**BC Hydro**
Power smart

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March 19, 2019

Mr. Patrick Wruck
Commission Secretary and Manager
Regulatory Support
British Columbia Utilities Commission
Suite 410, 900 Howe Street
Vancouver, BC V6Z 2N3

Dear Mr. Wruck:

**RE:     British Columbia Utilities Commission (BCUC or Commission)**
**British Columbia Hydro and Power Authority (BC Hydro)**
**E$^x$ponent Report on Electric and Magnetic Fields and Health: Review of the**
**Scientific Research from January 2017 to December 2018 (the Report)**
**Compliance with Directive 4 of Commission Order No. C-4-06**

BC Hydro writes in compliance with Directive 4 of the Commission's Order No. C-4-06
dated July 7, 2006 in regards to the British Columbia Transmission Corporation
Vancouver Island Transmission Reinforcement Project and encloses the Report.

The enclosed report prepared by Exponent is the fifth such report reviewing and
updating the scientific research pertaining to the potential health impacts of exposure to
Extremely Low Frequency Electric and Magnetic Fields (**ELF-EMF**) to be submitted to
the Commission. BC Hydro notes that consistent with all previous reports, the recent
research results, including the scientific literature that has been reviewed in this Report,
does not provide new evidence to alter the conclusion that long-term exposure to
ELF-EMF is not known to cause any adverse health effects, including cancer or other
illnesses.

The cost of each of these Reports is approximately $25,000 (USD). Given that the
research results reviewed over the past 12 years has consistently concluded that
long-term exposure to ELF-EMF is not known to cause any adverse health effects,
including cancer or other illnesses, BC Hydro is requesting relief from Directive 4 of
Order C-4-06, requiring BC Hydro to file a report every two years. Based on the results
from the last five reports, BC Hydro respectfully submits incurring this frequency of
reporting, and the inherent cost, is no longer warranted going forward.

The purpose of the Exponent report was to keep the Commission up to date on the
research into the health impacts of exposure to ELF-EMF. Based on the consistent
findings showing that long-term exposure to ELF-EMF is not known to cause any
adverse health effects, continuing to require BC Hydro to provide a report every two
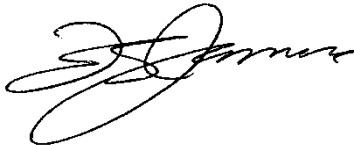
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Mr. Patrick Wruck
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Exponent Report on Electric and Magnetic Fields and Health: Review of the Scientific
Research from January 2017 to December 2018 (the Report)
Compliance with Directive 4 of Commission Order No. C-4-06          **Page 2 of 2**

years imposes, in BC Hydro's view, unnecessary costs on BC Hydro ratepayers. As a result, BC Hydro recommends either eliminating the requirement to continue to report on the long-term health effects of exposure to ELF-EMF, or at the very least, reduce the frequency of the required reporting.

BC Hydro may produce the Exponent Report on an as-needed basis in support of stand-alone capital project applications that involve the addition to or modification of the bulk transmission system. In transmission project applications, stakeholders often question the impacts of such a project on the local community in relation to ELF-EMF exposure. If needed, BC Hydro would update the review of the literature on health effects to support these major project applications. BC Hydro would determine the appropriate timeframe to update the report in support of its transmission projects, and would include the updated report in its project applications. BC Hydro submits this should be sufficient to continue to keep the Commission updated on the research into the health effects of exposure to ELF-EMF.

For further information, please contact Geoff Higgins at 604-623-4121 or by email at bchydroregulatorygroup@bchydro.com.

