimate average magnetic-field exposure over the measurement period. Since this type of measurement may be cost prohibitive in some locations, the investigators of a study of Canadian children evaluated what proxy exposure measures might best predict the child's 48-hour average magnetic-field exposure (Armstrong et al., 2001). Stationary 24-hour measurements in a child's bedroom were a good predictor of 48-hour personal exposure, and spot measurements around the perimeter of the child's home were a moderately good predictor. Wire code categories, on the other hand, were not found to be an accurate predictor of a child's exposure (Armstrong et al., 2001).

It is important to note that estimates of magnetic-field exposure in epidemiology studies, while given in units of mG, are not the same as the magnetic-field values at a single, fixed location, such as at the edge of a transmission line ROW. The difference is that the exposure estimate in epidemiology studies is intended to reflect a person's exposure to magnetic fields from all sources at all locations over a long period of time. It is evident then that brief encounters with higher magnetic fields (for example, walking under a distribution or transmission line, at home in front of a refrigerator or television, or at a grocery store near the freezer) would not significantly alter the long-term exposure of a person to magnetic fields, as reflected in their TWA exposure, because they spend such a small fraction of their time at these locations.

Much of the research on EMF is related to occupational exposures, given the higher range of exposure levels 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 [JEM]). The latter method, while an advance over earlier methods, still has some important limitations, as highlighted in a review by Kheifets et al. (2009) summarizing an expert panel's findings.[8] 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. A study of the 48-hour exposure of 543 workers in Italy found that JEMs were a poor indicator of actual occupational, magnetic-field exposure levels (Gobba et al. 2011). A recent study by Mee and colleagues (2009) also confirmed that JEMs could be improved by linking occupational classifications with industry or information on participation in certain tasks of interest (e.g., use of welding equipment or work near power lines) based on their measurements of personal occupational magnetic-field exposures in the United Kingdom.

[8] 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.

2.4 Evaluating experimental research

2.4.1 General research methods

Experimental studies of humans, animals, and cells and tissues complement epidemiology studies. Both epidemiologic and experimental approaches are needed because, although people are the species of interest, they have large variations in their genetic makeup, exposures, dietary intake, and health-related behaviors. In laboratories, these variables can be controlled to provide more precise information regarding the effects of an exposure. In epidemiology studies, it is difficult to control for these variables because scientists are merely observing individuals going about their ordinary lives. Taken together, epidemiology, *in vivo*, and *in vitro* studies provide a more complete picture of a possible disease etiology than any one of these study types alone.

A wide variety of approaches is available for assessing the possible adverse effects associated with exposures in experimental studies. The two, general types of experimental studies are studies of the effects of planned exposures on human volunteers (usually short-term studies) or whole animals (usually long-term studies, i.e., *in vivo* studies), and studies of isolated cells and tissues, i.e., *in vitro* studies. *In vitro* studies are designed to evaluate the way that the exposure acts on cells and tissues outside of the body, also known as the mechanism of action.

In vivo studies

Studies in which laboratory animals receive high exposures in a controlled environment provide an important basis for evaluating the safety of environmental, occupational, and drug exposures. These approaches are widely used by health agencies to assess risks to humans from medicines, chemicals, and physical agents (Health Canada, 1994; WHO, 1994; IARC, 2002 preamble; USEPA, 2002; USEPA, 2005). From a public health perspective, long-term (chronic) studies in which animals undergo exposure over most of their lifetime, or during their entire pregnancy, are of high importance in assessing potential risks of cancer and other adverse effects. In these long-term studies, researchers examine a large number of anatomical sites to assess changes and adverse effects in body organs, cells, and tissues.

These data are used in the hazard identification step of the risk assessment process to determine whether an environmental exposure is likely to produce cancer or damage organs and tissues. Health Canada mandates that lifetime *in vivo* or *in vivo* studies of exposures during critical sensitive periods are conducted to assess potential toxicity to humans (Health Canada, 1994). Furthermore, the EPA's position is that, "…the absence of tumors in well-conducted, long-term animal studies in at least two species provides reasonable assurance that an agent may not be a carcinogenic concern for humans" (USEPA, 2005, pp. 2-22).

In vitro studies

In vitro studies are used to investigate the mechanisms for effects that are observed in living organisms. The relative value of *in vitro* tests to human health risk assessment is less than that of *in vivo* and epidemiology studies because responses of cells and tissues outside the body may not reflect the response of those same cells if maintained in a living system, so their relevance cannot be assumed (IARC, 1992). It may be difficult to extrapolate from simple cellular systems to complex, higher organisms to predict risks to health because the mechanism underlying effects observed *in vitro* may not correspond to the mechanism underlying complex processes like carcinogenesis. In addition, the results of *in vitro* studies cannot be interpreted in terms of potential human health risks unless they are performed in a well-studied and validated test system. For these reasons, the IARC and other agencies treat data from *in vitro* studies as supplementary to data obtained from epidemiology and *in vivo* studies.

Convincing evidence for a mechanism that explains an effect observed in experimental or epidemiology studies can add weight to the assessment of cause and effect, and in some cases may clarify reasons for different results among species, or between animals and humans. *In vitro* studies are not used directly, however, by any health agency to assess risks to human health. Therefore, this report emphasizes epidemiology studies and experimental research conducted *in vivo* and relies on the conclusions of scientific panels with regard in vitro data.

2.4.2 Experimental methods for cancer research

Cancer research in the laboratory includes studies of various stages of cancer development. Research has established that cells may take several steps to change from ordinary cells to the uncontrolled growth typical of cancer. Cancer usually begins with a mutation, that is, an irreversible change in the genetic material of the cell, a process called initiation or induction. Other steps, or stages, must occur for a cancerous cell to develop into a tumor, including promotion. Some exposures cause only initiation or only promotion. Exposures that affect both initiation and promotion are complete carcinogens.

In vitro assays isolate specific cells or microorganisms in glassware in the laboratory to assess the likelihood that exposure to the agent can cause mutations, a step necessary in the initiation of cancer. Initiation tests have also been developed in animals, in which scientists expose them for less than lifetime periods to determine whether an exposure caused changes typical for early stage cancers in specific tissues such as liver, breast, or skin.

Other tests are designed to ascertain whether a specific exposure can stimulate tumor growth (i.e., promotion) in an animal in which the cellular changes typical of initiation have already occurred. Studies of promotion include two steps: first, exposing the experimental animals to a chemical known to initiate cancer, and second, exposing the animals to the agent to be tested as a promoter. The occurrence of cancer in animals exposed to an initiator and promoter is compared to the occurrence of cancer that develops in animals exposed only to the initiator.

The failure of early EMF research to produce mutations in the DNA of cells *in vitro* was a factor in directing scientists to focus on studies of promotion.

2.4.3 Experimental methods for developmental toxicity

Studies in animals are also used to assess whether an exposure can pose a risk to the unborn children of pregnant women. Experimental studies in pregnant animals provide a means for isolating the exposure in question from the myriad of other factors that can affect prenatal development. The results of these well-controlled *in vivo* studies are used by regulatory

agencies to assess prenatal risk and help set human exposure limits (NTP, 2011; USEPA, 1998; USEPA, 1991).

To test the potential for an exposure to affect fetal development, pregnant mammals such as mice, rats, or rabbits are exposed from the time the embryo is implanted in the uterus to the day before delivery. Variations in study design include preconception exposure of the female in addition to exposure during gestation, and even further exposure after the animal is born. Protocols generally specify that doses be set below the levels known to cause maternal toxicity, that unexposed controls are maintained at the same time period, and that the animals' health is monitored throughout the study. Endpoints measured include maternal body weight and weight change, the numbers and percent of live offspring, fetal body weight, the sex ratio, and external, soft tissue, or skeletal variations and malformations. The uterus can also be examined to assess the number of implantations and fetuses that have been lost, as an indication of miscarriage (USEPA, 1998).

2.4.4 Evaluating the cumulative body of experimental evidence

Key factors in evaluating individual experimental studies for a weight-of-evidence review include the details of the protocol; the plan for selecting animals and conducting and analyzing the study; the adequacy of the dose levels selected; the way in which the study was actually conducted, including adherence to good laboratory practices in animal housing and monitoring; and the evaluation of the effects on toxicity, tumors, or malformations, considering both biological and statistical issues (USEPA, 2005).

As an example of a protocol, consider the long-term *in vivo* study, a major tool for determining whether a chemical can produce cancer in humans. Standard protocols usually specify at least 50 animals of each sex per dose level, in each of three different dose groups. One of these is a high level dose group termed the "maximum tolerated dose," which is close to, but below, the level that increases mortality or produces significant morbidity. Additional dose levels are used below this maximum. An unexposed group, or control, is maintained under the same conditions during the same time period for comparison. This study design permits a separate evaluation of the incidence rate for each tumor type in the exposed group compared to the unexposed control

group. Statistical methods are used to assess the role of chance in any differences in the rates between exposed and unexposed, or among the dose groups. If effects are observed in a study, other studies are conducted because similarity of results in different studies, laboratories, and species strengthens the evidence.

Specific methods are used to reduce subjectivity and avoid systematic error, or bias, in scientific experiments (NRC, 1997). These are summarized in Table 2, including the random assignment of subjects to control or comparison groups, the unbiased collection of information (e.g., researchers are not aware of, or are "blind" to the exposure), and the need for replication of results. As with *Hill's criteria*, each guideline for evaluating causation in experimental studies is not met with a simple "yes" or "no," rather, they serve as guidance for weighing the evidence to reach a decision about cause-and-effect. The more firmly these criteria are met by the studies, the more convincing the evidence.

Table 2. Criteria for evaluating experimental studies as applied to EMF exposures

Avoiding unwanted effects	Experimental techniques should be chosen to avoid effects of intervening factors such as microshocks, noise, corona discharges, vibrations and chemicals.
Exposure classification	Extreme care should be taken to determine the effective EMF field, voltage, or current in the organism.
Sensitivity	The sensitivity of the experiments should be adequate to ensure a reasonable probability that an effect would be detected if it existed.
Objectivity	The experimental and observational techniques, methods and conditions should be objective. "Blind" scoring (where the investigator making the observations is unaware of the experimental variable being tested) should be used whenever there is a possibility of investigator bias. "Double-blind" protocols (where neither the investigator making the observations nor the experimental subject are aware of the experimental variable being tested) should be used in studies of people when the experimental subjects' perceptions may be unwittingly influenced.
Statistical significance	If an effect is claimed, the result should be demonstrated at a level where chance is an unlikely explanation.
Consistency	The results of a given experiment should be internally consistent among different ways of analyzing the data, and consistent across studies with respect to the effects of interest.
Quantifiable results	The results should be quantifiable and replicable. In the absence of independent confirmation, a result should not be viewed as definitive.
Appropriateness of methodologies	The biological and engineering methodologies should be sound and appropriate for the experiment.

Source: NRC, 1997

3 Conclusions of weight-of-evidence reviews of EMF and health

Scientists, scientific organizations, and regulatory agencies worldwide use the weight-of-evidence approach to assess potential health risks associated with exposures. These expert groups typically include many scientists with diverse skills that reflect the different research approaches required to answer questions about health. Using a weight-of-evidence approach as an analytic framework, each group provides its scientific consensus based on a review of the evidence.

3.1 Weight of evidence reviews by national and international scientific agencies

The following scientific organizations have assembled multidisciplinary panels of scientists to conduct weight-of-evidence reviews and arrive at conclusions about the possible risks associated with ELF EMF (in ascending, chronological order of their most recent publication):[9]

- The National Institute for Environmental Health Sciences (NIEHS) assembled a 30-person Working Group to review the cumulative body of epidemiologic and experimental data and provide conclusions and recommendations to the US government (NIEHS, 1998, 1999).
- The IARC completed a full carcinogenic evaluation of EMF in 2002.
- The Federal-Provincial-Territorial Radiation Protection Committee (FPTRPC), an intergovernmental, Canadian committee assembled to harmonize the standards and practices for radiation protection within federal,

[9] We are aware of other published summaries of the EMF research. With an increase in transmission infrastructure development and the advent of the Internet, the release of reviews and summaries now occurs regularly. This update is restricted to summaries that used a weight-of-evidence approach, and for which a multidisciplinary scientific panel reviewed the epidemiologic and experimental evidence (either in its entirety or since the organization's previous report), and offered conclusions about causality. Other reviews and summaries that did not follow this approach are not addressed because they do not assist in making science-based risk assessments and conclusions. In particular, a highly publicized posting on the Internet by the BioInitiative Group is not included.

provincial, and territorial jurisdictions, conducted a review in 1998 and an update in 2005 (FPTRPC 1998; FPTRPC 2005). The FPTRPC most recently released a statement from their Working Group in November 2008 summarizing their opinion on exposure to EMF (FPTRPC, 2008). [10]

- The National Radiological Protection Board (NRPB)[11] of the United Kingdom (UK) issued full evaluations of the research in 1992, 2001 and 2004, with supplemental updates and topic-specific reports published in the interim and subsequent to their last full evaluation in 2004 (NRPB, 1992, 1994a, 1994b, 2001a, 2001b, 2004; HPA, 2006). In a letter addressing a related topic in 2009, the Director of the HPA reiterated their position with regard to ELF EMF and appropriate precautionary measures (HPA, 2009).

- The World Health Organization (WHO) released a review in June 2007 as part of its International EMF Program to assess the scientific evidence of possible health effects of EMF in the frequency range from 0 to 300 GHz.

- The Health Council of Netherlands (HCN), using other major scientific reviews as a starting point, evaluated recent studies in several periodic reports (HCN, 2001; HCN, 2004; HCN, 2005; HCN, 2007; HCN, 2009a). The HCN also released an advisory letter that addressed the topic of power lines and Alzheimer's disease (HCN, 2009b).

- The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) issued a report to the Health Directorate of the European Commission (EC) in March 2007 and March 2009 updating previous conclusions (SSC, 1998; CSTEE, 2001; SCENIHR, 2007, 2009).

[10] Health Canada refers to the FTPRPC as the authority on issues related to EMF. The FPTRPC established an ELF Working Group to carry out periodic reviews, recommend appropriate actions and provide position statements that reflect the common opinion of intergovernmental authorities.

[11] The NRPB merged with the Health Protection Agency (HPA) in April 2005 to form its new Radiation Protection Division.

- The EC has also funded the European Health Risk Assessment Network on Electromagnetic Fields Exposure (EFHRAN), a network of experts convened to perform health risk assessments and provide scientifically-based recommendations to the Commission. EFHRAN consulted other major reviews and evaluated epidemiologic and experimental research published after August 2008 to provide an updated health assessment (EFHRAN, 2010a, 2010b).

- 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 exposure guidelines in 2010 that updated their 1998 exposure guidelines. For both guidelines, they relied heavily on previous reviews of the literature related to long-term exposure, but provided some relevant conclusions as part of their update process (ICNIRP, 1998, 2010).

- The Swedish Radiation Protection Authority (SSI), using other major scientific reviews as a starting point, evaluated current studies in three annual reports (SSI, 2007; SSI, 2008; SSM, 2010). [12]

The most comprehensive assessment of EMF was conducted by the WHO and published in June 2007; their report updated a previous evaluation of ELF EMF by the IARC in 2002. Exponent's 2007 Report focused on the conclusions of WHO (2007) and provided an update by reviewing literature published December 2005 (the approximate cut-off date for WHO) through September 2007. Exponent's 2010 report reviewed the research through mid-January 2010. While a few scientific organizations have published updates or statements since January 2010, no comprehensive risk assessment of the caliber of WHO (2007) has been published. This report

[12] The Swedish Radiation Safety Authority (Sträl säkerhets myndigheten [SSM]) has superseded the SSI, which ceased to exist on 30 June 2008. The SSM is a managing authority of Sweden's Ministry of the Environment and has "national collective responsibility within the areas of radiation protection and nuclear safety," which includes EMF research (http://www.stralsakerhetsmyndigheten.se).

will again focus on describing and updating the conclusions of the WHO (2007) report, while noting the other scientific organizations that have published material since January 2010. From January 15, 2010 through March 1, 2012, ICNIRP, EFHRAN, and SSM have published updates and statements with regard to ELF EMF.

Overall, the published conclusions of scientific review panels have been consistent. None of the panels concluded that either electric fields or magnetic fields are a known or likely cause of any adverse health effect at the long-term, low exposure levels found in the environment. As a result, no standards or guidelines have been recommended to prevent this type of exposure. Existing guidelines from ICNIRP include limits on short-term exposure at levels higher than those encountered in public locations, including publicly-accessible areas near electrical facilities.

Most of the uncertainty and controversy surrounding magnetic-field exposure is related to the research on childhood leukemia. Some epidemiology 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; other epidemiology studies did not report this statistical association. When a number of relevant studies were combined in a single analysis, no association was evident at lower exposure levels, but a weak association was reported between childhood leukemia and estimates of average magnetic-field exposure greater than 3-4 mG (Ahlbom et al., 2000; Greenland et al., 2000). These pooled analyses provide some evidence for an association between magnetic fields and childhood leukemia; however, because of the inherent uncertainty associated with observational epidemiology studies, the results of these pooled analyses were considered to provide only limited epidemiologic support for a causal relationship; chance, bias and confounding could not be ruled out with reasonable confidence. Further, *in vivo* studies have not found that magnetic fields induce or promote cancer in animals exposed for their entire lifespan under highly-controlled conditions, nor have *in vitro* studies found a cellular mechanism by which magnetic fields could induce carcinogenesis.

Considering all the evidence together, the WHO, as well as other scientific panels, classified magnetic fields as a *possible* cause of childhood leukemia (NRPB, 2001a; IARC, 2002;

ICNIRP, 2003; HCN, 2004; WHO, 2007). The term "*possible*" denotes an exposure for 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) and experimental evidence does not support a cause-and-effect relationship (Figure 3).

Despite additional research, it has not prompted scientific organizations to recommend that the classification of "possible carcinogen" be changed to any other IARC category such as "probable" or "known human carcinogen" (FPTRPC, 2009; HPA, 2009; SCENIHR, 2009; EFHRAN, 2010a; ICNIRP, 2010; SSM, 2010). The WHO and these more recent reviews have stressed the importance of reconciling the epidemiologic data on childhood leukemia and the lack of evidence from experimental studies through innovative research. Researchers believe that the development of childhood leukemia, like any other cancer, is influenced by a multitude of different factors, e.g., genetics, environmental exposures, and infectious agents (Buffler et al., 2005; McNally et al., 2006).

The WHO and other scientific organizations, however, have not found any *consistent* associations with regard to EMF exposure and any other cancerous or non-cancerous outcomes, nor have they concluded that there is a cause-and-effect link with any health effect, including childhood leukemia (WHO, 2007; HPA, 2009; SCENIHR, 2009; EFHRAN, 2010a; ICNIRP, 2010; SSM, 2010).

Although some questions remain, the epidemiologic evidence does not support a cause-and-effect relationship between magnetic fields and adult leukemia/lymphoma or brain cancer, with the data being described as inadequate or weak (WHO, 2007; SCENIHR, 2009; EFHRAN, 2010a). Scientific organizations have concluded that there is strong evidence in support of *no* relationship between magnetic fields and breast cancer or cardiovascular disease (WHO, 2007; SSI, 2008; ICNIRP, 2010; EFHRAN, 2010a; SSM, 2010). Although two epidemiology studies reported a statistical association between peak magnetic-field exposure and miscarriage, a serious bias in how these studies were conducted was identified and various scientific panels concluded that these biases preclude making any conclusions about associations between magnetic-field exposure and miscarriage (HCN, 2004; NRPB, 2004; WHO, 2007; ICNIRP, 2010). While an association between some neurodegenerative diseases (i.e., Alzheimer's

disease and Amyotrophic Lateral Sclerosis [ALS]) and estimates of higher average occupational magnetic-field exposure has been reported, scientific panels have described this research as weak and inadequate and recommended more research in this area (SCENIHR, 2007; WHO, 2007; SCENIHR, 2009; HCN, 2009b; ICNIRP, 2010; EFHRAN, 2010a; SSM, 2010).

In summary, reviews published by scientific organizations using weight-of-evidence methods have concluded that the cumulative body of research to date does not support the hypothesis that electric or magnetic fields cause any long-term adverse health effects at the levels we encounter in our everyday environments.

The Working Group of the FPTRPC concluded the following with respect to ELF EMF and health in a statement released in 2008:

> In summary, it is the opinion of the Federal-Provincial-Territorial Radiation Protection Committee that there is insufficient scientific evidence showing exposure to EMFs from power lines can cause adverse health effects such as cancer.

The FPTRPC conclusion is consistent with statements by Health Canada on their website, which were updated in January 2010 (http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/environ/magnet-eng.php). The website concludes, "In summary, when all of the studies are evaluated together, the evidence suggesting that EMFs may contribute to an increased risk of cancer is very weak."

3.2 Standards and guidelines for limiting exposure to EMF

3.2.1 Status of EMF guidelines

Two international scientific organizations, ICNIRP and the International Committee for Electromagnetic Safety (ICES), have published guidelines for limiting public exposure to EMF (ICES, 2002; ICNIRP, 2010). The health outcomes examined in most EMF epidemiology and *in vivo* studies primarily have addressed magnetic fields, mainly because structures and vegetation provide some shielding that limits residential exposure to electric fields from power lines; however, these EMF guidelines recommend limits for both electric and magnetic fields.

These guidelines set limits at high EMF levels to protect against the short-term direct, acute health effects (i.e., perception, annoyance, and the stimulation of nerves and muscles) that can occur at these high levels of exposure. Although ICNIRP and ICES have the same objectives[13] and used similar methods, the recommended limits for exposure of the general public to EMF at the frequencies used to transmit electricity differ, as seen in Table 3. Exposure standards were set based on acute effects—those that occur from short-term exposure to high levels—because both organizations judged that evidence for effects from long-term exposure to ELF EMF was insufficient for setting exposure standards. These reference levels are updated from Exponent's 2010 report to reflect ICNIRP's updated guidance (ICNIRP, 2010). ICNIRP increased the magnetic-field restriction level from 833 mG to 2,000 mG for the general public, but electric field restriction levels remain the same.

Table 3. Reference levels for whole body exposure to 60-Hz fields: general public

Organization recommending limit	Magnetic fields	Electric fields
ICNIRP restriction 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 rights of way 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).

ICNIRP recommends screening values for magnetic fields of 2,000 mG for the general public and 4,200 mG for workers (ICNIRP, 2010). The ICES recommends a screening value of 9,040 mG for magnetic-field exposure (ICES, 2002). The ICNIRP screening value for general public exposure to electric fields is 4.2 kV/m, and the ICES screening value for general public exposure to electric fields is 5 kV/m. Both organizations allow higher exposure levels if it can

[13] The scope of ICES is the "Development 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." ICES encourages balanced international volunteer participation of the public, the scientific and engineering community, agencies of governments, producers, and users. ICNIRP is an independent group of approximately 40 experts assembled from around the world. It is the formally recognized, non-governmental organization charged with developing safety guidance for non-ionizing radiation for the WHO, the International Labour Organization, and the European Union.

be demonstrated that exposure does not produce current densities or electric fields within tissues that exceed basic restrictions on internal current densities or electric fields.

In Canada, there are no national standards or guidance for limiting residential or occupational exposure to 60-Hz ELF EMF based on either acute or long-term health effects. Rather, the only Canadian standards specify maximum levels and duration of exposure to *radio frequency fields*, that is, fields with a frequency over 3,000 Hz (Health Canada, Safety Code 6). Health Canada, which monitors the scientific research on EMF and human health as part of its mission to improve the health of Canadians, takes the following position:

> At present, there are no Canadian government guidelines for exposure to EMFs at ELF. Health Canada does not consider guidelines for the Canadian public necessary because the scientific evidence is not strong enough to conclude that exposures cause health problems for the public. Some national and international organizations have published health based exposure guidelines for EMFs at ELF. However, these guidelines are not based on a consideration of risks related to cancer. Rather, the point of the guidelines is to make sure that exposures to EMFs do not cause electric currents or fields in the body that are stronger than the ones produced naturally by the brain, nerves and heart. EMF exposures in Canadian homes, schools and offices are far below these guidelines (Health Canada, 2010).

The sections below discuss the similarities and differences between the ICNIRP and ICES standards, and the public health implications of the differences.

3.2.2 Similarities between ICES and ICNIRP guidelines

In both the ICES and ICNIRP standard setting process, a group of scientists conducted extensive reviews of the scientific research regarding health effects. The scientists reviewed the epidemiologic and experimental evidence and concluded that the evidence was insufficient to warrant the development of standards on the basis of hypothesized long-term health effects, such as cancers. Each organization reached a consensus that the most sensitive endpoints – the substantiated adverse effects that would occur at the lowest level of exposure – are short-term reactions to electrostimulation of nerve and muscle. These are direct, acute reactions to high levels of exposure, not severe or life-threatening events.

Each organization developed its recommended exposure limit in two steps. The first step was to identify the lowest level of electrical forces inside the body that is likely to produce the stimulation of nerve and muscle. This internal level, or dose, is further lowered by safety factors to develop what is referred to as the basic restriction. As the term indicates, the basic restriction is the internal 'dose' recommended for exposed populations. This internal level is the foundation of both the ICNIRP and ICES standards because both electric and magnetic fields can induce electrical forces in the body.

The ICNIRP and ICES basic restrictions are set well below the value at which an adverse effect was observed in experiments; as a result, these exposure limits are conservative.[14] This is because they incorporate dose reduction factors, also known as safety factors, to account for potential sources of uncertainty. For example, both groups consider the potentially higher sensitivity in vulnerable groups as a reason for using a safety factor.

The second step in the standard setting process involves developing the reference level. A reference level is developed because a basic restriction cannot be directly measured. The reference level is the measurable level of electric fields at the location of interest; these levels are outside of the body, and are used as a screening value to maintain the internal level identified as the basic restriction.

3.2.4 Implications for human health

The underlying question for people who make decisions about public health and safety is whether the ICNIRP reference value (4.2 kV/m) implies greater safety simply because it is lower and includes a larger "safety factor." In developing public health standards, safety factors are used when uncertainty is recognized, and the general rule is that smaller safety factors are needed as the relevant information on risk to humans is improved. Although ICNIRP uses a larger safety factor, it applies that factor to a higher level of exposure as the estimated threshold

[14] In this context "conservative" means that if the reference level (i.e., the screening level) is exceeded, it does not necessarily follow that the basic restriction is exceeded. ICNIRP explains: "In many practical exposure situations external power frequency electric fields at the reference levels will induce current densities in central nervous tissues that are well below the basic restrictions. Recent dosimetry calculations indicate that the reference levels for power-frequency magnetic fields are conservative guidelines relative to meeting the basic restrictions on current density for both public and occupational exposures" (ICNIRP, 1999).

level. ICES uses a smaller safety factor, but has used highly specific data on human responses, leading to a lower, presumably more precise, estimated threshold level. It is essential to understand that for effects like these that have a threshold; the goal of the standard setting process is to set the exposure limit where no effects will occur in the population. Therefore, further lowering of the exposure limit is not expected to have any health benefit. For additional perspective on the question of the safety of exceeding ICNRIP exposure limits up to the level of the ICES limits, consider that ICNIRP states that EMF guidelines are conservative, and that the ICNIRP recommended limit for occupational exposure is 8.3 kV/m (ICNIRP, 1998, 2010).

3.3 Precautionary approaches

3.3.1 General definition

A precautionary policy for risk management of possible, but unproven, adverse effects emerged in Europe in the 1970s regarding environmental issues. The precautionary principle refers to the idea that, when evidence does not support the suggestion that an exposure is a cause of a particular disease but where a risk is perceived or uncertainty exists, precautionary measures may be taken that are proportional to the perceived level of risk, with science as the basis for estimating that risk. A key element of precautionary approaches is the recognition that a real risk from the exposure may not exist, and its necessary corollary is that the reduction of exposure may not decrease any adverse effects in the population.

The EC prepared a report in 2000 to clarify "the precautionary principle" because this idea had been subject to controversy and variability in interpretation.[15] The EC report explained that the implementation of the precautionary principle should be science based, starting with a complete scientific evaluation, and the range of actions taken should depend on the extent of the risk and the degree of uncertainty surrounding the occurrence of adverse effects. The EC provided guidelines for the application of the precautionary principle or other risk management measures

[15] Commission of the European Communities, Communication on the Precautionary Principle, Brussels 03 February 2000 (http://europa.eu.int/comm./off/com/health_consumer/precaution.htm)

as five general principles: proportionality, non-discrimination, consistency, examination of costs and benefits of actions, and examination of scientific developments.[16]

A variant of the precautionary principle called "prudent avoidance" has been favored as a policy option for EMF by some national and local governments. The WHO describes this as "using simple, easily achievable, low to modest (prudent) cost measures to reduce individual or public EMF exposure, even in the absence of certainty that the measure would reduce risk" (WHO, 2002).

3.3.2 WHO recommendations regarding precautionary measures for EMF

The scientific evaluation completed by the WHO also discusses general policy strategies for risk management, and provides a summary table of different policy strategies worldwide specifically for EMF exposure in the general public (WHO, 2007, Chapter 13). The WHO recommended the following precautionary measures:

- Countries are encouraged to adopt international science-based guidelines.
- 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.

[16] Proportionality: "Measures...must not be disproportionate to the desired level of protection and must not aim at zero risk."

Nondiscrimination: "comparable situations should not be treated differently and... different situations should not be treated in the same way, unless there are objective grounds for doing so."

Consistency: "measures...should be comparable in nature and scope with measures already taken in equivalent areas in which all the scientific data are available."

Examination of the benefits and costs of action or lack of action: "This examination should include an economic cost/benefit analysis when this is appropriate and feasible. However, other analysis methods...may also be relevant."

Examination of scientific developments: "The measures must be of a provisional nature pending the availability of more reliable scientific data"... "Scientific research shall be continued with a view to obtaining more complete data."

- 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 reductions 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 programs to reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure. (WHO, 2007, adapted from pp. 372-373)

In summary, the general recommendation of the WHO is as follows:

> Countries are encouraged to adopt international science-based guidelines. In the case of EMF, the international harmonization of standard setting is a goal that countries should aim for (WHO, 2006). If precautionary measures are considered to complement the standards, they should be applied in such a way that they do not undermine the science-based guidelines (WHO, 2007, p. 367).

3.3.3 Canadian perspective on precautionary approaches

The Government of Canada has published "A Framework for the Application of Precaution in Science-based Decision Making About Risk" (2003). One of the basic general principles is that sound scientific information must be the basis for both deciding whether or not to implement precautionary measures and determining what precautionary measures, if any, are implemented. The document clarifies that "Scientific advisors should give weight to peer-reviewed science and aim at sound and reasonable evidence on which to base their judgments" (p. 8).

The FPTRPC stated the following with respect to precautionary measures in 2008: "In the context of power-frequency EMFs, health risks to the public from such exposures have not been established; therefore, it is the opinion of the FPTRPC that any precautionary measures applied to power lines should favour low cost or no cost options."

Health Canada recommended no precautionary measures to the public in a 2010 statement: "You do not need to take action regarding daily exposures to electric and magnetic fields at extremely low frequencies. There is no conclusive evidence of any harm caused by exposures at levels found in Canadian homes and schools, including those located just outside the boundaries of power line corridors."

A framework for applying the precautionary principle to public health issues in Canada has been proposed by four Canadian public health physicians that closely matches the conceptual approach recommended by the EC and the approach of the FPTRPC and Health Canada in addressing EMF health concerns (Weir et al., 2010).

4 Human Health Research

This section provides an up-to-date summary assessment of the current literature to determine whether recent findings are consistent with the conclusions of the scientific panels presented in Section 3, particularly the conclusions of the WHO's evaluation (WHO, 2007). Exponent reviewed the literature through September 2007 (Exponent, 2007) and subsequently reviewed the literature through mid-January 2010 (Exponent, 2010). This assessment reviews literature indexed in Pub Med between January 15, 2010 and March 1, 2012. In carrying out this update, we considered the totality of the science (not just the new information) to determine if changes in the national and international health risk assessments were warranted. This assessment uses a weight-of-evidence approach with standard epidemiologic principles and *Hill's criteria* as an analytic foundation. All relevant research discussed below is taken into consideration and more weight is assigned to studies that are well-designed and well-conducted, because studies with better methods provide stronger evidence. Therefore, this assessment reflects the current knowledge of research related to EMF and the health concerns reviewed.

As noted by the ICNIRP and IARC, there has been no consistent or strong evidence to explain how EMF exposure could affect biological processes in cells and tissues. In addition, such data are supplementary to epidemiology and *in vivo* studies, and are used rarely by health agencies to directly identify hazards to human health. For that reason, this review systematically addresses epidemiology studies and *in vivo* studies, but relies largely on reviews and the conclusions of scientific panels with regard to studies of mechanism.

A structured literature review was conducted to identify new epidemiologic and *in vivo* peer-reviewed research published on 50- or 60-Hz alternating current (AC) ELF EMF between January 15, 2010 and March 1, 2012. A large number of search strings referencing the exposure and health outcomes of interest, as well as authors that regularly publish in this area, were included as search terms in the PubMed database.[17] This report focuses on the health outcomes that have received the

[17] PubMed is 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 back to the 1950s. PubMed includes links to full text articles and other related resources (http://www.ncbi.nlm.nih.gov/PubMed/).

most attention—cancer, reproductive or developmental effects, and neurodegenerative diseases. To be included in this review, epidemiology studies on these health outcomes must have assessed EMF exposure beyond a self-reported job title.[18] Many other health effects have been studied (suicide, depression, cardiovascular effects, etc.), but for brevity and because research on these topics evolves slowly, they are not summarized here. Electrical hypersensitivity is discussed separately in Section 5. The WHO report provides a good resource for the status of research on these additional health effects (WHO, 2007).

4.1 Cancer

4.1.1 Childhood leukemia

What was previously known about childhood leukemia?

Since the late 1970s, numerous epidemiology studies have evaluated the relationship between childhood leukemia and some proxy of magnetic-field exposure. As a group of independent studies, a clear and consistent association was not apparent. The largest and most advanced studies did not show a clear relationship between magnetic-field exposure and leukemia (Linet et al., 1997; UKCCS, 2000), including a study of Canadian children by McBride and colleagues (1999). When two, independent pooled analyses combined the data from these studies, however, results showed an approximate 2-fold statistically significant association between average magnetic-field exposure above 3-4 mG and childhood leukemia (Ahlbom et al., 2000; Greenland et al., 2000). This result means that the children with leukemia in these studies were about 2 times more likely to have had average magnetic-field exposure above 3-4 mG, compared to the children in the control group. Average exposure at this level is rare; several surveys show that approximately 0.5 – 7 percent of children have time-averaged exposures in

[18] Studies that only report associations between the health outcome under investigation and job titles that are presumed to have high levels of magnetic field exposure were identified and scanned, but are not evaluated further in this report for several reasons. First, job titles are a crude method of estimating exposure because they do not capture the variety of a person's occupational history or the variety of exposures a person may encounter within one occupation. Furthermore, hypothesis-generating case-control analyses that calculate associations for many occupations are subject to the bias associated with multiple comparisons. These studies provide relatively little information in a weight-of-evidence review, particularly when studies are available with more thorough exposure evaluations (as is the case for the large number of studies related to magnetic field exposures).

excess of 3 mG and 0.4 – 3.3 percent have time-averaged exposures in excess of 4 mG (WHO, 2007).[19] Because of the rarity of exposure to magnetic fields in the 3-4 mG range, analyses have suggested that a small proportion of childhood leukemia cases would be attributed to magnetic fields, if a true relationship existed (Greenland and Kheifets, 2006; Kheifets et al., 2006).

These studies were limited in many ways, such that chance, bias and confounding could not be ruled out as explanations for the association. Thus, it was unclear whether exposure to magnetic fields in the range of 3-4 mG had any relationship with the development of childhood leukemia or whether the association was simply a consequence of an error in study design. In addition, experimental studies did not suggest that magnetic fields are carcinogenic—these studies did not indicate any consistent increase in cancer in animals when they were exposed to high levels of magnetic fields over the course of their lifetime (see section "*In vivo* studies of carcinogenesis"), and there was no known mechanism by which magnetic fields cause cancer (see section "*In vitro* studies of carcinogenesis"). The IARC concluded in 2002 that the data on childhood leukemia provided "limited" evidence of carcinogenicity. In 2007, the WHO reviewed studies published since the 2002 IARC review and concluded that the new epidemiology studies were consistent with the classification of "limited" evidence and, together with the largely negative *in vivo* and *in vitro* research, consistent with the classification of magnetic fields as a possible carcinogen.[20]

As described in Exponent 2010, no studies have been published since the pooled analyses that provide strong evidence in support of the association, although the results of some subsequent studies suggest a promotional effect of magnetic fields at the same exposure level (i.e., > 3-4 mG). These studies reported that children with leukemia and estimates of average magnetic-field exposure greater than 3-4 mG had poorer survival rates; children with Down's syndrome

[19] The failure to understand the difference between calculated or measured 'spot' values of the magnetic field and estimates of long-term average magnetic-field exposure above 4 mG has been discussed by Bailey and Wagner (2008).

[20] The WHO concluded that, "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" (p. 355-6, WHO, 2007a).

and childhood leukemia were more likely to have estimates of magnetic-field exposure greater than 6 mG; and children with leukemia and a particular genetic polymorphism were more likely to live closer to an electrical installation. Further research on these new research topics is required.

Since it is unclear whether the association between magnetic fields and childhood leukemia is a cause and effect relationship, the WHO report described 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. The status of research on each of these factors is summarized below:

- ✓ **Chance**. The WHO report concluded that chance is an unlikely explanation since the pooled analyses had larger sample sizes and decreased variability.

- ✓ **Control selection bias**. Control selection bias occurs when the controls that decide to participate in a study do not represent the true exposure experience of the non-diseased population. In the case of magnetic fields, the WHO speculated that controls with a higher socioeconomic status (SES) may participate in studies more often than controls with a lower SES and, since persons with a higher SES may have lower magnetic-field exposure or tend to live farther away 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, it appears that the case group has higher exposures when, in fact, the difference is an artifact of the study. The WHO stated that control selection bias would result in an overestimate of the true association, but would not explain the entire observed association. A study published after the WHO review found that control selection bias is operating to some extent (Mezei et al., 2008a).

- ✓ **Confounding**. The WHO panel concluded that it is less likely that confounding is causing the observed association, although the possibility that some yet-to-be identified confounder is responsible for the association cannot be fully excluded. Suggested risk factors that may be acting as confounders include SES, residential mobility, contact

currents, and traffic density.[21] Preliminary research on contact currents suggests that they have some features of a confounder (Kavet and Hooper, 2009).

- ✓ **Exposure misclassification**. The WHO stated that the possible effects of exposure misclassification are the most difficult to predict. 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 provide an entire explanation for the association. A recent study found that there is substantial exposure misclassification when distance is used as a surrogate for magnetic-field exposure (Maslanyj et al., 2009).

What relevant studies have been published since Exponent 2010?

Eight studies have evaluated the association between childhood leukemia and magnetic fields since our previous review. While some recent studies were innovative in their approach, overall they lacked the methodological improvements (e.g., a large sample size or improved exposure assessment) necessary to advance this field, and the association between magnetic fields and childhood leukemia remains unexplained.

The most noteworthy study is a pooled analysis of studies published after 2000 on childhood leukemia and residential magnetic-field exposure (Kheifets et al., 2010a). The need for a pooled analysis was identified by the WHO as a high research priority to evaluate whether newer studies are consistent with the classification of magnetic fields as a possible carcinogen (WHO, 2007). The intent of a pooled analysis is to provide a more reliable estimate of an association because of the larger sample size. Despite the large number of childhood leukemia cases (10,818) enrolled in the analysis, however, a relatively small number of cases (26 [0.2%]) were classified in the highest exposure category (> 3 mG) (Table 4). Compared to the earlier pooled

[21] For example, if dwellings near power lines encounter higher traffic density and pollution from traffic density causes childhood leukemia, traffic density may cause an observed association between magnetic-field exposure and childhood leukemia.

analyses (Ahlbom et al., 2000; Greenland et al., 2000), the association between childhood leukemia and magnetic-field exposure levels greater than 3 mG was weaker (OR=1.44) and not statistically significant (95% CI=0.88–2.36). The authors concluded that the results of this analysis are consistent with the classification of magnetic fields as a possible carcinogen, but carry less weight because of the weakness and imprecision of the risk estimate and possible bias in the underlying studies. A recent quantitative analysis suggests that the data best fits a model assuming cases of childhood leukemia could occur below the 3-4 mG range if a true relationship existed, although there were many limitations to the analysis (Kheifets et al., 2011).

Table 4. Number of childhood leukemia cases (by study and exposure level) and resultant odds ratios from pooled analysis by Kheifets et al. (2010a)

Study*	Total cases	Cases <1 mG	Cases >3mg	OR <1 vs. >3 mG (95% CI)
Studies that measured fields				
Wünsch-Filho et al., 2012	162	120	11	1.26 (0.61-2.62)
Kabuto et al., 2006	312	279	8	1.40 (0.56-3.49)
Schüz et al., 2001	514	474	4	3.05 (0.68-13.8)
Studies that calculated fields				
Malagoli et al., 2010	46	45	1	2.26 (0.20-25.9)
Kroll et al., 2010	9,665	9,657	2	0.98 (0.14-6.97)
Bianchi et al., 2000	119	116	0	-
All studies				
Pooled analysis	10,818	10,691	26	1.44 (0.88-2.36)
Pooled analysis without Wünsch-Filho et al., 2012	10,656	10,571	15	1.56 (0.78-3.10)

*Studies published after Exponent 2010 are in bold and are summarized in this report.

Three of the six studies included in the Kheifets et al. (2010a) pooled analysis were published since Exponent 2010 and are, therefore, described further (i.e., Kroll et al., 2010; Malagoli et al., 2010; Wünsch-Filho et al., 2011).