Yours sincerely,

Fred James
Chief Regulatory Officer

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Enclosure

*Health Sciences Practice*

**Electric and Magnetic Fields
and Human Health:
Review and Update of the
Scientific Research from
January 1, 2017 to December
31, 2018**

# E<sup>x</sup>ponent®

**Electric and Magnetic Fields
and Human Health:
Review and Update of the
Scientific Research from
January 1, 2017 to December
31, 2018**

Prepared for

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March 4, 2019

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# Acronyms and Abbreviations

| | |
|---|---|
| µT | Microtesla |
| AC | Alternating current |
| ACGIH | American Conference of Governmental Industrial Hygienists |
| ALL | Acute lymphoblastic leukemia |
| ALS | Amyotrophic lateral sclerosis |
| CI | Confidence interval |
| CNS | Central nervous system |
| DMBA | 7, 12-dimethylbenz[a]anthracene |
| EFHRAN | European Health Risk Assessment Network on Electromagnetic Fields Exposure |
| ELF | Extremely low frequency |
| EMF | Electric and magnetic fields |
| EMI | Electromagnetic interference |
| FPTRPC | Federal-Provincial-Territorial Radiation Protection Commission |
| G | Gauss |
| Hz | Hertz |
| IARC | International Agency for Research on Cancer |
| ICD | mplantable cardioverter-defibrillator |
| ICES | International Committee for Electromagnetic Safety |
| ICNIRP | International Commission on Non-Ionizing Radiation Protection |
| IEI | Idiopathic environmental intolerance |
| kV/m | Kilovolts per meter |
| MDA | Malondialdehyde |
| mG | Milligauss |
| OR | Odds ratio |
| RR | Relative risk |
| SCENIHR | Scientific Committee of Emerging and Newly Identified Health Risks |
| SOD | Superoxide dismutase |
| TWA | Time-weighted average |
| V/m | Volts per meter |
| 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 electric and magnetic field exposure and health. The findings presented herein are made to a reasonable degree of scientific certainty. This report is limited to the papers reviewed and may not include all information in the public domain. 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.

# Executive Summary

This report was prepared at the request of BC Hydro to provide a summary and overview on the status of scientific research related to extremely low frequency (ELF) electric and magnetic fields (EMF) exposure and health. This report also fulfills a recurring directive from the British Columbia Utilities Commission to monitor and report on ELF EMF research on a regular basis.

Electric and magnetic fields are produced by both natural and man-made sources that surround us in our daily lives. Power-frequency EMF, part of the ELF range of the electromagnetic spectrum that includes frequencies up to 300 Hertz (ICNIRP, 1998), are invisible fields surrounding all objects that generate, use, or transmit electricity. People are almost constantly exposed to ELF EMF in their homes, workplaces, schools, hospitals, and other environments, because the use of electricity and the supporting electricity network are essential parts of technologically advanced societies. Sources of ELF EMF in our everyday environment include, for example, appliances, wiring in homes, and electric motors, as well as distribution and transmission lines.

This report provides an overview of scientific methods used for studying potential health effects of environmental exposures, specifically reviews the scientific disciplines most relevant for human health (epidemiologic and laboratory animal studies), and reviews methods used for health risk assessments. This report then identifies relevant studies of childhood cancers, adult cancers, reproductive and developmental effects, neurodegenerative diseases, electromagnetic hypersensitivity, *in vivo* experimental studies on carcinogenesis, and fauna/flora studies published from January 1, 2017 to December 31, 2018. These studies were systematically reviewed and evaluated.

Since the late 1970s, potential health effects related to ELF EMF have been the focus of extensive scientific research. Because of the amount and complexity of the scientific studies in this area, comprehensive evaluations of the available scientific evidence have been performed for health and scientific agencies by panels comprised of independent scientists with expertise in relevant scientific disciplines. The general public and policy makers should look to the

conclusions of reviews such as these for guidance. In the past two decades a number of national and international health and scientific agencies have assembled panels of scientists that conducted comprehensive evaluations of the scientific literature to assess if the evidence supports a causal relationship between exposure to ELF EMF and adverse human health effects.