Wünsch-Filho et al. (2011) is the only recent study to use long-term measurements to estimate magnetic-field exposure. This study had a significant influence on the results of the pooled analysis because it contributed a relatively large proportion of the cases with estimated exposures $\geq$ 3 mG (11 cases [7%], Table 4). Prior to publication of the Wünsch Filho study,

Kheifets et al. (2010a) used their raw data to calculate an OR equal to 1.26 (95% CI=0.61-2.62) for 24-hour residential exposure $\geq$ 3 mG, but Wünsch-Filho et al. actually reported a lower OR of 1.09 (95% CI=0.33-3.61) for the same exposure level.[22] The authors concluded that although their results do not support an association between childhood leukemia and magnetic fields, this conclusion carries less weight because of the study's weaknesses. The most significant limitation was selection bias that may have artificially reduced the OR (i.e., low participation rates and some evidence that the excluded controls had higher magnetic-field exposures). Since this study was influential to the pooled analysis, analyses were conducted by Kheifets et al. without the data from the Wünsch-Filho study; substantially higher (but still imprecise) ORs were reported, similar to those from the earlier pooled analyses (Table 4).

Two case-control studies published in 2010 estimated magnetic-field exposure using calculations of magnetic fields from nearby power lines (Kroll et al., 2010; Malagoli et al., 2010). These studies are less susceptible to the type of selection bias found in Wünsch-Filho et al. (2011), but do not taken into account all sources of residential magnetic fields. Both Kroll et al. (2010) and Malagoli et al. (2010) reported a positive association with a wide CI due to the rarity of elevated exposure from nearby power lines; Kroll et al. (2010) reported an OR of 2.00 (95% CI=0.18-22.04) for childhood leukemia and calculated exposure greater than 4 mG in their study of childhood cancers in the United Kingdom from 1962-1995.[23] Malagoli et al. (2010) reported an OR of 2.10 (95% CI=0.2-26.2) for childhood leukemia and residence in a home 6 months prior to diagnosis with calculated exposure greater than 4 mG in a study of childhood lymphohematopoietic malignancies in two Italian municipalities from 1986-2007. Neither of these studies provides strong evidence in support of an association. In Kroll et al. (2010), nearly 25% of the residences with possible magnetic-field exposure from power lines lacked the data necessary to calculate the actual magnetic-field levels. Malagoli et al. (2010) had complete

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[22] Pooled analyses often report results that differ substantially from those reported in the underlying studies because of differences in inclusion/exclusion criteria.

[23] Kroll et al. (2010) was conducted as a follow-up to an earlier study (Draper et al., 2005) that reported a statistically significant association between childhood leukemia and distance from home address at birth to high-voltage power lines. This association was not readily explained by magnetic fields because it extended to over 600 m. To address this discrepancy, Kroll et al. (2010) directly estimated magnetic fields from nearby high-voltage power lines to assess whether they were related to the risk of childhood leukemia in the same study population as Draper et al. (2005).

residential histories and exposure information, but only one case of leukemia and two controls had estimated exposures greater than 4 mG.

Kroll et al. (2010) contributed the vast majority (89%) of the childhood leukemia cases to the Kheifets et al. (2010a) pooled analysis, but few of the cases had an estimated exposure $\geq$ 3 mG (2 cases [0.02%]) (Table 4). While Kroll et al. (2010) reported a positive association at exposure levels greater than 4 mG, no association was observed in the pooled analysis for this study at exposure levels greater than 3 mG (Table 4). This discrepancy has been attributed to a change in the categorization of *one* control subject and highlights the instability of this association because of small sample size (Schmiedel and Blettner, 2010).

Another recent case-control study of childhood leukemia (Does et al., 2011) measured magnetic fields inside the home, but was not included in the pooled analysis because the exposure metric was substantially different from the other included studies (i.e., a 30-minute measurement in the room with the median spot measurement after a full survey of the home). There was no evidence of an association between childhood leukemia and residential magnetic-field levels in this Northern California study, although few children had measured levels above 3 mG, which limited the study's power to detect an association.

Kheifets et al. (2010a) also pooled data on distance from nearby power lines and childhood leukemia from five recent studies including Malagoli et al. (2010) and Wünsch-Filho et al. (2011).[24] The pooled analysis reported an elevated OR at residential distances $\leq$ 200 m, which reached statistical significance at distances $\leq$ 50 m. One other study published data on this association since Exponent 2010, but was excluded from the pooled analysis because of its hospital-based design. Sohrabi et al. (2010) reported an association between childhood leukemia and residence within 600 m of a transmission line in a case-control study in Iran. The study's strength was that a relatively large proportion of study subjects lived in close proximity to transmission lines, but it was severely limited by the lack of information on participation rates

[24] They included five studies in their analysis on distance from nearby power lines; the other three of these were discussed in Exponent 2010.

and adjustment for SES, both of which can introduce selection bias. In addition, similar to the much larger study by Draper et al. (2005) in England and Wales, the association was found at distances too far from the transmission lines to be fully explained by magnetic fields.

Studies have also investigated whether magnetic-field exposure of parents either prior to conception or during pregnancy may be relevant to the risk of childhood leukemia. A small body of literature is available on this topic with inconsistent findings, including two studies (Hug et al., 2010; Reid et al., 2011) that used advanced JEMs to compare the occupational exposure of the parents of children with leukemia to the exposure of parents of healthy children. No statistically significant association was found in either study with maternal or paternal magnetic-field exposure prior to or after birth. When the entire body of literature in this area is considered, small sample sizes, exposure uncertainties, and potential confounding with electromagnetic energy of different frequencies (as well as other occupational exposures, e.g., chemicals) prevent firm conclusions from being drawn. More research is required with improved exposure techniques.

Recent research also includes a case-control study by Does et al. (2011), discussed briefly above, which is the first case-control study of childhood leukemia to evaluate the possible confounding effect of contact currents. Contact currents occur when the water line provides the ground for the home's electrical system. The hypothesis is that a child may experience a contact current from touching surfaces at different potentials while bathing, and these contact currents may be responsible for the association between magnetic fields and childhood leukemia. Two criteria must be fulfilled for contact currents to have this confounding effect. First, there must be an independent causal relationship between contact currents and childhood leukemia, and second, there must be a strong association between residential magnetic fields and the voltage between bathtub plumbing fixtures and drains. While research suggests that the second criterion is met (e.g., Zaffanella, 1997; Kavet and Hooper, 2009; Kavet et al., 2011), Does et al. (2011) did not find an association between indoor or outdoor contact voltage and childhood leukemia, although the study was limited by poor participation rates. Further research should be conducted in study populations with a greater potential for elevated contact current and

magnetic-field exposure and with information available on the frequency of contact current exposure.

In summary, the association between childhood leukemia and magnetic fields remains unexplained. Recent studies have provided some evidence of an association with elevated magnetic fields, but the studies lacked notable methodological advancements to rule out bias and confounding; the small number of subjects in the upper exposure categories, including in the pooled analysis, continue to limit the robustness of the findings. In addition, recent studies continue to provide limited data for an association between childhood leukemia and residence near a power line. It is still unclear how to interpret this relationship, however, since residential distance is a poor proxy for magnetic-field exposure (Maslanyj et al., 2009) and the association is found at distances where magnetic fields from the power lines would have diminished completely. Thus, the results of these studies do not change the classification of the epidemiologic data as limited. This conclusion is supported by recent reviews (Calvente et al., 2010; Eden, 2010; Miller and Green, 2010) and conclusions from scientific organizations (SSM, 2010; EFHRAN, 2010a).

One editorial questioned whether studies of childhood leukemia and magnetic fields have exhausted the methods available to this field and stated that "better insights into this association cannot be expected" (Schmiedel and Blettner, 2010). Several areas of inquiry, however, may provide additional clarity. For example, an ongoing international epidemiologic study is being conducted on children with high magnetic-field exposure from residence above internal transformer stations in apartment buildings, which provides a more stable estimate of the association in upper exposure categories with less concerns of selection bias (Hareuveny et al., 2011). Agreement on the relevant exposure metric and exposure period has not been reached. In addition, further work on prenatal exposure may be warranted since research suggests that the first genetic changes linked to leukemia occur as part of fetal development (Eden, 2010).

It should be noted that magnetic fields are just one area in the large body of research on the possible causes of childhood leukemia. There are many other hypotheses under investigation that point to possible genetic, environmental, and infectious explanations for childhood

leukemia, which have similar or stronger support in epidemiology studies (Ries et al., 1999; McNally and Parker, 2006; Belson et al., 2007; Rossig and Juergens, 2008; Eden 2010).

Table 5. Studies of childhood leukemia published after Exponent 2010

Authors	Year	Study
Does et al.	2011	Exposure to electrical contact currents and the risk of childhood leukemia
Hug et al.	2010	Parental occupational exposure to extremely low frequency magnetic fields and childhood cancer: a German case-control study
Kheifets et al.	2010a	Pooled analysis of recent studies on magnetic fields and childhood leukaemia
Kheifets et al.	2011	Exploring exposure--response for magnetic fields and childhood leukemia
Kroll et al.	2010	Childhood cancer and magnetic fields from high-voltage power lines in England and Wales: a case-control study
Malagoli et al.	2010	Risk of hematological malignancies associated with magnetic fields exposure from power lines: a case-control study in two municipalities of northern Italy
Reid et al.	2011	Risk of childhood acute lymphoblastic leukaemia following parental occupational exposure to extremely low frequency electromagnetic fields
Sohrabi et al.	2010	Living near overhead high voltage transmission power lines as a risk factor for childhood acute lymphoblastic leukemia: a case-control study
Wünsch-Filho et al.	2011	Exposure to magnetic fields and childhood acute lymphocytic leukemia in São Paulo, Brazil

4.1.2 Childhood brain cancer

The evidence linking magnetic fields to childhood brain cancer is weaker than childhood leukemia. No consistent association has been found, although the studies are limited by the small number of participants since childhood brain cancer is rare. To address this limitation, the WHO recommended a pooled analysis.

A meta-analysis published after the WHO report is described in Exponent 2010 (Mezei et al., 2008b). A meta-analysis is similar to a pooled analysis, but the results from the individual studies are combined as opposed to the raw data. Overall, no association was reported in the meta-analysis, but an analysis of five studies with information on calculated or measured magnetic fields greater than 3-4 mG found a combined OR that was elevated but not statistically significant (OR=1.68, 95% CI=0.83-3.43). The authors stated that an increased risk of childhood brain tumors could not be excluded at this high exposure level, but that the similarity

of this result to the findings of the pooled analyses of childhood leukemia data suggests that control selection bias is operating in both analyses.

What relevant studies have been published since Exponent 2010?

Two studies of childhood brain cancer and magnetic-field exposure have been published since Exponent 2010 (Table 6). In response to the WHO's recommendation, Kheifets et al. (2010b) pooled data from 10 studies on childhood brain cancer and residential magnetic-field exposure. Similar to the recent pooled analysis of childhood leukemia (Kheifets et al., 2010a), there were few cases in the upper exposure categories. Some elevated ORs were observed, but they were not statistically significant and no dose-response patterns were observed. The authors concluded that their results provide little evidence for an association between magnetic fields and childhood brain cancer.

The vast majority of cases in the pooled analysis were from the large, UK case-control study of childhood cancers discussed above (Kroll et al., 2010). No association was found in Kroll et al. (2010) between central nervous system tumors or brain tumors and estimated exposures greater than 4 mG from nearby power lines (OR=0.80, 95% CI=0.43–1.51). This finding was limited by incomplete exposure data and the small number of subjects in the upper exposure categories. The results are similar to the findings from the study published in 2005 by Draper et al., which found no association with distance to power lines in the same underlying case and control groups.

These two new studies do not change the classification of the epidemiologic evidence in relation to childhood brain cancer as inadequate; this conclusion is consistent with a recent review by the EFHRAN (EFHRAN, 2010a). In particular, small sample size still limits the conclusions that can be drawn. Although the meta- and pooled analyses of brain cancer reported weak positive associations in some categories, they could not be distinguished from chance findings and the overall patterns did not suggest a real relationship. Similar to studies childhood leukemia, there are numerous methodological issues with the underlying studies (e.g., selection bias), which permit strong conclusions regarding an association.

A further complication inherent to this research area is that each histological subtype of brain cancer is thought to have a different mechanism of tumorigenesis and, therefore, different risk factors and relevant etiologic "windows." It is recommended that risk factors should be analyzed by histological type (Baldwin and Preston-Martin, 2004), although this is extremely challenging in relation to magnetic fields given the rarity of each histological subtype and exposure greater than 3-4 mG. In addition, evidence suggests that pre-conception and *in utero* exposures likely play a significant role in the development of childhood brain cancer (Olshan et al., 2000; Baldwin and Preston-Martin, 2004). Thus, further research on this question should take into account histological subtype and *in utero* exposures.

Table 6. Studies of childhood brain cancer published after Exponent 2010

Authors	Year	Study
Kheifets et al.	2010b	A pooled analysis of extremely low-frequency magnetic fields and childhood brain tumors.
Kroll et al.	2010	Childhood cancer and magnetic fields from high-voltage power lines in England and Wales: a case-control study

4.1.3 Breast cancer

What was previously known about breast cancer?

Early studies conducted on breast cancer and electric blanket use and residential and occupational magnetic-field exposure reported inconsistent findings. The WHO concluded that, since the body of research they reviewed was higher in quality compared with the early studies, there was strong support for consensus statements that magnetic-field exposure does not influence the risk of breast cancer.[25] Studies published after the WHO review and included in Exponent 2010 support this conclusion. The WHO recommended no further research with respect to breast cancer and magnetic-field exposure, although the epidemiologic evidence was still classified as inadequate.

[25] 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 2007, p. 307).

What relevant studies have been published since Exponent 2010?

Chen et al. (2010) conducted a meta-analysis to supplement an earlier meta-analysis by Erren (2001), which had reported weak, statistically significant associations for both female and male breast cancer (Table 7). The recent meta-analysis found no association between female breast cancer and magnetic-field exposure in 15 case-control studies published between 2000 and 2009. The authors stated that their findings are limited by the diversity of methods used for exposure assessment and data categorization in the underlying studies (Chen et al., 2010). The advantage of this meta-analysis, however, is the precision created by the large number of cases—a consequence of breast cancer being a relatively common cancer.

The meta-analysis of recent studies confirms the WHO's conclusion that the evidence does not support an association. Recent reviews also conclude that the evidence does not suggest a risk (EFHRAN, 2010a; SSM, 2010). Further studies are justified, however, if they address uncertainties about exposure assessment or concerns related to selection bias or confounding variables.

Table 7. Studies of breast cancer published after Exponent 2010

Authors	Year	Study
Chen et al.	2010	Extremely low-frequency electromagnetic fields exposure and female breast cancer risk: a meta-analysis based on 24,338 cases and 60,628 controls

4.1.4 Other adult cancers[26]

What was previously known about other adult cancers?

In general, scientific panels have concluded that there is not a strong or consistent relationship between other adult cancers (leukemia, lymphoma, or brain cancers) and exposure to magnetic fields; however, the possibility cannot be entirely ruled out because the findings have been inconsistent (IARC, 2002; WHO 2007). Since studies with better exposure assessment methods do not report stronger findings, scientific panels concluded that the evidence for an association

[26] A study of ELF EMF exposure and melanoma was identified (Behrens et al. 2010), but is not fully evaluated in this report because it is the first study to evaluate this cancer type.

is weak and the observed inconsistency is probably due to chance or bias. 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 the remaining uncertainty attributed mainly to limitations in exposure assessment methods.

Much of the research on EMF and adult cancers is related to occupational exposure, given the higher range of exposure levels encountered in the occupational environment. The main limitations of these studies, however, are 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 exposure for each occupation (i.e., a JEM). The latter method, while advanced, still has some important limitations. These limitations, as already mentioned in Section 2.3.4, were highlighted in a review summarizing an expert panel's findings by Kheifets et al. (2009). 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 also unknown.

Therefore, researchers have made specific recommendations in order to reduce the remaining uncertainty about whether there is an association between magnetic fields and these cancers. They recommend meta-analyses to clarify the likely reasons for inconsistencies in the data and use of exposure assessment methods that incorporate a greater level of detail on tasks and exposure characteristics such as spark discharge, contact current, harmonics, etc. (WHO, 2007; Kheifets et al., 2009; Mee et al., 2009).

4.1.4.1. Adult brain cancer

What was previously known about adult brain cancer?

As described above, the WHO classified the epidemiologic data on adult brain cancer as inadequate[27] and recommended (1) updating the existing cohorts of occupationally-exposed individuals in Europe and (2) pooling the epidemiologic data on brain cancer and adult leukemia to confirm the absence of an association. No association was found in an updated cohort of utility workers (Johansen et al., 2007) or in a case-control study of gliomas and meningiomas with improved exposure assessment (Coble et al., 2009). In a meta-analysis of occupationally-exposed cohorts performed by Khefeits et al. (2008), a small and statistically significant increase of leukemia and brain cancer was reported 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. For example, Khefeits et al. (2008) reported a weaker association than the previous meta-analysis, whereas a stronger association would be expected if there were a true relationship since the quality of the studies has improved 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" (p. 677).

What relevant studies have been published since Exponent 2010?

Two case-control studies of adult brain cancer and magnetic-field exposure have been published since Exponent 2010 (Table 8). Baldi et al. (2011) enrolled glioma, meningioma, and neurinoma cases in France and evaluated occupational magnetic-field exposure using a JEM and residential distance to nearby power lines at the time of diagnosis. The JEM utilized measurement data from Sweden and did not take into account job tasks or the frequency of contact with ELF EMF sources. Positive associations were observed with occupational ELF EMF exposure overall and residential proximity within 100 meters of a power line for most

[27] The WHO concluded, "In 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 disease remains inadequate" (p. 307, WHO 2007a).

brain tumor types, although a significant association was only reported for occupational ELF EMF exposure and meningiomas. No dose-response patterns were observed.

Marcilio et al. (2011) identified deaths from brain cancer among adults in a large, urban area of Brazil from 2001-2005. No associations were found between brain cancer mortality and living near a transmission line at death or calculated magnetic-field levels from these transmission lines. No analyses were done by histological subtype. The strengths of this study include its relatively large sample size (N=2,357) and, since the study calculated distance with GIS and did not entail voluntary participation, there was no possibility of selection and recall bias. Limitations include the use of cancer deaths, as opposed to incident cases, which limits generalizations to subtypes with a higher mortality rate; the consideration of homes only where participants lived at death; and the lack of information on occupational exposures. In addition, proximity to transmission lines appears to be a poor surrogate of magnetic-field exposure (e.g., Maslanyj et al., 2009).

While an association still cannot be ruled out *entirely*, recent studies do not provide strong evidence in support of a relationship between magnetic fields and brain cancer because of the remaining deficiencies in exposure assessment methods. The data remain inadequate (EFHRAN, 2010a).

Table 8. Studies of adult brain cancer published after Exponent 2010

Authors	Year	Study
Baldi et al.	2010	Occupational and residential exposure to electromagnetic fields and risk of brain tumors in adults: a case-control study in Gironde, France
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

4.2.4.2 Adult leukemia and lymphoma

What was previously known about adult leukemia/lymphoma?

Similar to adult brain cancer, the WHO classified the epidemiologic evidence with regard to adult leukemia as "inadequate" and recommended updating the existing occupationally exposed

cohorts in Europe and a meta-analysis of occupational magnetic field exposure[28] (WHO 2007, p. 307). The data published subsequent to WHO (2007) and reviewed in Exponent 2010 was responsive to these WHO recommendations (Johansen et al., 2007; Khefeits et al., 2008). As described above, a small and statistically significant increase of leukemia in relation to the highest estimate of magnetic-field exposure was reported in the meta-analysis (Kheifets et al., 2008), although the authors did not conclude that the overall pattern of data was suggestive of a true relationship (e.g., there was no consistency in findings by leukemia subtype).

What relevant studies have been published since Exponent 2010?

The Brazilian case-control study discussed above also evaluated adult leukemia deaths (Marcilio et al., 2011). A statistically significant association was found between residence at death within 50 meters of a transmission line, but it was unclear how to interpret this association because it was restricted to lower voltage lines. In addition, proximity is a poor predictor of magnetic-field exposures. A positive association was also found with calculated exposures greater than 3 mG from these transmission lines, but the association was not statistically significant (OR=1.61, 95% CI=0.91-2.86). No analyses were conducted by leukemia subtypes.

Residential distance to power lines was also evaluated in a large, Chinese case-control study of Non-hodgkin's lymphoma (NHL); no statistically significant association was found by self-report of living within 100 meters of a power line and NHL overall or specific NHL subtypes (Wong et al., 2010)

Neither recent study provided strong evidence in support of an association. While the possibility that there is a relationship between adult lymphohematopoietic malignancies and magnetic-field exposure still cannot be entirely ruled out, because of the remaining deficiencies in study methods, the current database of studies provides weak evidence. The data remain inadequate (EFHRAN, 2010a).

[28] No specific conclusions were provided by the WHO with regard to lymphoma.

Table 9. Studies of adult leukemia/lymphoma published after Exponent 2010

Authors	Year	Study
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
Wong et al.	2010	A hospital-based case-control study of non-Hodgkin lymphoid neoplasms in Shanghai: Analysis of personal characteristics, lifestyle, and environmental risk factors by subtypes of the WHO classification

4.1.5 *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 cause cancer in laboratory animals. 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 their lifetime and performed tissue evaluations to assess the incidences 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).

It should be noted that no directly relevant animal model for childhood acute lymphocytic leukemia (ALL) currently has been validated, although some animals develop a type of lymphoma similar to childhood ALL and studies exposing transgenic mice predisposed to this lymphoma to ELF magnetic fields did not report an increased incidence of lymphoma. In general, animal long-term exposure studies reviewed by the WHO (2007) found no increases in any types of cancer (Mandeville et al., 1997; Yasui et al., 1997; Harris et al., 1998; McCormick et al., 1998; Boorman et al., 1999a, 1999b; McCormick et al., 1999; Sommer and Lerchel, 2004), with one exception. A series of investigations in Germany reported an increased incidence of 7,12-dimethylbenz[a]anthracene (DMBA)-induced mammary tumors with magnetic-field exposure (Löscher et al., 1993, 1994, 1997; Baum et al., 1995; Löscher and Mevissen, 1995; Mevissen et al., 1993a, 1993b, 1996a, 1996b, 1998); however, these results

could not be replicated in studies from other laboratories (Anderson et al., 1999; Boorman et al.1999a, 1999b; NTP, 1999). The WHO concluded that the inconsistent findings across laboratories may be due to differences in experimental protocols or the use of different rat sub-strains, only some of which may be susceptible to the promotional effects of magnetic fields on mammary tissue. Based on the research available at the time, the WHO concluded that, "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 2007, p. 322).

In light of the available evidence that exposure to magnetic fields *alone* does not increase the occurrence of cancer, studies published subsequently and reviewed in Exponent 2010 investigated the potential promotional or co-carcinogenic effects of magnetic-field exposure. These studies showed that long-term exposure to magnetic fields does not alter the carcinogenic response of rats or mice treated with the chemical initiator ethylnitrosourea (ENU) (Bernard et al., 2008; Chung et al., 2008) or DMBA (Negishi et al., 2008). Endpoints evaluated included brain tumors and lymphoma/leukemia. Another study showed that long term magnetic field exposure did not alter cancer incidence rates or survival time in a strain of mice genetically predisposed to develop leukemia (Chung et al., 2010). In contrast, further research from the German laboratory replicated earlier findings showing that the incidence of breast cancer in a particular rat strain was significantly elevated with magnetic-field exposure after initiation with DMBA (Fedrowitz and Löscher, 2008). These results are wholly inconsistent with those from other laboratories.

Another study suggested an increased genotoxic response in animals with magnetic-field exposure (Lai and Singh, 2004), but these results have not yet been replicated. Finally, Cakir et al. (2009) found that magnetic-field exposure did not alter total white cell or red cell counts in rats, which is consistent with a lack of association between ELF EMF exposure and signs of pre-leukemia or leukemia.

What relevant studies have been published since Exponent 2010?

Eleven studies published since the Exponent 2010 review investigated effects of magnetic-field exposures on carcinogenic processes in animals (Table 10). In an effort to determine why certain strains of rats develop breast cancer in response to magnetic-field exposure following initiation with DMBA while others do not, Fedrowitz and Löscher (2012) examined gene expression in the mammary gland following magnetic-field exposure. Fischer 344 rats (magnetic-field susceptible) and Lewis rats (magnetic-field resistant) were continuously exposed to a 1,000 mG magnetic field for 2 weeks, after which gene expression in the mammary tissue was analyzed using a whole-genome microarray. Only 22 out of >31,100 genes were altered by magnetic-field exposure and only one of these genes was altered in both strains of rats (albeit in different directions). Genes showing the greatest fold change in F344 rats were those for α-amylase and parotid secretory protein. More research is still needed to determine the potential role of these genes breast cancer. This study was conducted using sham exposures and blinded analyses.

A number of studies have been conducted since the Exponent 2010 report that involved the direct injection of cancerous cells into mice and their subsequent exposure to magnetic fields to assess whether such exposures reduced tumor size or increased animal survival. These studies were conducted to evaluate the hypothesis that magnetic-field exposure may preferentially kill tumor cells or augment the apoptotic effects of X-irradiation. Berg and colleagues (2010) reported that either treatment with bleomycin (an antibiotic used as an anti-cancer treatment) or exposure to a 200,000 mG, 50-Hz magnetic field reduced mean tumor size; combined treatment had an even greater effect. Likewise, Wen and colleagues (2011) reported that exposure to a 7,000 mG, 100-Hz magnetic field reduced tumor size and increased mean survival time of mice injected with hepatocellular carcinoma cells and subsequently treated with x-rays; a dose-response relationship was observed (i.e., the parameters were directly affected by the number of magnetic-field applications). Finally, Jiménez-Garcia et al. (2010) reported that exposure to a 45,000 mG, 120 Hz magnetic field (50 minutes per day for 32 days) inhibited development of pre-neoplastic lesions in rats initiated via treatment with N-diethylnitrosamine, 2-acetylaminofluorene, and partial hepatectomy. These studies used few animals per group and

none reported to have been conducted in a blinded manner. Nevertheless, these findings suggest a possible ameliorative role of magnetic-field exposure in cancer treatment.

Other studies investigated the role of magnetic-field exposures in the development of oxidative stress. Akdag et al. (2010) found that certain oxidative stress indices and markers of oxidative stress (catalase and malondialdehyde levels), but not others (myeloperoxidase levels), were altered in the brains of rats after exposure to a 5,000 mG magnetic field for 2 hours per day for 10 months. Chu et al. (2011) also reported differential effects on oxidative stress markers in the brains of mice after acute (3-hour) exposure to a 23,000 mG (60-Hz) magnetic field, with certain markers showing altered expression (malondialdehyde, hydroxyl radical, superoxide dismutase, ascorbic acid) and others being unaffected by treatment (glutathione peroxidase, glutathione). Exposure to a 70,000 mG (40-Hz) magnetic field for 60 minutes per day for 10 days significantly increased the concentration of free sulfydryl groups in the brains of rats and the concentration of thiobarbituric acid reactive substances (TBARs; a lipid peroxidation marker) was increased after both 30- and 60-minute exposures (Ciejka et al., 2011); hydrogen peroxide concentrations, however, were not significantly affected. Similarly, Goraca et al. (2010) reported that exposure to a 70,000 mG (40 Hz) magnetic field for 60 minutes per day for 2 weeks increased expression of lipid peroxidation markers in the hearts of rats and reduced plasma antioxidant capacity; no effect was observed when the exposures were reduced to only 30 minutes per day. Martínez-Sámano et al. (2010), on the other hand, found that certain oxidative stress markers (glutathione levels and superoxide dismutase activity), but not markers of lipid peroxidation, were altered in the livers of rats following an acute 2-hour exposure to a 24,000 mG (60 Hz) magnetic field; physical restraint of the rats produced a similar response. Only the study by Akdag et al. (2010) reported using methods to ensure that analyses were conducted blind.

Finally, several studies published since the Exponent 2010 report explored the role of magnetic-field exposure in DNA damage. Mariucci et al. (2010) reported that DNA damage was increased in all examined brain regions in CD-1 mice exposed to a 10,000 mG (50 Hz) magnetic field for 1 or 7 days. This damage was evident when animals were sacrificed immediately after exposure, but not if animals were sacrificed after a 24-hour recovery period, suggesting that the

findings may be reversible. In another study (Okudan et al., 2010), continuous exposure to much lower magnetic-field strengths of 10-50 mG (50 Hz) for 40 days did not cause a genotoxic response in Swiss albino mice. This latter study reported the use of procedures to blind the analyses.

Reviewers for EFHRAN (2010b) concluded that the *in vivo* research published up to July 2010 indicated a "lack of effect" of magnetic fields on cancer. For other *in vivo* studies, EFHRAN suggested that the evidence for effects on behavior or memory was "limited" while the hematology evidence was "inadequate."

Table 10. Studies of carcinogenesis published after Exponent 2010

Authors	Year	Study
Akdag et al.	2010	Effects of extremely low-frequency magnetic field on caspase activities and oxidative stress values in rat brain
Berg et al.	2010	Bioelectromagnetic field effects on cancer cells and mice tumors
Chu et al.	2011	Extremely low frequency magnetic field induces oxidative stress in mouse cerebellum
Ciejka et al.	2011	Effects of extremely low frequency magnetic field on oxidative balance in brain of rats
Fedrowitz and Löscher	2010	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
Goraca et al.	2010	Effects of extremely low frequency magnetic field on the parameters of oxidative stress in heart
Jiménez-Garcia	2010	Anti-proliferative effect of extremely low frequency electromagnetic field on preneoplastic lesions formation in the rat liver
Mariucci et al.	2010	Brain DNA damage and 70-kDa heat shock protein expression in CD1 mice exposed to extremely low frequency magnetic fields
Martinez-Samano	2010	Effects of acute electromagnetic field exposure and movement restraint on antioxidant system in liver, heart, kidney and plasma of Wistar rats: A preliminary report
Okudan et al.	2010	Effects of long-term 50 Hz magnetic field exposure on the micro nucleated polychromatic erythrocyte and blood lymphocyte frequency and argyrophilic nucleolar organizer regions in lymphocytes of mice
Wen et al.	2011	The effect of 100 Hz magnetic field combined with X-ray on hepatoma-implanted mice

4.1.6 *In vitro* studies of carcinogenesis

In vitro studies are supplementary to epidemiology and *in vivo* studies, and they are not directly used by health agencies to assess risk to human health. For that reason, Exponent reviews have relied largely on the discussions and the conclusions of scientific panels with regard to *in vitro* studies of potential mechanisms of interaction of EMF with cells and tissue (Exponent 2010).

What did the WHO and other scientific panels conclude with respect to *in vitro* studies of carcinogenesis?

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, 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 on the promotional effects of magnetic fields *in vitro* was also recommended, following suggestive findings from several laboratories. As noted by the SSI, however, 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, according to the WHO (p. 347, WHO, 2007).

What have scientific panels concluded about *in vitro* research since Exponent 2010?

Despite the publication of many new *in vitro* studies since 2010, the three reviews published by scientific panels do not indicate that this avenue of research has yielded new insights (EFHRAN, 2010b; ICNIRP, 2010; SSM, 2010). The conclusions presented in the SSM (2010) review of current research are similar to those expressed by the WHO (2007) and the other reviews.

> Many new findings have been published in the last years on ELF magnetic field bioeffects. Most of the in-vitro studies are dealing with DNA damage, production of ROS and expression of genes. They are mostly uncorrelated in terms of cell models and endpoints and performed under high-level exposure, i.e., in the mT range. Moreover, most of the in-vitro studies are not addressing directly the main issue, which are mechanistic explanations for the association between ELF exposure and childhood leukaemia. The conclusion on genotoxic effects is that the differences between ELF-exposed and sham exposed cells have been small with little biological relevance (although statistically significant in some studies) with very few exceptions. As stated above, the current interpretation of the positive results does not imply that there is direct damage caused by ELF exposure and the health risk assessment must be done accordingly (SSM, 2010, pp. 13-14).

The Exponent (2010) report cited a comprehensive and carefully controlled replication of DNA damage studies that used blinded analyses to examine the effects of multiple magnetic-field strengths produced by two different 50-Hz exposure systems and administered magnetic fields as either continuous or intermittent exposures up to 1 mT (Burdak-Rothkamm et al., 2009). This study evaluated multiple genotoxic endpoints, all of which were unaffected by magnetic-field exposure. Of the studies cited by SSM, the study by Focke et al. (2010) was the most notable because it also attempted to replicate the studies by Ivancsits et al. highlighted by the WHO review (2007).

The Focke et al. (2010) study of four different human cell lines suggests that intermittent, but not continuous, exposures to the same strength magnetic field (1 mT at a frequency of 50 Hz) may be associated with DNA fragmentation; however, subsequent evaluation of this study

suggested that the statistical methods used were inappropriate (Lerchl, 2010). When the data were reanalyzed by Lerchl using the appropriate statistical methods, the slight increase in DNA fragmentation was not statistically significant. The conclusion of SSM about this study was that "The amplitude of the effect depended on cell proliferation, suggesting DNA replication rather than direct damage may have been affected. The authors concluded that the effects induced by ELF exposure might be rationalized in terms of minor disturbances in S-phase processes and occasional triggering of apoptosis rather than by DNA damage" (SSM, 2010, p. 13).

The EFHRAN (2010a) concluded that "no mechanism (*sic*) have yet been established which could lead to adverse effects from exposures significantly below guideline values." The review only expressed interest in *in vitro* studies to the extent that they might suggest "possible interaction mechanisms that could underpin biological effects at low frequencies" that would be relevant to understanding the association between magnetic-field exposure and childhood leukemia. EFHRAN pointed to the general research topic on the detection of the geomagnetic field by birds and other animals, and in particular to the *in vitro* study by Maeda et al. (2008). This study reported that a 50 µT static magnetic field affected a radical pair reaction in frozen chemical solutions. EFHRAN did not discuss whether such results would apply to cellular biological systems exposed to 60-Hz magnetic fields or the limitation reported by Maeda et al. that "the magnetic field effect decreased as the temperature increases" and all but disappeared at about -26 ºC. Such a mechanism, as observed in this study, would not function at the body temperature of humans. Overall, EFHRAN (2010b) considered the evidence for EMF effects on calcium ions, reactive oxygen species, and genotoxicity as "limited".

The ICNIRP (2010) review of *in vitro* EMF research limited its discussion to studies of the central nervous system, which had also been reviewed by WHO (2007) except for a subsequent summary of that research by Saunders and Jeffries (2007). This latter paper suggested that theoretical estimates of the sensitivity of a network of neurons of about 1 mV/m were lower than thresholds around100 mV/m measured in recent *in vitro* studies of brain tissue.

4.2 Reproductive and developmental effects

What was previously known about reproductive and developmental effects?

Studies have evaluated the relationship between ELF EMF and fertility, pregnancy outcomes, and prenatal and postnatal developmental effects. The effect of occupational exposures and contact with video display terminals, electric blankets, and heated beds has been studied on miscarriage, infertility, low birth weight, and select birth defects (e.g., neural tube defects, cleft palate defects). The WHO described the inconsistent findings in this area as inadequate.[29]

Two studies received considerable attention because of a reported association between peak magnetic-field exposure greater than approximately 16 mG and miscarriage—a prospective cohort study of women in early pregnancy (Li et al., 2002) and a *nested case-control* study of women who miscarried compared to their late-pregnancy counterparts (Lee et al., 2002). The WHO concluded, "There is some evidence for increased risk of miscarriage associated with measured maternal magnetic field exposure, but this evidence is inadequate" and recommended further research in this area (WHO 2007, p. 254). As discussed in Exponent 2007, later studies supported the notion that the associations observed in Lee et al. (2002) and Li et al. (2002) were due to important biases in the collection of the data. The scientific panels that have considered these two studies concluded that the possibility of this bias precludes making any conclusions about the effect of magnetic fields on miscarriage (NRPB, 2004; FPTRPC, 2005; WHO, 2007; ICNIRP, 2009).

Five *in vivo* animal studies also examined the effect of electric or magnetic fields on reproductive or developmental endpoints. Two of these studies (Al-Akras et al., 2008; Aydin et al., 2009) showed no evidence of exposure-related adverse effects on female sex hormone levels and organ weights, although one of these studies (Aydin et al., 2009) is limited by its experimental design, which involved the exposure of one group of animals in a barn located under a transmission line. Three other studies reported exposure-related effects in rats or mice during pregnancy or during sexual development, or both (Anselmo et al., 2008, 2009; Dundar et

[29] The WHO stated: "On the whole, epidemiological studies have not shown an association between adverse human reproductive outcomes and maternal or paternal exposure to ELF fields … Overall the evidence for developmental effects and for reproductive effects is inadequate" (p. 254, WHO 2007).

al., 2009). In the studies by Anselmo et al. (2008, 2009), 30 mG magnetic-field exposure in combination with a nutrition-deficient regional diet was reported to cause a small delay in some postnatal developmental endpoints and in maternal thyroid hormone levels, but not in other maternal metabolic endpoints. Similarly, Dundar et al. (2009) reported delayed puberty and some histopathologic changes in reproductive organs of female rat offspring exposed to electric fields at 10 kV/m, 24-hours per day during both the prenatal and postnatal periods. IGF-1 levels were also reduced in the prenatally-exposed group. The authors concluded that electric field exposure of rats from conception until puberty resulted in growth restriction, delayed puberty, and reduced IGF-1 levels. Delayed puberty, however, is inconsistent with the study's reported absence of an effect on the reproductive hormones that influence this process.

These *in vivo* studies are all severely limited by small sample sizes, the absence of specific methods to control for litter-effects (i.e., the propensity of littermates to be more similar to each other than offspring from separate litters due to a shared maternal environment), and the lack of methods to ensure that the "scoring" of the tissues for damage was performed by someone blinded to the test status. Given that the effects observed are not consistent with previous research and the absence of adverse health effects in larger studies at higher exposure levels, these results do not modify previous conclusions. Based on long-term and multi-generational studies, the evidence does not support adverse effects of EMF exposure on reproduction and development.

What relevant studies have been published since Exponent 2010?

No new epidemiology studies on magnetic field exposure and miscarriage have been conducted. Three recent studies considered novel hypotheses regarding reproductive/developmental effects and magnetic-field exposure (Table 11). Li et al. (2010) described the first study of measured magnetic-field levels and semen abnormalities in a case-control study derived from healthy sperm donors in China. A two-fold, statistically significant association was reported between high magnetic-field exposure (90th percentile of 24-hour measurements ≥ 1.6mG) and poor sperm quality. The relationship exhibited dose-response patterns and other features associated with a valid relationship. The main strength of the study was the use of actual personal

magnetic-field measurements, although it is unclear how this 24-hour measurement reflects true magnetic-field exposure during spermatogenesis.

The first study of maternal residence near transmission lines and adverse birth outcomes was reported by Auger et al. in 2011. For all 700,000 live births in Montreal and Quebec City from 1990-2004, the authors compared the occurrence of adverse birth outcomes by distance of the child's home at birth to nearby transmission lines. No association with distances in 50 meter increments was found for any of the outcomes (pre-term birth, low birth weight, small for gestational age, or proportion of male births). The study was large and controlled for numerous potential confounders, but was limited by exposure deficiencies (the use of distance as a surrogate of magnetic-field exposure; the lack of information on occupational exposures; and incomplete residential histories).

Another recent publication was the first to evaluate the association between magnetic field exposure *in utero* and subsequent asthma in a prospective cohort of 626 pregnant women and their offspring in California (Li et al., 2011). Asthmatic children were more likely to have mothers with high magnetic-field levels during pregnancy, compared to healthy children (HR=3.52, 95% CI=1.68-7.35); the association was strong and increased in strength as estimated exposure increased. The design and methods of this study were relatively strong, although it is possible that an unknown confounder is responsible for the observed association. Low SES is associated with higher magnetic-field exposures and may play a role in the development of childhood asthma directly or as a surrogate of other environmental risk factors (e.g., indoor mold, allergen exposure, outdoor pollution) (Rona, 2000). The authors only adjusted for family income in their analyses, which may not entirely control for the effect of SES. Several scientists posted comments in the journal about the limitations of this study and the authors' interpretation of this study after publication. Further studies on this topic need to have more detailed information on risk factors for childhood asthma.

The three, new epidemiology studies in this research area do not change the classification of the data as inadequate. The two studies by Li et al. (2010, 2011) are relatively strong and suggest an association between magnetic fields on semen abnormalities and asthma, respectively, but

unless further research resolves issues in these studies, the data remain inadequate (EFHRAN, 2010a). Furthermore, a comprehensive modeling study of pregnant women and fetuses at different stages of gestation concluded that compliance with the ICNIRP Reference Levels for public exposure will produce internal electric fields and current densities substantially below the Basic Restriction values (Dimbylow and Findlay, 2010).

Eight *in vivo* animal studies published since the Exponent 2010 report evaluated the potential effects of magnetic-field exposure on reproductive and developmental parameters (Table 11). Rajaei et al. (2010) exposed female mice to a 5,000 mG magnetic field for 4 hours per day, 6 days per week for 2 weeks. The mice were super-ovulated after 8 days of exposure, and then mated. The numbers of blastocysts flushed from the uterus were significantly reduced with exposure; further, the height of the fallopian tube epithelium was reported to be significantly increased with treatment. The methods used to make these measurements, however, were not reported and the toxicological significance of the findings is unclear. In another study by the same group of investigators and using the same experimental design and exposure regimen, the reduction in the number of blastocysts flushed from the uterus following magnetic-field exposure was replicated (Borhani et al., 2011); further analysis indicated that magnetic-field exposure was associated with a significant increase in DNA fragmentation in the blastocysts. Bernabo et al. (2010) noted reduced fertilization in swine with short-term (4-hour) exposure to a 10,000 mG magnetic field. In this study, however, the female oviducts were surgically exposed to the magnetic fields outside of the body just prior to or immediately after insemination; thus, the findings may not be relevant to human health.

Saadeldin et al. (2011) reported reduced rat testes weights, increased seminiferous tubular damage and apoptosis, and reduced sperm quality after continuous exposure to a 1,000 mG magnetic field for 21 days; serum testosterone concentrations were also increased. In another study (Tenorio et al. 2011, 2012), the effects on the testes of exposure to a 10,000 mG magnetic field during gestation and early postnatal development were investigated. Although histomorphometric measures were altered on postnatal day (PND) 21, no pathologic alterations were noted but were observed at a later observation point (PND 90). Further, no changes in plasma testosterone concentrations were observed in this study.