One of the most comprehensive health risk assessments of the EMF ELF literature that critically reviewed the cumulative epidemiologic and laboratory research was published by the World Health Organization in a 2007 report. Similar evaluations also were conducted in prior years by the National Institute for Environmental Health Sciences in the United States, the International Agency for Research on Cancer, the Federal-Provincial-Territorial Radiation Protection Committee in Canada, and the National Radiological Protection Board in the United Kingdom, among others. More recent evaluations have been conducted by the Swedish Radiation Safety Authority and the European Union's Scientific Committee on Emerging and Newly Identified Health Risks. Overall, none of these agencies has concluded that long-term exposure to ELF EMF is known to cause any adverse health effect, including cancer and other illnesses. Recent research results, including the scientific literature that have been reviewed in this report, do not provide new evidence to alter this conclusion.

# 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. This report provides an update to Exponent's 2007, 2010, 2012, and 2017 reports.[1] The previous Exponent reports evaluated research results published up to December 31, 2016, and assessed their potential impact on the conclusions reached by the World Health Organization (WHO) in its comprehensive risk assessment that reviewed research through 2005 (WHO, 2007). The current report evaluates research published between January 1, 2017 and December 31, 2018, to determine if new research developments justify changes to the conclusions of previous weight-of-evidence reviews. This report also provides an update to the British Columbia Utilities Commission on the status of EMF health research since 2016. Health Canada also recognizes that *"the current state of scientific knowledge with respect to possible health effects from EMF exposure and a review of current exposure guidelines and/or position statements from health-related organizations"* is a key element for its assessment of the potential effects of [EMF exposure for] a proposed project on human health" (Health Canada, 2010, pp. 7, 4).

This report follows the general structure of the previous Exponent reports to BC Hydro and discusses the scientific topics covered in the previous reports. Sections 1 and 2 of this report 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 epidemiologic studies on selected health outcomes (childhood cancers, adult cancers, reproductive and developmental effects, neurodegenerative diseases), *in vivo* experimental studies on carcinogenesis, and the phenomena of electromagnetic hypersensitivity,

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[1] Electric and Magnetic Fields and Health: Review of the Scientific Research from March 1, 2012, to December 31, 2016 (Exponent, 2017); EMF and Health – Comprehensive Review and Update of the Scientific Research, January 15, 2010 through March 1, 2012 (Exponent, 2012); EMF and Health – Review and Update of the Scientific Research, September 2007 through January 2010 (Exponent, 2010); EMF and Health – Review and Update of the Scientific Research (Exponent, 2007).

published from January 1, 2017[2] to December 31, 2018, as identified through a systematic review of the literature. Sections 5 and 6 address additional topics with relevance to an EMF risk assessment. A glossary of scientific terms is included at the end of the report to provide additional clarification.

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[2]  A few studies published in 2016 were included in this review if they had not been included in the earlier review because they were not available at the time that review was completed.

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# 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 EMF.[3] Power-frequency EMF is part of the ELF range that includes frequencies up to 300 Hz (ICNIRP, 1998). Natural sources of EMF include, for example, the earth's static magnetic field and the electric 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 but plugged in; field strength diminishes quickly, however, as one increases distance from the source.

Magnetic fields are produced by the movement of electricity. 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.[4] 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

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

[4]  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 microtesla by dividing by 10 (i.e., 1 mG = 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 0.01 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 principally from indoor sources (Zaffanella, 1993). Based on a sample taken in the United States, 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 in a sample of 382 children from five provinces, including British Columbia, was measured as 1.2 mG using wearable personal magnetic-field meters (Deadman et al., 1999). While higher magnetic-fields levels may be measured immediately under distribution and transmission lines, the distance of most buildings from a power line's right-of-way 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, typical sources of the highest magnetic fields encountered indoors are electrical appliances. For example, a publication by the U.S. National Institute of Environmental Health Sciences (NIEHS, 2002) reported that the median magnetic field measured at 6 inches from a sample 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).[5]

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[5]  Mobile phones and their antennas, wireless communication networks, and radios of all types (AM, FM, police, and fire) operate using radiofrequency fields, which represent a frequency (i.e., millions and billions of Hz) within the electromagnetic spectrum much higher than ELF EMF.