De Bruyn and De Jager (2010) found no effect of exposure to a varying magnetic field of 5-770 mG through two generations of mice on sperm count or serum testosterone. Although sperm motility was reduced, other parameters related to fertility were unaffected. Finally, Vallejo and Hidalgo (2012) exposed mice to a 150 mG magnetic field starting 98 days prior to mating, through pregnancy, birth, lactation, and weaning, into adulthood (220 days). They reported no adverse effects on fertility or gestation. Statistically significant higher and lower body weights were noted in the exposed compared to unexposed mice during different periods of the study. Based on these results, the authors suggest that growth rates of the mice during certain life phases were affected by magnetic-field exposure; however, the biological significance of these differences, if any, is unknown.

Overall, the *in vivo* animal studies published since the Exponent 2010 report suffer from serious methodological and reporting deficiencies. Several studies failed to report whether they used methods to ensure that analyses were conducted in a blinded manner and none examined the effects at more than one magnetic-field strength. Although these studies suggest possible reproductive and developmental effects due to high magnetic-field exposure, because of the conflicting nature of the findings across studies and the questionable biological significance of some of these findings, no firm conclusions can be drawn. Further research in this area is warranted.

Table 11. Studies of reproductive and developmental effects published after Exponent 2010

Authors	Year	Study
Auger et al.	2011	The relationship between residential proximity to extremely low frequency power transmission lines and adverse birth outcomes
Bernabo et al.	2010	Extremely low frequency electromagnetic field exposure affects fertilization outcome in swine animal model
Borhani et al.	2011	Analysis of DNA fragmentation in mouse embryos exposed to an extremely low-frequency electromagnetic field
De Bruyn and De Jager	2010	Effect of long-term exposure to a randomly varied 50 Hz power frequency magnetic field on the fertility of the mouse
Dimbylow and Findlay	2010	The effects of body posture, anatomy, age and pregnancy on the calculation of induced current densities at 50 Hz
Li et al.	2010	Exposure to magnetic fields and the risk of poor sperm quality

Authors	Year	Study
Li et al.	2011	Maternal exposure to magnetic fields during pregnancy in relation to the risk of asthma in offspring
Rajaei et al.	2010	Effects of extremely low-frequency electromagnetic field on fertility and heights of epithelial cells in pre-implantation stage endometrium and fallopian tube in mice
Saadeldin et al.	2011	Effects of exposure to 50 Hz, 1 Gauss magnetic field on reproductive traits in male albino rats
Tenorio et al.	2011	Testicular development evaluation in rats exposed to 60 Hz and 1 mT electromagnetic field
Tenorio et al.	2012	Evaluation of testicular degeneration induced by low-frequency electromagnetic fields
Vallejo and Hidalgo	2012	Growth variations in OF1 mice following chronic exposure of parental and filial generations to a 15 μT, 50 Hz magnetic field

4.3 Neurodegenerative disease

What was previously known about neurodegenerative disease?

Research into the possible effect of magnetic fields on 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), which is also known as Lou Gehrig's disease. The inconsistency of the Alzheimer's disease studies prompted the NRPB to conclude in 2001 that there is "only very weak evidence to suggest that it [ELF magnetic fields] could cause Alzheimer's disease" (NRPB, 2001b, p. 21). 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, as well as electrical occupations. The review panels, however, were hesitant to conclude that the associations provided strong support for a causal relationship because they felt that an alternative explanation (i.e., electric shocks received at work) may be the source of the observed association.

The more recent studies discussed by the WHO continue to report statistically significant associations between occupational magnetic-field exposure and mortality from Alzheimer's disease and ALS, although the design and methods of these studies are relatively weak (e.g., disease status based on death certificate data, exposure based on incomplete occupational

information from census data, and no control for confounding factors). The WHO panel concluded that there is "inadequate" data in support of an association between magnetic fields and Alzheimer's disease or ALS.[30] The panel recommended more research in this area using better methods; in particular, studies that 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. A meta-analysis published since the WHO review and evaluated in Exponent 2010 confirmed the association between Alzheimer's disease and occupational magnetic-field exposure (Garcia et al., 2008), but was limited by the poor quality of the underlying studies included (Santibanez et al., 2007). Finally, an *in vivo* study of an ALS mouse model reported no effect of magnetic fields on ALS progression (Poulletier de Gannes et al., 2009).

What relevant studies have been published since Exponent 2010?

Three epidemiology studies have been published since Exponent 2010—one study of Alzheimer's disease and dementia and two studies of motor neuron disease (Table 12). Andel et al. (2010) utilized data from 9,508 subjects in the Study of Dementia in Swedish Twins, a nationwide registry of all twins residing in Sweden ≥65 years of age. Telephone screening of the registry participants and in-person clinical work-up were used to identify incident cases (216) and controls (9,292). Occupational exposure to ELF magnetic fields was based on the subjects' primary lifetime profession, which was self-reported or reported by a proxy, and linkage to a Swedish JEM. Overall, cases of dementia and Alzheimer's disease were more likely to have high and medium magnetic-field exposure, compared to the controls, but the associations were not statistically significant. Medium and high levels of magnetic-field exposure were, however, significantly associated with dementia beginning by age 75 (OR=1.94, 95% CI=1.07-3.65 for medium; OR=2.01, 95% CI=1.10-3.65 for high). There was also a significant association among cases whose primary profession was manual (OR=1.81, 95% CI=1.06-3.09 for medium; OR=1.75, 95% CI=1.00-3.05 for high), even though there was no difference in the median magnetic-field exposures between manual and non-manual workers.

[30] 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 or ALS] disease risk" (p. 194, WHO 2007).

Elevated, but non-significant, associations were also found for medium and high exposure in the 42 twin pairs discordant for dementia, an analysis that inherently controls for some genetic differences. Strengths of the study include the utilization of a cases from a large population-based study and the assessment of various risk factors (e.g., intellectually challenging job characteristics, cardiovascular risk factors, etc.) as possible confounders. The exposure assessment is limited by a crude JEM based on primary occupation only and measurements taken during a period when subjects had already retired. In addition, information on occupation was sometimes provided by proxies due to illness or other reasons, introducing the possibility for measurement error.

In a Brazilian case-control study, persons dying from ALS were no more likely to live close to power lines than controls (Marcilio et al., 2011).[31] In addition, a large cohort of the general US population assembled from five census surveys did not provide evidence that motor neuron disease mortality is associated with occupational magnetic-field exposure (Partlett et al., 2011). The cohort of nearly 300,000 persons was followed for a maximum of 9 years, and 40 deaths due to motor neuron disease were identified. The incidence of motor neuron disease was compared for different magnetic-field exposure categories based on the job reported at the time of the census. The population-based nature and large size of the study adds strength to the conclusions, but the analysis is limited by the generic JEM.

The recent epidemiology studies do not alter the conclusion that there is "inadequate" data on Alzheimer's disease or ALS. Little progress has been made to clarify these associations or address the WHO's recommendations. Andel et al. (2010) included incident cases of Alzheimer's disease and dementia, but both studies of motor neuron disease still relied on deaths (Marcilio et al., 2011; Partlett et al., 2011); no recent work has addressed the possible confounding effect of electrical shocks. The recent studies continue to be limited by uncertainties about the estimates of occupational magnetic-field exposure; both Marcilio et al. (2011) and Partlett et al. (2011) relied on generic JEMs that did not incorporate job tasks or reflect cumulative occupational magnetic field exposure. Further research in this area is still needed; the data remain inadequate (Kheifets et al., 2008; EFHRAN, 2010a; SSM, 2010).

[31] The details of this study are discussed in the adult cancer section above.

Eleven *in vivo* studies of EMF exposure in relation to neurological endpoints were published after the Exponent 2010 report (Table 12). The WHO (2007) recommended that studies of the effects of magnetic fields on the performance of mentally demanding tasks by human volunteers be conducted. A recent meta-analysis of such studies quantitatively summarized the results of seven human experimental studies on the cognitive performance of 445 subjects (Barth et al., 2010). The authors concluded that, in aggregate, the studies provided little evidence for any effects of magnetic fields on cognitive function. In another report, exposure to a 30,000 mG magnetic field had no effect on the speed and accuracy of performance on nine cognitive tasks in a large number of human subjects (Corbacio et al., 2011). This latter study was conducted in a blinded manner. These studies do not support the notion that magnetic-field exposure affects cognitive functions.

Three *in vivo* animal studies published since the Exponent 2010 report investigated the effects of magnetic-field exposures on responses thought to reflect memory recall. Foroozandeh et al. (2011) reported that after exposure to an 80,000 mG, 50-Hz magnetic field for 1 hour, mice stepped onto a grid where they had been shocked 24 hours earlier more frequently than controls, suggesting reduced retention or fear of the place where shocks had been administered. Another study found that chicks exposed to a 20,000 mG, 50-Hz magnetic field for 60 minutes per day on embryonic days 12-18 (while still in the egg) had reduced memory recall at 30 and 120 minutes, but not at 10 minutes post-training in a passive avoidance task. Both of these studies involved negative reinforcement; therefore, information on learning under positive reinforcement is not available. A third study exposed rats for 1 or 4 hours per day for 4 weeks or sham-control conditions to a 20 G magnetic field prior to Morris water maze tests (He et al., 2011). No differences between rats exposed for 1 hour per day or sham conditions were found, but the rats exposed for 4 hours per day showed improved training performance and improved memory retention compared to sham-exposed rats. None of these studies reported using methods to prevent investigator bias due to knowledge regarding exposure conditions.

Two studies published since the Exponent 2010 report examined the effect of 50-Hz magnetic-field exposure on behaviors thought to reflect enhanced emotional states. In one study, Szemersky et al. (2010) suggest that prolonged continuous magnetic-field exposure at 5,000 mG

may increase anxiety-like behaviors and stress responses, but hormonal and other physiological measures do not support the latter suggestion. The He et al. (2011) study also tested for effects of a 20 G magnetic field indicator of anxiety on the open field test and elevated plus maze test. Both tests suggested that the rats with daily 4 hour exposures were more anxious than sham controls on some measures but 1 hour exposure per day had no significant effect. These studies did not report using methods to ensure the analyses were blinded.

Another study examined the effects of magnetic-field exposure on electrical activity of the brain. Carrubba et al. (2010) reported that 60-Hz magnetic fields of 10 and 50 mG did not produce delayed evoked potentials in human subjects, as recorded from the scalp with onset or offset of the field. Magnetic-field stimuli, however, produced changes in brain electrical activity, suggesting that the fields were detected in a manner similar to that of other sensory stressors. This study was not reported to have implemented methods to ensure that the analyses were conducted in a blinded manner.

The WHO review recommended additional dosimetry to better estimate the electric-field levels induced in tissues. Hirata et al. (2011) used an advanced numerical dosimetry method to calculate the levels of electric fields produced in the brain and retina of human subjects exposed to an 81,000 mG, 20-Hz magnetic field, an exposure reported to stimulate visual phosphenes. The induced field levels were similar to those assumed by ICES and ICNIRP in previous modeling as a threshold for stimulation of the central nervous system. It should be noted, however, that both ICES and ICNIRP estimate that the threshold for stimulation would be considerably higher at 50-Hz or 60-Hz power frequencies.

Finally, a number of studies addressed other aspects related to brain function. Akdag et al. (2010) examined possible oxidative processes in the brain, which may be involved in mediating certain neurodegenerative diseases. This study found that certain oxidative stress indices and enzymes (catalase and malondialdehyde) were altered in the brains of rats after exposure to a 5,000 mG magnetic field for 2 hours per day for 10 months; other oxidative stress markers (myeloperoxidase) and apoptosis rates did not appear to be affected. Another study reported increased neural cell proliferation and maturation in the dentate gyrus of the hippocampus of mice following exposures to a 10,000 mG magnetic field (Cuccurazzu et al., 2010), suggesting a

new approach for regeneration of neural tissues. Frilot et al. (2011) indicated that a 2,500 mG, 60-Hz magnetic field increased the uptake of a glucose analog in the hindbrain of the rat brain during exposure; much greater uptake was seen when the field was intermittent than continuous over this period; increased uptake of glucose or its analog is interpreted as an indicator of increased local neural activity. Finally, Gulturk et al. (2010) showed that exposure to a 50,000 mG magnetic field for 165 minutes per day for 30 days increased blood-brain barrier permeability in rats and that this effect was similar to that observed in a diabetic rat model. With the exception of Akdag et al. (2010), these studies did not report that the analyses were conducted in a blinded manner.

Overall, the *in vivo* studies of magnetic-field exposure examined a variety of aspects of brain function. These studies fail to show consistent findings to support a role of magnetic-field exposures in the development of neurodegenerative diseases. Although a wide range of exposures were evaluated, most studies did not report biological responses to magnetic fields unless the exposure was between 10,000-20,000 mG; studies that reported repeated exposures over longer periods (i.e., 1 week, 1 month, or more than 1 month) at these levels were more likely to report biological responses.

Table 12. Studies of neurodegenerative disease published after Exponent 2010

Authors	Year	Study
Akdag et al.	2010	Effects of extremely low-frequency magnetic field on capsase activities and oxidative stress values in rat brain
Andel et al.	2010	Work-related exposure to extremely low-frequency magnetic fields and dementia: results from the population-based study of dementia in Swedish twins
Barth et al.	2010	Effects of extremely low-frequency magnetic field exposure on cognitive functions: Results of a meta-analysis
Carrubba et al.	2010	Numerical analysis of recurrence plots to detect effect of environmental-strength magnetic on human brain electrical activity
Corbacio et al.	2011	Human cognitive performance in a 3 mT power-line frequency magnetic field.
Cuccurazzu et al.	2010	Exposure to extremely low-frequency (50 Hz) electromagnetic fields enhances adult hippocampal neurogenesis in C57BL/6 mice
Foroozandeh et al.	2011	Effects of single, brief exposure to an 8 mT electromagnetic field on avoidance learning in male and female mice

Authors	Year	Study
Frilot et al.	2011	Transient and steady-state magnetic fields induce increased fluorodeoxyglucose uptake in the rat hindbrain
Gulturk et al.	2010	Effect of exposure to 50 Hz magnetic field with or without insulin on blood-brain barrier permeability in streptozotocin-induced diabetic rats
He et al.	2011	Effects of extremely low frequency magnetic field on anxiety level and spatial memory of adult rats
Hirata et al.	2011	An electric field induced in the retina and brain at threshold magnetic flux density causing magnetophosphenes
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
Szemersky et al.	2010	Stress-related endocrinological and psychopathological effects of short- and long-term 50 Hz electromagnetic field exposure in rats

4.4 Immune system

What was previously known about immune system effects?

The WHO concluded that findings concerning ELF EMF effects on the immune system, which plays an important role in protecting against infection and disease, were generally inconsistent across studies—possibly due to variations in experimental conditions and exposures applied, the typically small numbers of test subjects, and the extensive number of parameters assessed. Consequently, evidence to suggest that ELF EMF exposure affects the immune system was judged to be inadequate (WHO, 2007).

Since the WHO review, a couple of studies have been published that examine the effects of magnetic-field exposure on various aspects of immune function. Canseven et al. (2006) reported that the splenocytes of guinea pigs exposed short-term (4 hours per day for 5 days) to a 20,000 mG magnetic field exhibited a reduced cytotoxic response. This study was conducted in a blinded manner. In contrast, Cicekcibasi et al. (2008) indicated no effect of subchronic (40-day) exposure to a 10-50 mG magnetic field on mouse lymphoid organs and cells. These studies suffer from various methodological and reporting deficiencies, and do not merit strong weight in the evaluation of the cumulative body of literature. Therefore, the evidence remains inadequate to address the effects of ELF EMF on the immune system.

What relevant studies have been published since Exponent 2010?

Five *in vivo* animal studies have been published since the last Exponent report (Table 13). Okudan et al. (2010) evaluated the effects of continuous exposure to 10-50 mG magnetic fields for 40 days on markers of genetic damage on cells of the hematopoietic system of Swiss mice. They reported that magnetic-field exposure did not cause a genotoxic response. In another study, Rajkovic et al. (2010a) examined the effects of exposure to 1,000-5,000 mG (50 Hz) magnetic fields for 4 hours per day for 30 days on cutaneous mast cells, which mediate inflammatory and allergic reactions in the skin. These treatments were conducted alone or in combination with oral exposure to atrazine, a herbicide. In general, magnetic-field exposure alone had no effect on numbers of mast cells, except for a possible reduction in the numerical density of intact mast cells. In a study using the same exposure regimen (Rajkovic et al., 2010b), the same group of investigators reported a qualitative reduction in degranulated mast cells in the thyroid with magnetic-field exposure based on histological examination, but no quantitative analysis was conducted (i.e., the number of mast cells were not counted). Bayat et al. (2011) reported that exposure to a 60,000 mG (50 Hz) magnetic field during gestation caused a reduction in mouse newborn body weights, spleen volume, and the number of megakaryocytes. This exposure, however, is relatively high and it is not known if heat from the power supply may have been a source of environmental stress. These studies, with the exception of Bayat et al. (2011), were conducted in a blinded manner.

Finally, Selmaoui et al. (2011) examined cytokine levels in the blood of human subjects following either continuous or intermittent (1 hour "off," 1 hour "on" with the field switched on and off every 15 seconds) exposure to 100 mG (50 Hz) magnetic fields. Cytokines are important in regulating immune function. The cytokine interleukin-6 (IL-6) was reported to be significantly increased with intermittent, but not continuous, exposures. None of the other cytokines or associated molecules evaluated (IL-1β, IL-2, IL-1 receptor antagonist, and IL-2 receptor) was affected by exposure. Although the study subjects were blinded to their exposures, the study investigators were not.

Overall, the data published since the Exponent 2010 report address a variety of different endpoints related to immune function. For the most part, these studies report no or only limited

effects. The exception is the study by Bayat et al. (2011), which was conducted at a high magnetic-field strength.

Table 13. Studies of the immune system published after Exponent 2010

Authors	Year	Study
Bayat et al.	2011	Effect of exposure to extremely low electro-magnetic field during prenatal period on mice spleen
Okudan et al.	2010	Effects of long-term 50 Hz magnetic field exposure on the micro nucleated polychromatic erythrocyte and blood lymphocyte frequency and argyrophilic nucleolar organizer regions in lymphocytes of mice
Rajkovic et al	2010a	Studies on the synergistic effects of extremely low-frequency magnetic fields and the endocrine-disrupting compound atrazine on the thyroid gland
Rajkovic et al.	2010b	Combined exposure of peripubertal male rats to the endocrine-disrupting compound atrazine and power-frequency electromagnetic fields causes degranulation of cutaneous mast cells: A new toxic environmental hazard?
Selmaoui et al.	2011	Acute exposure to 50-Hz magnetic fields increases interleukin-6 in young healthy men

5 Electromagnetic 'hypersensitivity'

The WHO 2007 report discussed anecdotal accounts of persons who reported that they could perceive EMF at levels below accepted thresholds and accounts of persons who believed they had developed a variety of symptoms including sleep disturbances, general fatigue, difficulty concentrating, dizziness, and eyestrain due to EMF exposure. The WHO reviewed double-blind studies of human volunteers, office workers, and self-reported hypersensitive individuals and concluded that the perception of EMF and health complaints are not related to exposure. The WHO proposed that electromagnetic hypersensitivity should more appropriately be termed "idiopathic environmental intolerance (IEI) with attribution to EMF" and explained that "[t]hese symptoms are not explained by any known medical, psychiatric or psychological disorder, and the term IEI has no medical diagnostic value. IEI individuals cannot detect EMF exposure any more accurately than non-IEI individuals, and well-controlled and conducted double-blind studies have consistently shown that their symptoms are not related to EMF exposure per se" (WHO, 2007, p. 137).

Since the WHO report, only a few studies have been published on this topic. Four papers have been published on this topic since Exponent 2010—two review articles (Rubin et al., 2010, 2011) and two human exposure studies (McCarty et al., 2011; Kim et al., 2012).[32] The Rubin et al. (2010) review discussed two earlier studies on this topic, both of which reported that persons identified as IEI-EMF and controls could not discriminate between 50-Hz magnetic field or sham exposure conditions at intensities of 10 μT (100 mG) (David et al., 2006) or 96 mT (960 G) (Wenzel et al., 2005). The Rubin et al. (2011) review identified four, additional studies of IEI-EMF subjects and controls involving ELF EMF exposures, all published prior to 2005. None of these studies reported that IEI-EMF subjects and controls differed in their ability to distinguish EMF from sham exposures. No other responses were associated with exposure in either group, excluding one study that reported lower visual attention and processing scores for

[32] Electromagnetic hypersensitivity was not discussed in Exponent 2010, but the studies published since the time of that report are noted in Table 14 for consistency.

IEI-EMF subjects than controls but performance on multiple other measures was unaffected (Trimmel and Schweiger, 1998).

McCarty et al. (2011) studied a single subject who reported electromagnetic hypersensitivity. They exposed the subject to electric fields at 60 Hz and five higher frequencies in the kilohertz range and reported that the subject could not reliably detect the presence of a field during exposures lasting 1 second. No data or statistical testing was provided, however. In another experiment in which an electric field was presented for 100 seconds for 5 or 10 trials, the subject was described as reporting statistically significant higher symptom ratings when the field was present, compared to no electric-field exposure. The study has several, important limitations including the use of only a single subject, the lack of blinding in the analysis of the data, and errors in the statistical analysis.