Because the frequency of electromagnetic energy is a key factor in determining its interaction with living things, and the interaction mechanisms relevant for ELF EMF are very different from those relevant for higher frequency fields (e.g., radio frequency or solar energy), only studies of ELF EMF are directly relevant to assessing the potential biological and health effects of power-frequency fields. The focus of this report is on power-frequency EMF (i.e., the ELF EMF fields produced by the generation, transmission, and use of electricity); thus, only ELF EMF studies will be reviewed in this report.[6]

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

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# 2      Methods for evaluating scientific research

## 2.1      Heath risk assessment approach

The standard scientific method for determining whether an exposure in the environment (such as chemical, physical, or biological agents) can affect human health is a health risk assessment.[7] Health risk assessments include four general steps: hazard identification, dose-response assessment, exposure assessment, and specific risk characterization. The process starts with a systematic identification and evaluation of the entire relevant body of research to determine if any health risks are associated with an exposure (hazard identification/weight-of-evidence review).[8] 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 necessarily indicate a causal relationship. Scientists use systematic methods to evaluate observations and assess the potential impact of a specific agent on human health.

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[7]  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, 2009a; SSM, 2010; SCENIHR, 2012; SCHEER, 2018).

[8]  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.

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 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 search of the published literature to identify relevant studies, an evaluation of each identified study to determine its strengths and weaknesses, and an overall evaluation of the data, giving more weight to higher-quality studies.

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*). Epidemiologic and experimental studies complement one another because the inherent limitations of epidemiologic studies are addressed in experimental studies and *vice versa*. Similar to puzzle pieces, the results of epidemiologic 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 scientific discipline that studies the patterns of disease occurrence in human populations and the factors that influence those patterns. Epidemiologic studies are critical for determining the causes of diseases and play a primary role in a human health risk assessment. Epidemiologic studies are observational in nature, in that they examine and analyze people in their normal lives with the investigators having 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 fiber content compared to people without the disease (i.e., a negative association), or 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). Epidemiologic studies can identify factors that may contribute to the development of disease but typically they are not used as the sole basis for drawing inferences about cause-and-effect relationships. Additional results from experimental research needs to be considered as well.

In contrast to epidemiologic studies, experimental studies are conducted under controlled laboratory conditions designed to test specific hypotheses. *In vivo* studies can strictly control and measure the exposure levels in the exposed groups as well as control and measure other factors such as food intake, housing conditions, and temperature that may have an effect on the outcome in all groups of exposed and unexposed animals. 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 either *known* or *unlikely* causes of cancer (IARC, 2006).

## 2.3    Evaluation of epidemiologic studies

This section briefly describes the two most commonly used and most informative designs used in epidemiologic studies (cohort and case-control designs) 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 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 being exposed among the cases to the odds of being exposed among the controls. If an OR is equal to 1.0, the general interpretation is that 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. Epidemiologists typically quantify the precision of the estimated measures of association by calculating confidence intervals (CI), which is the margin of error, usually set at 95% by convention, around the point estimates. The 95% CI represents a range of values that are expected to include the underlying effect estimate in the population 95% of the time if samples for studies were repeatedly drawn from the underlying population. When the 95% CI for the effect estimate excludes the null value of 1.0, the result is also commonly referred to as statistically significant.

In a cohort study, the researchers start with the identification of a pre-defined study population (i.e., individuals who are free of the disease), determine their exposure status, then follow them over time to see if persons with a certain exposure develop disease at a higher or lower rate compared to 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 risk of disease in the exposed group divided by the risk of disease in the unexposed group, with values greater than 1.0 suggesting that the exposed group has a higher risk of disease.
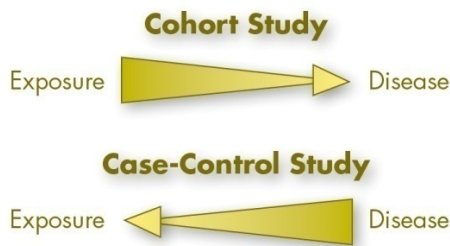
Figure 1. Basic design of cohort and case-control studies
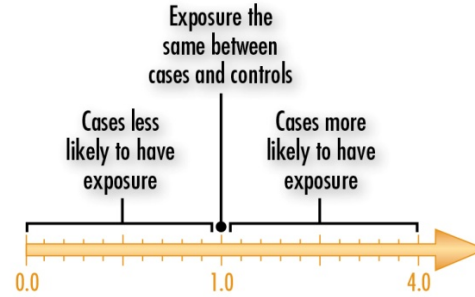
Figure 2. Interpretation of an odds ratio in a case-control study

A RR or OR value is simply a measure of association (i.e., 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 in epidemiologic studies refers to random error that may result from sampling variability, or imprecision in measurements of study variables, including exposure, outcome, and confounders. The probability that a given finding is due to chance may be estimated by statistical methods, such as significance testing, or calculation of CIs.

- 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 end up living closer to power lines than controls in the study sample just because of the selection process and the differential willingness to participate between cases and controls).

- 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, may 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 epidemiologic 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 epidemiologic 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 epidemiologic 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

As discussed earlier, an association is a relationship between two events, a finding that they occur together more often than expected by chance. A reported association, even a statistically significant 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 epidemiologic studies that have measured associations) in a weight-of-evidence review.

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. Hill also noted that, while formal tests of significance do not establish causation, the proposed guidelines were intended for evaluation of associations where chance was eliminated as a potential explanation (Hill, 1965).

**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. Smaller relative risks are more likely to be result of 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. |
|---|---|
| Experimental evidence | 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. |

\*These guidelines were adapted from Hill (1965).

## 2.3.2 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 statistically 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 and to examine factors that may explain differences between the results of studies analyzed.

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 that 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 assess heterogeneity in the results, that is, 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). In addition, the influence of individual studies on the overall results also could be assessed. For example, in a pooled 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 overall results. 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.

### 2.3.3     Assessment of EMF exposure in epidemiologic studies

One of the most crucial aspects in the review of any epidemiologic study is an evaluation of how exposure was measured or assessed. A good exposure metric should measure the element that is hypothesized to cause the disease at the etiologically relevant time in the disease process. Estimating exposure to EMF is difficult because 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 used different types of magnetic-field assessment methods, including measurements and calculations, to estimate a person's long-term 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 time spent in that environment, and divide that value by the total time of interest.

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

- Classification 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);

- Simple distance from overhead or underground power lines;

- Instantaneous, spot (short-term) measurements in particular locations of a home;

- Long-term stationary measurements of magnetic fields (typically over 24- or 48-hour periods) in a room where a person spends most of his or her time, or measurements taken by a device that is carried by the person (personal monitoring); and

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

In general, long-term exposure using personal magnetic-field measurements are frequently considered as the most appropriate measures, because they estimate exposure from all magnetic-field sources and directly estimate a person's total exposure. Personal monitoring results, however, are strongly influenced by behavior and the person's environment, thus, any change in behavior and the environment between the time of measurement and the etiologically relevant time period may still result in exposure misclassification. Also, even long-term measurements typically capture exposure during a 24- or 48-hour period, and may not fully represent average exposure over months or years. Other methods typically 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 epidemiologic studies represent estimates of long-term exposure potentially from all sources over months or years, and should not be compared to the magnetic-field values measured on a single occasion, and at a single, fixed location. It is evident 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 typically spend a very 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). The latter method, while it represents advancement over earlier methods, still has some important limitations, as noted in the Scientific Committee of Emerging and Newly Identified Health Risk's (SCENIHR's) 2015 review and highlighted in a review by Kheifets et al. (2009) summarizing an expert panel's findings.[9] 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. The 2015 review by SCENIHR noted that the validity of using an indirect indictor of exposure, such as job title, depends on the variability of exposure of people within similar occupations – the more the exposures differ across the same occupation, the higher the likelihood that the exposure level will be incorrectly estimated (SCENIHR, 2015). A study of the 48-hour exposure of 543 workers in Italy found that job exposure matrices were a poor indicator of actual occupational, magnetic-field exposure levels (Gobba et al., 2011). A study by Mee et al. (2009) also confirmed that job exposure matrices 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.