Kim et al. (2012) recorded heart rate and respiration rate before, during, and after a 38-minute exposure period involving sham exposure or exposure to a 60-Hz 12.4 μT (125 mG) magnetic field.[33] A measure of heart rate variability was computed from the recorded heart rate. Magnetic-field exposure was not associated with these measured responses and did not cause an increase in subjective symptoms in either normal subjects or those selected for high scores on a validated screening test for electromagnetic hypersensitivity.

In summary, both comprehensive reviews and individual studies of ELF EMF and electromagnetic hypersensitivity published after the 2007 WHO report support the conclusion that ELF EMF is not detected by self-reported 'sensitive' subjects or other subjects and that symptoms are not reliably elicited by exposure to ELF magnetic or electric fields over a range of exposure levels.

[33] A summary of this same study was presented by the authors at the 2011 Conference of the IEEE Engineering in Medicine and Biology Society (Nam et al., 2011).

Table 14. Studies of electromagnetic hypersensitivity published after 2010

Authors	Year	Study
Kim et al.	2012	Idiopathic environmental intolerance attributed to electromagnetic fields (formerly 'electromagnetic hypersensitivity'): An updated systematic review of provocation studies
McCarty et al.	2011	Electromagnetic hypersensitivity: Evidence for a novel neurological syndrome
Rubin et al.	2010	Idiopathic environmental intolerance attributed to electromagnetic fields (formerly 'electromagnetic hypersensitivity'): An updated systematic review of provocation studies
Rubin et al.	2011	Do people with idiopathic environmental intolerance attributed to electromagnetic fields display physiological effects when exposed to electromagnetic fields? A systematic review of provocation studies

6 Possible Effects of ELF Electric and Magnetic Fields on 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 can potentially 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 associated with ELF EMF to implanted cardiac devices such as pacemakers and defibrillators.

In the presence of electromagnetic fields, devices can respond in different ways, defined as modes. The likelihood of interference occurring and the mode of the response depend on the strength 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. Experimental research has been conducted to assess whether interference may occur when currents are induced in the patient's body by environmental electric and magnetic fields.

6.1 Electromagnetic interference: pacemakers and implanted cardiac devices

What was previously known about electromagnetic interference?

Both the American Conference of Governmental Industrial Hygienists (ACGIH) and the Electric Power Research Institute (EPRI) have suggested that exposures be kept below 1.5-2 kV/m for electric fields, and the ACGIH recommends an exposure limit of 1,000 mG for magnetic fields (ACGIH, 1998, 2001; EPRI, 2004). These recommendations are general in nature, however, and do not take into account that classes of pacemakers and devices from some manufacturers are quite immune to interference, even at levels much greater than their recommendations. These organizations recommend that the patient first consult their physician

and the respective pacemaker manufacturer, however. When a manufacturer does not specify any limits, the patient is then referred to their guidelines.

Manufacturers of pacemakers and other implantable devices will typically follow the AAMI PC69:2007 (North America) or IEC 45502-2-1/-2-2:2003 (Europe) standards. These standards require a test to verify that the function of the cardiac device is not affected to at least a 2 millivolt (mV) peak-to-peak signal applied to the sensing electrodes. This test verifies immunity of a cardiac device[34] of at least 0.94 G (root-mean-square magnetic field) and "to prevent incompatibility with higher magnetic fields than the reference levels of EC 519/99." At 60 Hz, the reference levels in EC 519/99 (also known as 1999/519/EC) are 838 mG and 4.167 kV/m (the standard assumes that only an electric or magnetic field is present at any time).

Moreover, the standard procedure to assess EMF exposure for workers with active implantable medical devices (AIMD) states that the "risk assessment is based on the approach that AIMDs are expected to work uninfluenced as long as the General Public Reference levels of 1999/519/EC (except for static magnetic fields) are not exceeded … , where the AIMD has been implanted and programmed following good medical practice" (EN 50527-1:2010). The procedure recommended by this standard contains steps for assessing that the field levels of EC 519/99 are not exceeded and that AIMD patients do not have higher than normal sensitivity settings on their device for clinical reasons.

What relevant studies have been published since Exponent 2010?

Tiikkaja et al. (2012) conducted an experimental study on the malfunction of pacemakers from external sources of magnetic fields. The researchers tested 16 pacemakers for their susceptibility to magnetic field interference in the frequency range of 2 to 1,000 Hz. The study was performed with devices only, not with patients. A mix of bipolar and unipolar lead configurations was used. Pacemakers were tested up to the ICNIRP 1998 occupational exposure limit of 500 μT (5,000 mG) at 50 Hz and 410 μT (4,100 mG) at 600 Hz. Of the 16

[34] Magnetic field value is calculated using an average area (200 cm^2) of a unipolar cardiac device. In rare cases, such as for a large patient with a unipolar implant, the immunity may be lower. For a patient with a bipolar lead configuration, the immunity will be higher.

pacemakers tested, 2 had interference recorded below the occupational exposure limit, but above the ICNIRP (2010) public exposure limit (2,000 mG) at powerline frequencies. At 50 Hz, the interference occurred at 410 µT (4,100 mG) and 450 µT (4,500 mG). At 60 Hz, interference occurred at 360 µT (3,600 mG) and 260 µT (2,600 mG). These values are greater than the public exposure limit by a factor of more than 3.

Souques et al. (2011) proposed a method for performing a risk assessment for workers with implantable cardiac devices (ICD) exposed to 50-Hz electromagnetic fields. Three patient case studies from an electric utility in France were presented. In the first case, the electric field was less than 3 kV/m and the maximum magnetic field was 650 µT (6,500 mG). No dysfunction of the device was recorded. In the second case, only field levels encountered by a colleague of the worker with the pacemaker were mapped. No cardiac device was present. In the third case, the maximum electric field was 12.2 kV/m and the maximum magnetic field was 76.8 µT (768 mG). No disruption of the ICD was observed.

Korpinen et al. (2012) tested 31 pacemakers placed inside a human-shaped phantom to detect if interference occurs after exposure to electromagnetic fields produced by a 400-kV power line operating at 50 Hz. Only one pacemaker in a unipolar configuration had a disturbance during its operation. This disturbance occurred in an electric field of 6.7 kV to 7.5 kV/m with a simultaneous magnetic field of 2.4 to 2.9 µT (24 to 29 mG), which was judged to be negligible and did not contribute to the disturbance. No disturbance occurred for this same pacemaker when operated in a bipolar configuration. Based on these results, the researchers concluded that the risk of disturbances to pacemakers near a 400-kV power line is not deemed to be high.

Katrib et al. (2011) created a numerical model of an ICD operating at maximum sensitivity (i.e., the worst case scenario for electromagnetic interference). The effect of a 50-Hz magnetic field on this ICD model was then investigated. The researchers found that no interference should occur below 7,000 mG.

Table 15. Studies of EMI published after Exponent 2010

Authors	Year	Study
Katrib et al.	2011	Implantable cardioverter-defibrillators exposed to low frequency magnetic fields
Korpinen et al.	2012	Cardiac pacemakers in electric and magnetic fields of 400-kV power lines
Souques et al.	2011	Implantable cardioverter defibrillator and 50-Hz electric and magnetic field exposure in the workplace
Tiikkaja et al.	2012	Experimental study on malfunction of pacemakers due to exposure to different external magnetic fields

7 Fauna and Flora Research

7.1 Fauna

What was previously known from fauna research?

Previous Exponent reports reviewed the relevant research and concluded that the research to date did not suggest that electric or magnetic fields result in any adverse effects on the health, behavior, or productivity of fauna, including livestock such as cows, sheep, and pigs, a variety of small mammals, deer, elk, birds, or bees. No relevant new studies have been published since Exponent 2010.

7.2 Flora

What was previously known from flora research?

Previous Exponent reports described the body of research on the possible effects of EMF on forest species and agriculture crops, concluding that researchers have found no adverse effects on plant responses at the levels of EMF produced by high-voltage transmission lines, excluding some corona-related effects from high-voltage lines on the growth of nearby trees. No relevant new studies have been published since Exponent 2010.

Glossary

Association – An association is a measure of how things vary together. They are measured by odds ratios and relative risks.

Basic restriction – The basic restriction is the electric field level or current density inside the body that is recommended as a limit to protect exposed populations. The term is used in standards or guidelines that recommend exposure limits.

Bias – Bias refers to any error in the design, conduct or analysis of a study that results in a distorted estimate of an exposure's effect on the risk of disease. For example, the characteristics of persons selected by telephone calls to participate in a study may not accurately reflect those of the entire community and this can introduce error into the study's findings.

Carcinogenesis – Carcinogenesis describes the process of the progression of normal cells to cancerous cells.

Causation or cause – A cause is an exposure or condition of the individual that has been proven through a sound weight-of-evidence review to increase risk of a disease.

Cause-and-effect relationship – A cause-and-effect relationship between an exposure and a disease is a statistically significant association that is determined through a weight-of-evidence review to be causal in nature.

Case-control study – A case-control study compares persons without a disease (controls) to persons with a disease (cases) to see if they differ on any factors or exposures of interest.

Chance – Chance refers to random sampling variation, like a coincidence. An association can be observed between an exposure and disease that is simply the result of a chance occurrence.

Cohort study – A cohort study follows a group of people over a long period of time to observe whether the occurrence of disease differs among exposed and unexposed persons in the group.

Confidence interval – A confidence interval is a range of values for an estimate of effect that has a specified probability (e.g., 95%) of including the "true" estimate of effect. A 95% confidence interval indicates that, if the study were conducted a very large number of times, 95% of the measured estimates would be within the upper and lower confidence limits.

Confounding – Confounding is a situation in which an association is distorted because the exposure is associated with other risk factors for the disease. For example, a link between coffee drinking in mothers and low birth weight babies has been reported in the past. However, some women who drink coffee also smoke cigarettes. It was found that when the smoking habits of the mothers are taken into account, coffee drinking was not associated with low birth weight babies because of the confounding effect of smoking.

Dose-response assessment/relationship – Data from scientific research in which a change in amount, intensity, or duration of exposure is associated with a change in risk of a specified outcome. A pattern of a stronger association with increasing exposure, or dose.

Electric field – The electric field is a property of a location or point in space and its electrical environment, and describes the forces that would be experienced by a charged body in that space by virtue of its charge. The electric field is expressed in measurement units of volts per meter (V/m) or kilovolts per meter (kV/m); a kilovolt per meter is equal to 1,000 V/m.

Electromagnetic spectrum – The range of wavelengths of electromagnetic energy, including visible light, arranged by frequency. Wavelength decreases with increasing frequency; the ELF range includes the power frequencies of 50/60-Hz.

Electromagnetic hypersensitivity – Self-reported responses to or perception of electromagnetic fields, including ELF-EMF, at levels far below exposure limits that may include a wide range symptoms, including sleep disturbances, general fatigue, difficulty in concentrating, dizziness, and eyestrain.

Epidemiology – The study of the frequency and distribution of disease and health events in human populations and the factors that contribute to disease and health events.

Exposure assessment – The step in risk assessment that characterizes the exposure circumstances of the situation under analysis.

Extremely low frequency (ELF) fields – Extremely low frequency refers to electromagnetic fields in the range of 0-300 Hz.

Hazard identification – The identification of adverse effects on health from a specific exposure based on a weight-of-evidence review of the scientific research.

In vitro – Laboratory studies of isolated cells that are artificially maintained in test tubes or culture dishes are called *in vitro* studies, literally "in glass." Researchers expose isolated cells or groups of cells (tissues) to a specific agent under controlled conditions. These studies help explain the mechanisms by which exposures might affect biological processes.

In vivo – Studies in living animals or experimental studies of processes in whole living organisms are called *in vivo* studies. Scientists expose laboratory animals to a specific agent under controlled conditions and look for effects on body function, measures of health, or disease. Experience has shown that effects in laboratory animals can help to predict effects that occur in people.

Initiation – The first stage in the development of cancer, initiation typically results from exposure to an agent that can cause mutations in a cell. Initiation is believed to be irreversible, and increases the likelihood of cancer occurring.

Job-exposure matrix – A job-exposure matrix cross-classifies job titles and exposure estimates. Job-exposure matrices are used to estimate cumulative occupational exposure (e.g., magnetic field exposure) based on an individual's job history.

Magnetic fields – The magnetic field is a state of region in space, and describes the forces that would be experienced by a moving charge (or magnetic material) in proportion to its charge and velocity. The strength of magnetic fields is expressed as magnetic flux density in units called gauss (G), or in milligauss (mG), where 1 G = 1,000 mG.

Meta-analysis – An analytic technique that combines the results of many studies into one summary estimate of the association between a particular exposure and disease.

Nested case-control study – A case-control study in which the cases and controls are drawn from a cohort study's population.

Odds ratio – An odds ratio is a measure of association that describes the ratio of the odds of exposure among persons with a disease to the odds of exposure among persons without a disease. For example, an odds ratio of two would suggest that persons with the disease are two times more likely to have had exposure than persons without the disease.

Pooled analysis – A pooled analysis combines individual-level data across many studies and analyzes the data together to get a summary estimate of the association between a particular exposure and disease.

Precautionary principle – The precautionary principle refers to the idea that, when evidence does not support the suggestion that an exposure is a cause of a particular disease but where a risk is perceived, precautionary measures may be taken that are proportional to the perceived level of risk, with science as the basis for measuring that risk.

Promotion – Promotion is a later stage in cancer development, following initiation. If there is sufficient exposure to the agent, promoters increase the frequency of tumor formation that occurs after initiation.

Reference level – The reference level is a measurable level of electric or magnetic field outside of the body that is used as a screening value. It is a practical measure to determine whether the internal level identified as the basic restriction is likely to be exceeded.

Relative risk – A relative risk is an estimate that compares the risk of disease among persons who are exposed to the risk of disease among persons who are unexposed. For example, a relative risk of two means that that exposed persons in the study is two times more likely to develop the disease than unexposed persons.

Risk characterization – A quantitative estimation of the likelihood of adverse effects that may result from exposure to a specific agent in a specific situation.

Safety factor – A multiplicative factor (usually less than 1.0) incorporated into risk assessments or safety standards to allow for unpredictable types of variation, such as variability in responses from test animals to humans or person-to-person variability.

Selection bias – Selection bias occurs when there are differences in the type of person who participates in the study compared to the type of person who doesn't participate in the study. Selection bias introduces systematic error into a study, and limits the conclusions and generalizations that can be drawn.

Spot measurement – A spot measurement is an instantaneous magnetic or electric field reading that is taken at one location as an estimate of exposure.

Statistically significant – An association is statistically significant if one can conclude (with an established level of confidence using standard statistical tests) that the association is not due to a chance occurrence.

Time-weighted average (TWA) - The average exposure over a given specified time period (i.e., an 8-hr workday or a 24-hr day) of a person's exposure to a chemical or physical agent. The average is determined by sampling the exposure of interest throughout the time period.

Voltage – Voltage is the difference in electric potential between any two conductors of a circuit. It is the electric 'pressure' that exists between two points and is capable of producing the flow of current through an electrical conductor.

Weight-of-evidence review – A weight-of-evidence review critically evaluates the strength of the evidence for causality for a particular exposure and disease. It entails a comprehensive assessment of *all* relevant scientific research, in which each of the studies is critically evaluated, and more weight is given to studies of better quality.

Wire code categories – Wire coding categories are based on a classification system of homes using characteristics of power lines outside the home (e.g., thickness of the wires) and their distances from the home. This information is used to code the homes into categories based on their predicted magnetic field level.

References

Ahlbom A, Day N, Feychting M, Roman E, Skinner J, Dockerty J, Linet M, Michealis J, Olsen JH, Tynes T, Verkasalo PK. A pooled analysis of magnetic fields and childhood leukemia. Br J Cancer 83:692-698, 2000.

Akdag MZ, Dasdag S, Ulukaya E, Uzunlar AK, Kurt MA, Taskin A. Effects of extremely – frequency magnetic field on caspase activities and oxidative stress values in rat brain. Biol Trace Elem Res 138:238-249, 2010.

Al-Akhras MA. Influence of 50 Hz magnetic field on sex hormones and body, uterine, and ovarian weights of adult female rats. Electromagn Biol Med 27:155-163, 2008.

American Conference of Governmental Industrial Hygienists (ACGIH). Documentation of the threshold limit values for physical agents in the work environment. 1998.

American Conference of Government Industrial Hygienists (ACGIH). Documentation of the Threshold Limit Values and Biological exposure Indices, 7th edition. Publication No. 0100. Cincinnati, OH: American Conference of Government Industrial Hygienists. 2001.

Andel R, Crowe M, Feychting M, Pedersen NL, Fratiglioni L, Johansson B, Gatz M. Work-related exposure to extremely low-frequency magnetic fields and dementia: Results from the population-based study of dementia in Swedish Twins. J Gerontol A Biol Sci Med Sci 65:1220-1227, 2010.

Anderson LE, Boorman GA, Morris JE, Sasser LB, Mann PC, Grumbein SL, Hailey JR, McNally A, Sills RC, Haseman JK. Effect of 13 week magnetic field exposures on DMBA-initiated mammary gland carcinomas in female Sprague-Dawley rats. Carcinogenesis 20:1615-1620, 1999.

Anselmo CS, Silva TL, Holanda TG, Prado LV, Cabral-Filho JE, Catanho MT, Medeiros MC. Influence of a 60 Hz, microT, electromagnetic field on the somatic maturation of Wistar rat offspring fed a regional basic diet during pregnancy. Braz J Biol 68:641-648, 2008.

Anselmo CS, Pereira PB, Ctanho MT, Medeiros MC. Effects of the electromagnetic field, 60 Hz, 3 microT, on the hormonal and metabolic regulation of undernourished pregnant rats. Braz J Biol 69:397-404, 2009.

Armstrong BG, Deadman J, McBride ML. The determinants of Canadian children's personal exposure to magnetic fields. Bioelectromagnetics 22:161-169, 2001.

Auger N, Joseph D, Goneau M, Daniel M. The relationship between residential proximity to extremely low frequency power transmission lines and adverse birth outcomes. J Epidemiol Commun Health 65:83-85, 2011.

Aydin M, Cevik A, Kandemir FM, Yuksel M, Apaydin AM. Evaluation of hormonal change, biochemical parameters, and histopathological status of uterus in rats exposed to 50-Hz electromagnetic field. Toxicol Ind Health 25:352-158, 2009.

Bailey WH and Wagner ME. IARC evaluation of ELF magnetic fields: Public understanding of the 0.4-μT exposure metric. J Expo Sci Environ Epidemiol 18: 233-235, 2008.

Baldi I, Coureau G, Jaffre A, Gruber A, Ducamp S, Provost D, Lebailly P, Vital A, Loiseau H, Salamon R. Occupational and residential exposure to electromagnetic fields and risk of brain tumours in adults: a case-control study in Gironde, France. Int J Cancer 129:1477-1484, 2011.

Baldwin RT and Preston-Martin S. Epidemiology of brain tumors in children—a review. Toxicol Appl Pharmacol 199:118-131, 2004.

Barth A, Ponocny I, Ponocny-Seliger E, Vana N, Winker R. Effects of extremely low-frequency magnetic field exposure on cognitive functions: results of a meta-analysis. Bioelectromagnetics 31:173-179, 2010.

Baum A, Mevissen M, Kamino K, Mohr U, Löscher W. A histopathological study on alterations in DMBA-induced mammary carcinogenesis in rats with 50 Hz, 100 mT magnetic field exposure. Carcinogenesis 16:119-125, 1995.

Bayat PD, Ghanbari A, Babaei S, Khazaei M, Ghorbani R, Ayubian M. Effect of exposure to extremely low electro-magnetic field during prenatal period on mice spleen. Indian J Exp Biol 49:634-638, 2011.

Belson M, Kingsley B, Holmes A. Risk factors for acute leukemia in children: A review. Environ Health Perspect 115:138-43, 2007.

Berg H, Günther B, Hilger I, Radeva M, Traitcheva N, Wollweber L. Bioelectromagnetic field effects on cancer cells and mice tumors. Electromag Biol Med 29:132-143, 2010.

Bernabò N, Tettamanti E, Russo V, Martelli A, Turri M, Mattoli M, Barboni B. Extremely low frequency electromagnetic field exposure affects fertilization outcome in swine animal model. Theriogenology 73:1293-1305, 2010.

Bernard N, Alberdi AJ, Tanguy ML, Brugere H, Helissey P, Hubert C, Gendrey N, Guillosson JJ, Nafziger J. Assessing the potential leukemogenic effects of 50 Hz and their harmonics using an animal leukemia model. J Radiat Res 49:565-577, 2008.

Boorman GA, Anderson LE, Morris JE, Sasser LB, Mann PC, Grumbein SL, Hailey JR, McNally A, Sills RC, Haseman JK. Effects of 26-week magnetic field exposure in a DMBA initiation-promotion mammary glands model in Sprague-Dawley rats. Carcinogenesis 20:899-904, 1999a.

Boorman GA, McCormick DL, Findlay JC, Hailey JR, Gauger JR, Johnson TR, Kovatch RM, Sills RC, Haseman JK. Chronic toxicity/oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in F344/N rats. Toxicol Pathol 27:267-78, 1999b.

Borhani N, Rajaei F, Salehi Z, Javadi A. Analysis of DNA fragmentation in mouse embryos exposed to an extremely low-frequency electromagnetic field. Electromagn Biol Med 30: 246 – 252, 2011.

Buffler PA, Kwan ML, Reynolds P, Urayama KY. Environmental and genetic risk factors for childhood leukemia: appraising the evidence. Cancer Invest 23:60-75, 2005.

Burdak-Rothkamm S, Rothkamm K, Folkard M, Patel G, Hone P, Lloyd D, Ainsbury L, Prise KM. DNA and chromosomal damage in response to intermittent extremely low frequency magnetic fields. Mutat Res 672:82-89, 2009.

Calvente I, Fernandez MF, Villalba J, Olea N, Nuñez MI. Exposure to electromagnetic fields (non-ionizing radiation) and its relationship with childhood leukemia: a systematic review. Sci Total Environ 408:3062-3069, 2010.

Cakir DU, Yokus B, Akdag MZ, Sert C, Mete N. Alterations of hematological variations in rats exposed to extremely low frequency magnetic fields (50 Hz). Arch of Med Res 40:352-356, 2009.

Canseven AG, Seyhan N, Mirshahidi S, Imir T. Suppression of natural killer cell activity on *candida stellatoidea* by a 50 Hz magnetic field. Electromagn Biol Med 25:79-85, 2006.

Carrubba S, Frilot C, Chesson AL, Marino AA. Numerical analysis of recurrence plots to detect effect of environmental-strength magnetic fields on human brain electrical activity. Med Eng Phys 32:898-907, 2010.

Chen C, Ma X, Zhong M, Yu Z. Extremely low frequency electromagnetic fields exposure and female breast cancer risk: a meta-analysis based 24,338 cases and 60,628 controls. Breast Cancer Res Treat 123:569-576, 2010.

Chu LY, Lee JH, Nam YS, Lee YJ, Park WH, Lee BC, Kim D, Chung YH, Jeong JH. Extremely low frequency magnetic field induces oxidative stress in mouse cerebellum. Gen Physiol Biophys 30:415-421, 2011.

Chung M-K, Yu W-J, Cicekcibasi AE, Celik, I, Salbacak A, Ozkan Y, Okudan N, Buyukmumcu M. Determination of the effects of extremely low frequency electromagnetic fields on the percentages of peripheral blood leukocytes and histology of lymphoid organs of the mouse. Saudi Med J 29:36-41, 2008.

Chung M-K, Kim Y-B, Ha C-S, Myung S-H. Lack of a co-promotion effect of 60 Hz rotating magnetic fields on n-ethyl-n-nitrosourea induced neurogenic tumors in F344 rats. Bioelectromagnetics 29:539-548, 2008.

Chung M-K, Yu W-J, Kim Y-B, Myung S-H. Lack of a co-promotion effect of 60 Hz circularly polarized magnetic fields on spontaneous development of lymphoma in AKR mice. Bioelectromagnetics 31:130-139, 2010.

Cicekcibasi AE, Celik I, Salbacak A, Ozkan Y, Okudan N, Buyukmumcu M. Determination of the effects of extremely low frequency electromagnetic fields on the percentages of peripheral blood leukocytes and histology of lymphoid organs of the mouse. Saudi Med J 29:36-41, 2008.

Ciejka E, Kleniewska P, Skibska B, Goraca A. Effects of extremely low frequency magnetic field on oxidative balance in brain of rats. J Physiol Pharmacol 62: 657 – 661, 2011.

Coble JB, Dosemeci M, Stewart PA, Blair A, Bowman J, Fine HA, Shapiro WR, Selker RG, Loeffler JS, Black PM, Linet MS, Inskip PD. Occupational exposure to magnetic fields and the risk of brain tumors. Neuro Oncol 11:242-249, 2009.

Corbacio M, Brown S, Dubois S, Goulet D, Prato FS, Thomas AW, Legros A. Human cognitive performance in a 3 mT power-line frequency magnetic field. Bioelectromagnetics 32: 620-633, 2011.

Cuccurazzu B, Leone L, Podda MV, Piacentini R, Riccardi E, Ripoli C, Azzena GB, Grassi C. Exposure to extremely low-frequency (50 Hz) electromagnetic fields enhances adult hippocampal neurogenesis in C57BL/6 mice. Exp Neurol 226:173-182, 2010.

David E, Reissenweber J, Wojtysiak A. Provocation studies in electromagnetically hypersensitive persons. In Hansson Mild K, Repacholi M, van Deventer E, Ravazzani P (editors). Electromagnetic Hypersensitivity. Proceedings: International Workshop on EMF Hypersensitivity, pp. 123–133. Prague: WHO, 2006.

Deadman JE, Armstong BG, McBride ML, Gallaher R, Theriault G. Exposures of children in Canada to 60-Hz magnetic and electric fields. Scand J Work Environ Health 25:368-375, 1999.

De Bruyn L and De Jager L. Effect of long-term exposure to a randomly varied 50 Hz power frequency magnetic field on fertility in the mouse. Electromagn Biol Med 29:52-61, 2010.

Dimbylow P and Findlay R. The effects of body posture, anatomy, age and pregnancy on the calculation of induced current densities at 50 Hz. Radiation Protection Dosimetry 139: 532-538, 2010.

Does M, Scélo G, Metayer C, Selvin S, Kavet R, Buffler P. Exposure to electrical contact currents and the risk of childhood leukemia. Radiat Res 175:390-396, 2011.

Draper G, Vincent T, Kroll ME, Swanson J. Childhood cancer in relation to distance from high voltage power lines in England and Wales: a case-control study. BMJ 330:1290, 2005.

Dundar B, Cesur G, Comlekci S, Songur A, Gokcimen A, Sahin O, Ulukut O, Yilmaz HR, Sutcu R, Caliskan S. The effect of the prenatal and post-natal long-term exposure to 50 Hz

electric field on growth, pubertal development and IGF-1 levels in female Wistar rats. Toxicol Ind Health 25:479-487, 2009.

Eden T. Aetiology of childhood leukaemia. Cancer Treat Rev 36:286-297, 2010.

Electric Power Research Institute (EPRI). Electromagnetic Interference with Implanted Medical Devices: 1997-2003. Report No.1005570, 2004. A summary can be found at: http://my.epri.com/portal/server.pt?space=CommunityPage&cached=true&parentname=ObjMgr&parentid=2&control=SetCommunity&CommunityID=221&PageIDqueryComId=0

Erren TC. A meta-analysis of epidemiologic studies of electric and magnetic fields and breast cancer in women and men. Bioelectromagnetics Suppl 5:S105-S119, 2001.

European Health Risk Assessment Network on Electromagnetic Fields Exposure (EFHRAN). Risk Analysis of Human Exposure to Electromagnetic Fields. Report D2 of the EFHRAN project, July 2010a.

European Health Risk Assessment Network on Electromagnetic Fields Exposure (EFHRAN). Report on the Analysis of Risks Associated to Exposure to EMF: In Vitro and In Vivo (animals) Studies. Report D3 of the EFHRAN project, July 2010b.

Exponent. Response to Evidence Presented by Magda Havas. Report prepared for British Columbia Transmission Corporation, November, 2005.

Exponent. EMF and Health: Review and Update of the Scientific Research. Report prepared for British Columbia Transmission Corporation, October 30, 2007.

Exponent. EMF and Health: Comprehensive Review and Update of the Scientific Research September 2007 through January 2010. Report prepared for British Columbia Transmission Corporation, February, 2010.

Federal-Provincial-Territorial Radiation Protection Committee. Health effects and exposure guidelines related to extremely low frequency (ELF) 50/60 Hz electric and magnetic fields – an overview. Prepared by the ELF Working Group, 1998.

Federal-Provincial-Territorial Radiation Protection Committee (FPTRPC). Heath Effects and Exposure Guidelines Related to Extremely Low Frequency Electric and Magnetic Fields - An Overview. Prepared by The ELF Working Group, 2005.

Federal-Provincial-Territorial Radiation Protection Committee (FPTRPC). Response Statement to Public Concerns Regarding Electric and Magnetic Fields (EMFs) from Electric Power Transmission and Distribution Lines. November 8, 2008. http://www.hc-sc.gc.ca/ewh-semt/radiation/fpt-radprotect/emf-cem-eng.php)

Fedrowitz M and Löscher W. Exposure of Fischer 344 rats to a weak power frequency magnetic field facilitates mammary tumorigenesis in the DMBA model of breast cancer. Carcinogenesis 29:186-193, 2008.

Fedrowitz M and Löscher W. 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. Int J Radiat Biol 88:425-429, 2012.

Focke F, Schuermann D, Kuster N, Schar P. DNA fragmentation in human fibroblasts under extremely low frequency electromagnetic field exposure. Mutat Res 683:74-83; 2010.

Foroozandeh E, Ahadi H, Askari P, Naeini MS. Effects of single, brief exposure to an 8 mT electromagnetic field on avoidance learning in male and female mice. Psychol Neurosci 4:143-148, 2011.

Frilot C, Carrubba S, Marino AA. Transient and steady-state magnetic fields induce increased fluorodeoxyglucose uptake in rat hindbrain. Synapse 65:617-623, 2011.

García AM, Sisternas A, Hoyos SP. Occupational exposure to extremely low frequency electric and magnetic fields and Alzheimer disease: a meta-analysis. Int J Epidemiol 37:329-40, 2008.

Gobba F, Bravo G, Rossi P, Contesa GM, Scaringi M. Occupational and environmental exposure to extremely low frequency-magnetic fields: a personal monitoring study in a large group of workers in Italy. J Expo Sci Environ Epidemiol 21:634-645, 2011.

Goraca A, Ciejka E, Piechota A. Effects of extremely low frequency magnetic field on the parameters of oxidative stress in heart. J Physiol Pharmacol 61:333-338, 2010.

Government of Canada. A Framework for the Application of Precaution in Science-based Decision Making about Risk. C2003-98208

Greenland S and Kheifets L. Leukemia attributable to residential magnetic fields: results from analyses allowing for study biases. Risk Anal 26:471-482, 2006.

Greenland S, Sheppard AR, Kelsh MA, Kaune WT. A pooled analysis of magnetic fields, wire codes, and childhood leukemia. Epidemiology 11:624-634, 2000.

Gulturk S, Demirkazik A, Kosar I, Cetin A, Dokmetas HS, Demir T. Effect of exposure to 50 Hz magnetic field with or without insulin on blood-brain barrier permeability in strptozotocin-induced diabetic rats. Bioelectromagnetics 31:262-269, 2010.

Hareuveny R, Kandel S, Yitzhak N-M, Kheifets L, Mezei G. Exposure to 50 Hz magnetic fields in apartment buildings with indoor transformer stations in Israel. J Expo Sci Environ Epidemiol 21:365-371, 2011.

Harris AW, Basten A, Gebski V, Noonan D, Finnie J, Bath ML, Bangay MJ, Repacholi MH. A test of lymphoma induction by long-term exposure of E mu-Pim1 transgenic mice to 50 Hz magnetic fields. Radiat Res 149:300-307, 1998.

Health Canada. Human Health Risk Assessment for Priority Substances. Environmental Health Directorate. Canadian Environmental Protection Act. Ottawa: Health Canada, 1994.

Health Canada (HC). It's Your Health – Electric and Magnetic Fields at Extremely Low Frequencies. 2010.

Health Council of the Netherlands (HCN). ELF electromagnetic fields committee. electromagnetic fields: annual update 2001. The Hague: Health Council of the Netherlands. Publication No. 2001/14, 2001.

Health Council of the Netherlands (HCN). ELF Electromagnetic Fields Committee. Electromagnetic fields: Annual Update 2003. The Hague: Health Council of the Netherlands. Publication No. 2004/1, 2004.

Health Council of the Netherlands (HCN). ELF Electromagnetic Fields Committee. Electromagnetic fields: Annual Update 2005. The Hague: Health Council of the Netherlands. Publication No. 2005/14, 2005.

Health Council of the Netherlands (HCN). ELF Electromagnetic Fields Committee. Electromagnetic fields: Annual Update 2006. The Hague: Health Council of the Netherlands. Publication No. 2007/06, 2007.

Health Council of the Netherlands (HCN). Electromagnetic Fields: Annual Update 2008. The Hague: Health Council of the Netherlands. Publication No. 2009/02, 2009a.

Health Council of the Netherlands (HCN). Advisory letter – Power lines and Alzheimer's disease. The Hague: Health Council of the Netherlands. Publication No. 2009/05E, 2009b

Health Protection Agency (HPA). Power frequency electromagnetic fields, melatonin and the risk of breast cancer: report of an independent advisory group on non-ionising radiation. Doc HPA. Series B: Radiation, Chemical and Environmental Hazards. RCE-1, 2006.

He LH, Shi HM, Liu TT, Xu YC, Ye KP, Wang S. Effects of extremely low frequency magnetic field on anxiety level and spatial memory of adult rats. Chin Med J 124:3362-3366, 2011.

Hill AB. The environment and disease: association or causation? Proc R Soc Med 58:295-300, 1965.

Hirata A, Takano Y, Fujiwara O, Dovan T, Kavet R. An electric field induced in the retina and brain at threshold magnetic flux density causing mangetophosphenes. Phys Med Biol 56:4091-4101, 2011.

Hug K, Grize L, Seidler A, Kaatsch P, Schüz J. Parental occupational exposure to extremely low frequency magnetic fields and childhood cancer: A German case-control study. Am J Epidem 171:27-35, 2010.

International Agency for Research on Cancer (IARC). Mechanisms of Carcinogenesis in Risk Identification. No. 116. Lyon, France: IARC Press, 1992.

International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 80: Static and extremely low-frequency (ELF) electric and magnetic fields. Lyon, France: IARC Press, 2002.

International Agency for Research on Cancer (IARC). IARC monographs on the evaluation of carcinogenic risks to humans. Preamble. Lyon, France: IARC Press, 2006.

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

International Commission on Non-Ionizing Radiation Protection (ICNIRP). Review of the epidemiologic literature on EMF and health. Environ Health Perspect 109:S911-S933, 2001.

International Commission on Non-Ionizing Radiation Protection (ICNIRP). General approach to protection against non-ionizing radiation. Health Phys 82:540-548, 2002.

International Commission on Non-Ionizing Radiation Protection (ICNIRP). Exposure to Static and Low Frequency Electromagnetic Fields, Biological Effects and Health Consequences (0-100 kHz) – Review of the Scientific Evidence on Dosimetry, Biological Effects, Epidemiological Observations, and Health Consequences Concerning Exposure to Static and Low Frequency Electromagnetic Fields (0-100 kHz). Matthes R, McKinlay AF, Bernhardt JH, Vecchia P, Beyret B (eds.). International Commission on Non-Ionizing Radiation Protection, 2003.

International Commission on Non-ionizing Radiation Protection (ICNIRP). Draft Guidelines for limiting exposure to time-varying electric and magnetic fields (1 Hz to 100 kHz). Health Phys 96:504-514, 2009.

International Commission on Non-Ionizing Radiation Protection (ICNIRP). ICNIRP Statement—Guidelines for limiting exposure to time-varying electric and magnetic fields 1 Hz to 100 kHz. Health Phys 99: 818-836, 2010.

International Committee on Electromagnetic Safety (ICES). IEEE Standard for Safety Levels with Respect to Human Exposure to Electromagnetic Fields 0 to 3 kHz C95. 6-2002. Piscataway, NJ: IEEE, 2002.

Ivancsits S, Diem E, Pilger A, Rüdinger HW, Jahn O. Induction of DNA strand breaks by intermittent exposure to extremely-low-frequency electromagnetic fields in human diploid fibroblasts. Mutat Res 519:1-13, 2002a.

Ivancsits S, Pilger A, Diem E, Schaffer A, Rüdinger HW. Vanadate induces DNA strand breaks in cultured human fibroblasts at doses relevant to occupational exposure. Mutat Res 519:25-35, 2002b.

Ivancsits S, Diem E, Jahn O, Rüdiger HW. Age-related effects on induction of DNA strand breaks by intermittent exposure to electromagnetic fields. Mech Aging Dev 124:847-850, 2003a.

Ivancsits S, Diem E, Jahn O, Rüdiger HW. Intermittent extremely low frequency electromagnetic fields cause DNA damage in a dose-dependent way. Int Arch Occup Environ Health 76:431-436, 2003b.

Jiménez -Garcia MN, Robledo JA, Aparicio-Bautists DI, Rodriguez-Segura MA, Villa-Trevino S, Godina-Nava JJ. Anti-proliferative effect of extremely low frequency electromagnetic field on preneoplastic lesions formation in the rat liver. BMC Cancer 10: 1-12, 2010.

Johansen C, Raaschou-Nielsen O, Olsen JH, and Schuez J. Risk for leukaemia and brain and breast cancer among Danish utility workers - A second follow-up. Occup Environ Med 64:782-784, 2007.

Kabuto M, Nitta H, Yamamoto S, Yamaguchi N, Akiba S, Honda Y, Hagihara J, Isaka K, Saito T, Ojima T, Nakamura Y, Mizoue T, Ito S, Eboshida A, Yamazaki S, Sokejima S, Kurokawa Y, and Kubo O. Childhood leukemia and magnetic fields in Japan: a case-control study of childhood leukemia and residential power-frequency magnetic fields in Japan. Int J Cancer 119:643-50, 2006.

Katrib J, Schmitt P, Magne I, Kourtiche D, Souques M, Nadi M. Implantable cardioverter-defibrillators exposed to low frequency magnetic fields. IEEE General Assembly and Scientific Symposium, 13-20 Aug 2011.

Kavet R and Hooper HC. Residential magnetic fields and measures of neutral-to-earth voltage: Variability within and between residences. Health Phys 97:332-341, 2009.

Kavet R, Hooper C, Buffler P, Does M. The relationship between residential magnetic fields and contact voltage: a pooled analysis. Radiat Res 176:807-815, 2011.

Kheifets L, Monroe J, Vergara X, Mezei G, Afifi A. Occupational electromagnetic fields and leukemia and brain cancer: An update to two meta-analyses. JOEM 50:677-88, 2008.

Kheifets L, Bowman JD, Checkoway H, Feychting M, Harrington JM, Kavet R, Marsh G, Mezei G, Renew DC and van Wijngaarden E. Future needs of occupational epidemiology of extremely low frequency electric and magnetic fields: review and recommendations. Occup Environ Med 66:72-80, 2009.

Kheifets L, Ahlbom A, Crespi CM, Draper G, Hagihara J, Lowenthal RM, Mezei G, Oksuzyan S, Schüz J, Swanson J, Tittarelli A, Vincenti M, Wünsch-Filho V. Pooled analysis of recent studies on magnetic fields and childhood leukaemia. Br J Cancer 103:1128-1135, 2010a.

Kheifets L, Ahlbom A, Crespi CM, Feychting M. Johansen C, Monroe J, Murphy MFG, Oksuzyan S, Preston-Martin S, Roman E, Saito T, Savitz D, Schüz J, Simpson J, Swanson J, Tynes T, Merkasalo V, Mezei G. A pooled analysis of extremely low-frequency magnetic fields and childhood brain tumors. Am J Epidemiol 172:752-761, 2010b.

Kheifets L, Afifi A, Monroe J, Swanson J. Exploring exposure--response for magnetic fields and childhood leukemia. J Expo Sci Environ Epidemiol. 21 :625-33, 2011.

Kim DW, Choi JL, Nam KC, Yang DI, Kwon MK. Origins of electromagnetic hypersensitivity to 60 Hz magnetic fields: A provocation study. Bioelectromagnetics. 2011 Oct 19. doi: 10.1002/bem.20711Korpinen L, Kuisti H, Elovaara J, Virtanen V. Cardiac pacemakers in electric and magnetic fields of 400-kV power lines. Pacing Clin Electrophysiol 35: 422-430, 2012.

Kroll ME, Swanson J, Vincent TJ, Draper GJ. Childhood cancer and magnetic fields from high-voltage power lines in England and Wales: a case-control study. Br J Cancer 103:1122-1127, 2010.

Lai H and Singh NP. Magnetic-field-induced DNA strand breaks in brain cells of the rat. Environ Health Perspect 112:687-694, 2004.

Lee GM, Neutra RR, Hristova L, Yost M, Hiatt RA. A nested case-control study of residential and personal magnetic field measures and miscarriages. Epidemiology 13:21-31, 2002.

Lerchl A. Inappropriate statistical analyses lead to erroneous results [Focke et al., Mutat Res 683 (2010) 74-83]. Mutat Res 692: 61-2; author reply 63-64, 2010.

Li DK, Odouli R, Wi S, Janevic T, Golditch I, Bracken TD, Senior R, Rankin R, Iriye R. A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of miscarriage. Epidemiology 13:9-20, 2002.

Li DK, Yan B, Li Z, Gao E, Miao M, Gong D, Weng X, Ferber JR, Yuan W. Exposure to magnetic fields and the risk of poor sperm quality. Reprod Toxicol 29:86-92, 2010.

Li DK, Chen H, Odouli R. Maternal exposure to magnetic fields during pregnancy in relation to the risk of asthma in offspring. Arch Pediatr Adolesc Med 165:945-950, 2011.

Linet MS, Hatch EH, Kleinerman A, Robinson LL, Kaune WT, Friedman DR, Severson RK, Haines CM, Hartsock CT, Niwa S, Wachholder S, and Tarone RE. Residential exposure to magnetic fields and acute lymphoblastic leukemia in children. N Engl J Med 337:1-7, 1997.