## 2.4     Evaluation of experimental research

### 2.4.1     General research methods

Experimental studies of humans, animals, and cells and tissues complement epidemiologic 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 that may affect health outcomes. In laboratory animals,

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[9]     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.

these variables can be well controlled to provide more precise information regarding the effects of an exposure. In epidemiologic 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 *in vivo* and *in vitro* studies. *In vivo* studies include studies that examine the potential effects of exposures on human volunteers (usually short-term studies examining short-term effects) and studies of whole animals that could also examine long-term effects. *In vitro* studies are designed to evaluate the way that the exposure may interact with cells and tissues outside of the body, which may provide information on mechanism of action.

### 2.4.1.1  *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, 2000; WHO, 2010; 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 parameters and 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* studies or *in vivo* studies of exposures during critical sensitive periods are conducted to assess potential toxicity to humans (Health Canada, 1994). Furthermore, the U.S. Environmental Protection Agency'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).

### 2.4.1.2 *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 epidemiologic studies because responses of cells and tissues outside the body may not reflect the response of those same cells if maintained in an intact 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 epidemiologic and *in vivo* studies.

Convincing evidence for a mechanism that explains an effect observed in experimental or epidemiologic 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, however, are not used directly by any health agency to assess risks to human health. Therefore, this report focuses on epidemiologic studies and also discusses *in vivo* experimental research with relevance to carcinogenesis but does not address *in vitro* research nor the conclusions of scientific panels regarding *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 also called cancer initiation or cancer induction. Additional steps (also called cancer promotion), must also occur for a cancerous cell to develop into a tumor. A carcinogenic agent may affect either or both the

initiation and promotion phases of cancer development. Exposures that affect both initiation and promotion are sometimes called 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 considered 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 typically 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 the potential 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 also are 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, 2015; USEPA, 1991, 1998).

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. |

\*These criteria were adapted from 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 and background 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):[10]

- The National Institute for Environmental Health Sciences 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, provincial, and territorial jurisdictions, conducted a review in 1998 and an update in 2005 (FPTRPC, 1998; FPTRPC, 2005). The FPTRPC most recently

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[10] 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. Specifically, the Bioinitiative (BI) Group's report that was posted on the internet is not included in our report, because, among other shortcomings, the BI report is not a comprehensive review of the literature and is not based on the scientific weight-of-evidence method.

released a statement from their Working Group in November 2008 summarizing their opinion on exposure to EMF (FPTRPC, 2008).[11]

- The National Radiological Protection Board[12] of the United Kingdom 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 (HMG, 2009).

- The 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 Gigahertz.

- The Health Council of the Netherlands, 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 European Commission 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, 2010, 2012).

- 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,

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[11] 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.

[12] The National Radiological Protection Board merged with the Health Protection Agency in April 2005 to form its Radiation Protection Division, and in April 2013, the Health Protection Agency became part of Public Health England.

but provided some relevant conclusions as part of their update process (ICNIRP, 1998, 2010).

- The European Union's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) issued its most recent report to the Health Directorate of the European Commission in 2015 that updated previous conclusions (SSC, 1998; CSTEE, 2001; SCENIHR, 2007, 2009, 2015).