Löscher W and Mevissen M. Linear relationship between flux density and tumor co-promoting effect of prolonged magnetic field exposure in a breast cancer model. Cancer Lett 96:175-180, 1995.

Löscher W, Mevissen M, Lehmacher W, Stamm A. Tumor promotion in a breast cancer model by exposure to a weak alternating magnetic field. Cancer Lett 71:75-81, 1993.

Löscher W, Wahnschaffe U, Mevissen M, Lerchl A, Stamm A. Effects of weak alternating magnetic fields on nocturnal melatonin production and mammary carcinogenesis in rats. Oncology 51:288-295, 1994.

Löscher W, Mevissen M, Haussler B. Seasonal influence on 7,12-dimethylbenz[a]anthracene-induced mammary carcinogenesis in Sprague-Dawley rats under controlled laboratory conditions. Pharmacol Toxicol 81:265-270, 1997.

Maeda K, Henbest KB, Cintolesi F, Kuprov I, Rodgers CT, Liddell PA, Gust D, Timmel CR, Hore PJ. Chemical compass model of avian magnetoreception. Nature 453: 387-90, 2008.

Malagoli C, Fabbi S, Teggi S, Calzari M, Poli M, Ballotti E, Notari B, Bruni M, Plazaai G, Paolucci P, Vinceti M. Risk of hematological malignancies associated with magnetic fields exposure from power lines: A case control study in two municipalities of northern Italy. Environ Health 9:16, 2010.

Mandeville R, Franco E, Sidrac-Ghali S, Paris-Nadon L, Rocheleau N, Mercier G, Desy M, Gaboury L. Evaluation of the potential carcinogenicity of 60 Hz linear sinusoidal continuous-wave magnetic fields in Fisher F344 rats. FASEB Journal 11:1127-1136, 1997.

Marcilio I, Gouveia N, Filho ML, Kheifets L. Adult mortality from leukemia, brain cancer, amyotrophic lateral sclerosis and magnetic fields from power lines: a case control study in Brazil. Rev Bras Epidemiol 14:580-588, 2011.

Mariucci G, Villarini M, Moretti M, Taha E, Conte C, Minelli A, Aristei C, Ambrosini MV. Brain DNA damage and 70-kDa heat shock protein expression in CD1 mice exposed to extremely low frequency magnetic fields. Int J Radiat Biol 86:701-710, 2010.

Martínez-Sámano J, Torres-Durán PV, Juárez-Oropeza MA, Elías-Viñas D, Verdugo-Díaz L. Effects of acute electromagnetic field exposure and movement restraint on antioxidant system in liver, heart, kidney and plasma of Wistar rats: A preliminary report. Int J Radiat Biol 86:1088-1094, 2010.

Maslanyj M, Simpson J, Roman E, Schüz J. Power frequency magnetic fields and risk of childhood leukaemia: Misclassification of exposure from the use of the distance from power line' exposure surrogate. Bioelectromagnetics 30:183-188, 2009

McBride ML, Gallagher RP, Thériault G, Armstrong BG, Tamaro S, Spinelli JJ, Deadman JE, Fincham S, Robson D, Choi W. Power-frequency electric and magnetic fields and risk of childhood leukemia in Canada. Am J Epidemiol 149:831-842, 1999.

McCarty DE, Carrubba S, Chesson AL, Frilot C, Gonzalez-Toledo E, Marino AA. Electromagnetic hypersensitivity: Evidence for a novel neurological syndrome. Int J Neurosci 12: 670-676, 2011.

McCormick DL, Ryan BM, Findlay JC, Gauger JR, Johnson TR, Morrissey RL, Boorman GA. Exposure to 60 Hz magnetic field and risk of lymphoma in PIM transgenic and TSG-p53 (p53 knockout) mice. Carcinogenesis 19:1649-1653, 1998

McCormick DL, Boorman GA, Findlay JC, Hailey JR, Johnson TR, Gauger JR, Pletcher JM, Sills RC, and Haseman JK. Chronic toxicity/oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in B6C3F1 mice. Toxicol Pathol 27:279-85, 1999.

McNally RJ and Parker L. Environmental factors and childhood acute leukemias and lymphomas. Leuk Lymphoma 47(4):583-98, 2006.

Mee T, Whatmough P, Broad L, Dunn C, Maslanyj M, Allen S, Muir K, McKinney PA, Van Tongeren M. Occupational exposure of UK adults to ELF magnetic fields. Occup Environ Med 66:619-617, 2009.

Mevissen M, Stamm A, Buntenkotter S, Zwingelberg R, Wahnschaffe U, Löscher W. Effects of magnetic fields on mammary tumor development induced by 7,12-dimethylbenz(a)anthracene in rats. Bioelectromagnetics 14:131-143, 1993a.

Mevissen M, Wahnschaffe U, Löscher W, Stamm A, Lerchl A. Effects of AC magnetic field on DMBA-induced mammary carcinogenesis in Sprague-Dawley rats. In: Electricity and Magnetism in Biology and Medicine, pp. 413-415. Blank M (ed). San Francisco: San Francisco Press, 1993b.

Mevissen M, Lerchl A, Löscher W. Study on pineal function and DMBA-induced breast cancer formation in rats during exposure to a 100-mG, 50 Hz magnetic field. J Toxicol Environ Health 48:169-185, 1996a

Mevissen M, Lerchl A, Szamel M, and Löscher W. Exposure of DMBA-treated female rats in a 50 Hz, 50-μT magneticfield: effects on mammary-tumor growth, melatonin levels, and T-lymphocyte activation. Carcinogenesis 17:903-910, 1996b.

Mevissen M, Haussler M, Lerchl A, Löscher W. Acceleration of mammary tumorigenesis by exposure of 7,12-dimethylbenz[a]anthracene-treated female rats in a 50 Hz, 100-microT magnetic field: replication study. J Toxicol Environ Health A 53:401-418, 1998.

Mezei G, Spinelli JJ, Wong P, Borugian M, McBride ML. Assessment of selection bias in the Canadian case-control study of residential magnetic field exposure and childhood leukemia. Am J Epidemiol 167:1504-10, 2008a.

Mezei G, Gadallah M, Kheifets L. Residential magnetic field exposure and childhood brain cancer: a meta-analysis. Epidemiology 29:424-30, 2008b.

Miller AG and Green LM. Electric and magnetic fields at power frequencies. Chronic Diseases in Canada 29 Suppl 1:69-83, 2010.

Nam KC, Choi JL, Kwon MK, Jang KH, Kim DW. Physiological variables and subjective symptoms by 60 Hz magnetic field in EHS and non-EHS persons. Conf Proc IEEE Eng Med Biol Soc:1925-8, 2011.

National Institute of Environmental Health Sciences (NIEHS). Assessment of health effects from exposure to power-line frequency electric and magnetic fields: working group report. NIH Publication No. 98-3981. Research Triangle Park, NC: National Institute of Environmental Health Sciences of the U.S. National Institutes of Health, 1998.

National Institute of Environmental Health (NIEHS). Health effects from exposure to power line frequency electric and magnetic fields. NIH Publication No. 99-4493. Research Triangle Park, NC: National Institute of Environmental Health Sciences of the U.S. National Institutes of Health, 1999.

National Radiological Protection Board (NRPB). Electromagnetic fields and the risk of cancer. Report of an Advisory Group on Non-ionising Radiation. National Radiological Protection Board 3(1):1-138, 1992.

National Radiological Protection Board (NRPB). Electromagnetic fields and the risk of cancer. Supplementary report by the Advisory Group on Non-ionising Radiation. National Radiological Protection Board 5(2):77-81, 1994a.

National Radiological Protection Board (NRPB). Health effects related to the use of visual display units. Report of an Advisory Group on Non-ionising Radiation. National Radiological Protection Board 5(2):1-75, 1994b.

National Radiological Protection Board (NRPB). ELF electromagnetic fields and the risk of cancer: Report of an advisory group on non-ionising radiation. National Radiological Protection Board. Volume 12, No 1, 2001a.

National Radiological Protection Board (NRPB). ELF electromagnetic fields and neurodegenerative disease. National Radiological Protection Board. Volume 12, No 4, 2001b.

National Radiological Protection Board (NRPB). Review of the scientific evidence for limiting exposure to electromagnetic fields (0-300 GHz). National Radiological Protection Board. Volume 15, No 3, 2004.

National Research Council (NRC). Committee on the Possible Effects of Electromagnetic Fields on Biologic Systems. Possible Health Effects of Exposure to Residential Electric and Magnetic Fields. Washington DC: National Academy Press, 1997.

National Toxicology Program (NTP). NTP technical report on the toxicology and carcinogenesis studies of 60 Hz magnetic fields in F344/N rats and B6C3F1 mice. Washington DC: National Toxicology Program. NTP TR 488, NIH Publication No. 99-3979. 1999.

National Toxicology Program (NTP). Description of NTP study types, 2011. http://ntp.niehs.nih.gov/index.cfm?objectid=72015D9F-BDB7-CEBA-F4EB4F9BF507820C

Negishi T, Imai S, Shibuya K, Nishimura I, Shigemitsu T. Lack of promotion effects of 50 Hz magnetic fields on 7,12-dimethylbenz(a)anthracene-induced malignant lymphoma/lymphatic leukemia in mice. Bioelectromagnetics 29:29-38, 2008.

Okudan N, Celik I, Salbacak A, Cicekcibasi AE, Buyukmumcu M, Gokbel H. Effects of long-term 50 Hz magnetic field exposure on the micronucleated polychromatic erythrocyte and blood lymphocyte frequency and argyrophilic nucleolar organizer regions in lymphocytes of mice. Neuroendocrinol Lett 31:208-214, 2010.

Olshan AF, Anderson L, Roman E, Fear N, Wolff M, Whyatt R, Vu V, Diwan BA, Potischman N. Workshop to identify critical windows of exposure for children's health: cancer work group summary. Environ Health Perspect 108 Suppl 3:595-597, 2000.

Parlett LE, Bowman JD, van Winjgaarden E. Evaluation of occupational exposure to magnetic fields and motor neuron disease mortality in a population-based cohort. JOEM 53:1447-1451, 2011.

Poulletier de Gannes F, Ruffie G, Taxile M, Ladeveze E, Hurtier A, Haro E, Duleu S, Charlet de Sauvage R, Billaudel B, Geffard M, Veyret B, Lagroye I. Amyotrophic lateral sclerosis (ALS) and extremely-low frequency (ELF) magnetic fields: a study in the SOD-1 transgenic mouse model. Amyotroph Lateral Scler 10:370-373, 2009.

Rajaei F, Borhani N, Sabbagh-Ziarani F, Mashayekhi F. Effects of extremely low-frequency electromagnetic field on fertility and heights of epithelial cells in pre-implantation stage endometrium and fallopian tube in mice. J Chinese Integr Med 8:56-60, 2010.

Rajkovic V, Matavulj M, Johansson O. Studies on the synergistic effects of extremely low-frequency magnetic fields and the endocrine-disrupting compound atrazine on the thyroid gland. Int J Radiat Biol 86:1050-1060, 2010a.

Rajkovic V, Matavulj M, Johansson O. Combined exposure of peripubertal male rats to the endocrine-disrupting compound atrazine and power-frequency electromagnetic fields causes degranulation of cutaneous mast cells: A new toxic environmental hazard? Arch Environ Contam Toxicol 59:334-341, 2010b.

Reid A, Glass DC, Bailey HD, Milne E, de Klerk NH, Downie P, Fritschi L. Risk of childhood acute lymphoblastic leukaemia following parental occupational exposure to extremely low frequency electromagnetic fields. Br J Cancer 10:1409-1413, 2011.

Ries LAG, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR (eds). Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995, National Cancer Institute, SEER Program. Bethesda, MD: NIH Pub. No. 99-4649, 1999.

Rona RJ. Asthma and poverty. Thorax 55:239-244, 2000.

Rossig C and Juergens H. Aetiology of childhood acute leukaemias: Current status of knowledge. Radiat Prot Dosimetry 132:114-118, 2008.

Rothman KJ and Greenland S. Modern epidemiology. Philadelphia, PA: Lippincott-Raven Publishers, 1998.

Rubin GJ, Nieto-Hernandez R, Wessely S. Idiopathic environmental intolerance attributed to electromagnetic fields (formerly 'electromagnetic hypersensitivity'): An updated systematic review of provocation studies. Bioelectromagnetics 31:1-11, 2010.

Rubin GJ, Hillert L, Nieto-Hernandez R, van Rongen E, Oftedal G. Do people with idiopathic environmental intolerance attributed to electromagnetic fields display physiological effects when exposed to electromagnetic fields? A systematic review of provocation studies. Bioelectromagnetics 32 :593-609, 2011.

Saadeldin IM, Fadel AM, Hamada MMZ, E-Badry AA. Effects of exposure to 50 Hz, 1 gauss magnetic field on reproductive traits in male albino rats. Acta Vet Brno 80:107-111, 2011.

Saito T, Nitta H, Kubo O, Yamamoto S, Yamaguchi N, Akiba S, Honda Y, Hagihara J, Isaka K, Ojima T, Nakamura Y, Mizoue T, Ito S, Eboshida A, Yamazaki S, Sokejima S, Kurokawa Y, Kabuto M. Power-frequency magnetic fields and childhood brain tumors: A case-control study in Japan. J Epidemiol 20:54-61, 2010.

Santibáñez M, Bolumar F, García AM. Occupational risk factors in Alzheimer's disease: a review assessing the quality of published epidemiological studies. Occup Environ Med 64:723-732, 2007.

Saunders RD and Jeffers JG. A neurobiological basis for ELF guidelines. Health Phys 92:596-603, 2007.

Scarfi MR, Sannino A, Perrotta A, Sarti M, Mesirca P, Bersani F. Evaluation of genotoxic effects in human fibroblasts after intermittent exposure to 50 Hz electromagnetic fields: a confirmatory study. Radiat Res 164:270-276, 2005.

Schmiedel S and Blettner M. The association between extremely low-frequency electromagnetic fields and childhood leukaemia in epidemiology: enough is enough? Br J Cancer 103:931-932, 2010.

Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Possible Effects of Electromagnetic Fields (EMF) on Human Health. European Commission. Directorate C – Public Health and Risk Assessment, 2007.

Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) for the Directorate-General for Health & Consumers of the European Commission. Health Effects of Exposure to EMF. January 2009.

Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). Opinion on Possible Effects of Electromagnetic Fields (EMF), Radio Frequency Fields (RF) and Microwave Radiation on Human Health. Brussels: European Commission, 2001.

Scientific Steering Committee of the European Commission (SSC). Opinion on possible health effects from exposure to electromagnetic fields (0 Hz- 300 GHz) - Report and opinion adopted at the meeting of the Scientific Steering Committee of 25-26 June 1998. http://ec.europa.eu/food/fs/sc/ssc/out19_en.html

Selmaoui B, Lambrozo J, Sackett-Lundeen L, Haus E, Touitou Y. Acute exposure to 50-Hz magnetic fields increases interleukin-6 in healthy young men. J Clin Immunol 31:1105-1111, 2011.

Sohrabi M-R, Tarjoman T, Abadi A, Yavari P. Living near overhead high voltage transmission power lines as a risk factor for childhood acute lymphoblastic leukemia: a case-control study. Asian Pac J Cancer Prev 11:423-427, 2010.

Sommer AM and Lerchl A. The risk of lymphoma in AKR/J mice does not rise with chronic exposure to 50 Hz magnetic fields (1 microT and 100 microT). Radiat Res 162:194-200, 2004.

Soques M, Magne I, Lambrozo J. Implantable cardioverter defibrillator and 50-Hz electric and magnetic field exposure in the workplace. Int Arch Occup Environ Health 84:1-6, 2011.

Susser M. What is a cause and how do we know one? A grammar for pragmatic epidemiology. Am J Epidemiol 133:635-648, 1991.

Swedish Radiation Protection Authority (SSI). Fourth annual report from SSI's Independent Expert Group on Electromagnetic Fields, 2006: Recent Research on EMF and Health Risks. SSI Rapport 2007:04.

Swedish Radiation Protection Authority (SSI). Fifth annual report from SSI's Independent Expert Group on Electromagnetic Fields, 2007: Recent Research on EMF and Health Risks. SSI Rapport 2008:12.

Swedish Radiation Safety Authority (SSM). Recent Research on EMF and Health Risks: Seventh annual report from SSMs independent Expert Group on Electromagnetic Fields 2010. Report number: 2010:44, December 2010.

Szemerszky R, Zelena D, Barna I, Bárdos G. Stress-related endocrinological and psychopathological effects of short- and long-term 50 Hz electromagnetic field exposure in rats. Brain Res Bull 81:92-99, 2010.

Tenorio BM, Jiménez GC, Morais RN, Torres SM, Nogueira RA, Silva, VA, Jr. Testicular development evaluation in rats exposed to 60 Hz and 1 mT electromagnetic field. J Appl Toxicol 31:223-230, 2011.

Tenorio BM, Jiménez GC, Morais RN, Peixoto CA, Nogueira RA, Silva, VA, Jr. Evaluation of testicular degeneration induced by low-frequency electromagnetic fields. J Appl Toxicol 32:210-218, 2012.

Tiikkaja M, Alanko T, Lindholm H, Hietanen M, Hartikainen J, Tolvonen L. Experimental study on malfunction of pacemakers due to exposure to different external magnetic fields. J Interv Card Electrophysiol 34:19-27, 2012.

Trimmel M and Schweiger E. Effects of an ELF (50 Hz, 1 mT) electromagnetic field (EMF) on concentration in visual attention, perception and memory including effects of EMF sensitivity. Toxicol Lett 96-97:377-382, 1998.

United Kingdom Childhood Cancer Study Investigators (UKCCS). Childhood cancer and residential proximity to power lines. Br J Cancer 83:1573-1580, 2000.

US Environmental Protection Agency (USEPA). US EPA Guidelines for Developmental Toxicity Risk Assessment. EPA/56 FR 63798-63826, 1991.

US Environmental Protection Agency (USEPA). EMF in your environment. 1992.

US Environmental Protection Agency (USEPA). Health effects test guidelines – Prenatal developmental toxicity study. EPA/712-C-98-207, 1998.

US Environmental Protection Agency (USEPA). A review of the reference dose and reference concentration process. EPA/630/P-02/002F, 2002.

US Environmental Protection Agency (USEPA). Guidelines for carcinogen risk assessment and supplemental guidance for assessing susceptibility from early-life exposure to carcinogens. EPA/630/P-03/001F, 2005.

Vallejo D and Hidalgo MA. Growth variations of OF1 mice following chronic exposure of parental and filial generations to a 15 μT, 50 Hz magnetic field. Electromagn Biol Med 31:19-33, 2012.

Weir E, Schabas R, Wilson K, Mackie C. Commentary: A Canadian framework for applying the precautionary principle to public health issues. Revue Canadienne de Santé Publique 101:396-398.

Wen J, Jiang S, Chen B. The effect of 100Hz magnetic field combined with X-ray on hepatoma-implanted mice. Bioelectromagnetics 32:322-324, 2011.

Wenzel F, Reissenweber J, David E. Cutaneous microcirculation is not altered by a weak 50 Hz magnetic field. Biomed Tech (Berl) 50:14–18, 2005.

Wong O, Harris F, Wang Y, Fu H. A hospital-based case-control study of non-Hodgkin lymphoid neoplasms in Shanghai: analysis of personal characteristics, lifestyle, and

environmental risk factors by subtypes of the WHO classification. J Occup Environ Med 52:39-53, 2010.

World Health Organization (WHO). Environmental Health Criteria 35. Extremely Low Frequency (ELF) Fields. Published under the joint sponsorship of the United Nations Environment Programme, the World Health Organization and the International Radiation Protection Association, 1984.

World Health Organization (WHO). Environmental Health Criteria 170. Assessing human health risks of chemicals: Derivation of guidance values for health-based exposure limits. International Programme on Chemical Safety, 1994

World Health Organization (WHO). WHO Handbook on: Establishing a dialogue on risks from electromagnetic fields. Geneva, Switzerland: World Health Organization, 2002.

World Health Organization (WHO). Framework for Developing Health-Based Standards. Geneva, Switzerland:World Health Organization, 2006.

World Health Organization (WHO). Environmental Health Criteria 238: Extremely Low Frequency (ELF) Fields. Geneva, Switzerland: World Health Organization, 2007.

Wünsch-Filho V, Pelissari DM, Barbieri FE, Sant'Anna L, de Oliveira CT, de Mata JF, Tone LG, Lee ML, de Andrea ML, Bruniera P, Epelman S, Filho VO, Kheifets L. Exposure to magnetic fields and childhood acute lymphocytic leukemia in São Paulo, Brazil. Cancer Epidemiol 35:534-539, 2011.

Yasui M, Kikuchi T, Ogawa M, Otaka Y, Tsuchitani M, Iwata H. Carcinogenicity test of 50 Hz sinusoidal magnetic fields in rats. Bioelectromagnetics 18:531-540, 1997.

Zaffanella LE. Survey of residential magnetic field sources. Vol. 1: Goals, results, and conclusions. (EPRI TR-102759-V1, Project 3335-02). Palo Alto, CA: Electric Power Research Institute, 1993.

Zaffanella LE, Kavet R, Pappa JR, Sullivan TP. Modeling magnetic fields in residences: validation of the resicalc program. J Expo Anal Environ Epidemiol 7:241-259, 1997.