- The Swedish Radiation Protection Authority, using other major scientific reviews as a starting point, evaluated current studies in several annual reports published in 2007 and 2008 (SSI, 2007, 2008). The Swedish Radiation Safety Authority, which superseded the Swedish Radiation Protection Authority in 2008, and has "national collective responsibility within the areas of radiation protection and nuclear safety" including EMF research, continues to publish annual reports (SSM, 2010, 2013, 2014, 2015, 2016, 2018).

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 from December 2005 (the approximate cut-off date for WHO) through September 2007. Exponent's 2010 report reviewed research through January 2010; the 2012 report reviewed the research through March 1, 2012; and the 2017 report reviewed the research through December 31, 2016. The current report will again focus on describing and updating the conclusions of the WHO (2007) report, while noting the other scientific organizations that have published their reviews in the interim.

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. The only known effects of exposure to EMF are acute or short-term effects (such as nerve and muscle stimulation). Existing guidelines from ICNIRP are set to limit short-term exposure at levels much 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 epidemiologic studies reported that children with

leukemia were more likely to live closer to power lines, or have higher estimates of magnetic-field exposure, compared to children without leukemia; other epidemiologic 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 analyses provide some evidence for an association between magnetic fields and childhood leukemia; however, because of the inherent uncertainty associated with observational epidemiologic 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).

While much additional research has been published since the WHO evaluation, the main conclusions of scientific organizations remained consistent—the scientific evidence does not establish that exposure to low level ELF EMF is the cause of any cancer (including childhood leukemia) or non-cancer adverse health effects (WHO, 2007; HMG, 2009; EFHRAN, 2012; ICNIRP, 2010; SCENIHR, 2015; SSM, 2018). The WHO and more recent reviews, however, continue to recommend further research to reconcile results from epidemiologic studies 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, such as genetics, environmental exposures, and infectious agents (see, e.g., Buffler et al., 2005; McNally and Parker, 2006).

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; EFHRAN, 2012; SCENIHR, 2015; SSM, 2016, 2018). 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, 2012; SSM, 2016). Although two epidemiologic 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; SCENIHR, 2015). 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 in earlier studies, more recent studies showed mixed results; scientific panels have described this research as weak and inadequate and recommended additional research in this area (WHO, 2007; HCN, 2009b; ICNIRP, 2010; EFHRAN, 2012; SCENIHR, 2015; SSM, 2016).

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 its website:

> 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.[13]

## 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 epidemiologic 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 guideline limits are set to prevent known and established effects after consideration of the scientific evidence regarding potential effects of both long-term and short-term exposures. Because the only established effects are the short-term direct, acute health effects (i.e., perception, annoyance, and the stimulation of nerves and muscles) that can occur at high levels of exposure, the guidelines are set to protect against these acute effects. With respect to long-term effects, the ICNIRP review concluded the following:

> It is the view of ICNIRP that the currently existing scientific evidence that prolonged exposure to low frequency magnetic fields is causally related with an increased risk of childhood leukemia is too weak to form the basis for exposure guidelines. In particular, if the relationship is not causal, then no benefit to health will accrue from reducing exposure. (ICNIRP, 2010; p. 824)

> Although ICNIRP and ICES have the same objectives[14] and used similar methods, the recommended limits for exposure of the general

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[13]   https://www.canada.ca/en/health-canada/services/home-garden-safety/electric-magnetic-fields-power-lines-electrical-appliances.html; website update on July 6, 2016; accessed on February 20, 2019.

[14]   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

public to EMF at the frequencies used to transmit electricity differ, as seen in Table 3.

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

| Organization recommending limit | Magnetic fields | Electric fields |
|---|---|---|
| ICNIRP restriction level (2010) | 2,000 mG | 4.2 kV/m |
| ICES maximum permissible exposure (2002) | 9,040 mG | 5 kV/m<br>10 kV/m* |

*This is an exception within transmission line rights of way because people do not spend a substantial amount of time in rights of way 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 10,000 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 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, 2015). 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 and references the ICNIRP guidelines on its website:

> Health Canada does not consider that any precautionary measures are needed regarding daily exposures to EMFs at ELFs. 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. … International exposure guidelines for exposure to EMFs at ELFs have been established by

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safety guidance for non-ionizing radiation for the WHO, the International Labour Organization, and the European Union.

the International Commission on Non-Ionizing Radiation Protection (ICNIRP). 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.[15]

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    Comparison of 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 nerves 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 nerves 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 limit for internal dose recommended for exposed populations. This internal dose limit is the foundation of both the ICNIRP and ICES standards because both electric fields 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. This is because they incorporate dose reduction factors, also

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[15]    https://www.canada.ca/en/health-canada/services/home-garden-safety/electric-magnetic-fields-power-lines-electrical-appliances.html; website updated on July 6, 2016; accessed on February 20, 2019.

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, i.e., the biological exposure limit, cannot be directly measured. The reference level is the measurable level of electric field or magnetic field at the location of interest; these levels are outside of the body, and are used as a screening value to ensure that the internal level identified as the basic restriction in not exceeded under any circumstance. Nevertheless, these reference levels represent conservative limits, meaning that if the reference level (i.e., the screening level) is exceeded, it does not necessarily follow that the basic restriction is exceeded. As 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, 1998).

### 3.2.3    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 safety factor to a higher estimated threshold 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 where thresholds are identified, 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 additional 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 considerably higher at 8.3 kV/m than the 5 kV/m for the general public (ICNIRP, 1998, 2010). Clearly, ICNIRP meant neither workers nor the public to be harmed by electric fields.

## 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 unconfirmed adverse effects in the population.

The European Commission prepared a report in 2000 to clarify the precautionary principle because this idea had been subject to controversy and variability in interpretation.[16] Their 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. They provided guidelines for the application of the precautionary principle or other risk management measures specifying five general principles: proportionality, non-discrimination, consistency, examination of costs and benefits of actions, and examination of scientific developments.[17]

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[16] 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).

[17] 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."

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 employed worldwide specifically for EMF exposure in the general public (WHO, 2007, Chapter 13). The WHO recommended the following precautionary measures (WHO, 2007, adapted from pp. 372-373):

- 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.

- 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.

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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."

- 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.

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 statement updated in 2016:

> Health Canada does not consider that any precautionary measures are needed regarding daily exposures to EMFs at ELFs. 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.[18]

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 European Commission and the approach of the FPTRPC and Health Canada in addressing EMF health concerns (Weir et al., 2010).

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[18] https://www.canada.ca/en/health-canada/services/home-garden-safety/electric-magnetic-fields-power-lines-electrical-appliances.html; website update on July 6, 2016; accessed on February 15, 2019.

# 4    Human Health Research

This section provides a summary and assessment of the literature published up to December 31, 2018, to determine whether recent findings are consistent with the conclusions of the scientific panels reviewed in Section 3, particularly the conclusions of the WHO's evaluation. In several previous reports, Exponent reviewed the literature through December 31, 2016 (Exponent, 2007, 2010, 2012, 2017).

This assessment reviews literature indexed in Pub-Med between January 1, 2017, and December 31, 2018. 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 epidemiologic 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 epidemiologic studies of various health concerns and *in vivo* studies relevant for carcinogenesis,

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 1, 2017, and December 31, 2018. 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.[19]  This report focuses on the health outcomes that have received the most attention—cancer, reproductive or developmental effects, and neurodegenerative diseases – as well as electrical hypersensitivity. To be included in this review, epidemiologic studies on these health outcomes must have assessed EMF exposure beyond a self-reported job title.[20]  Many other health effects have been studied (suicide, depression, cardiovascular effects, effects on the immune system, etc.), but for brevity and because research on these topics have evolved slowly, they are not summarized here. We note, however, that for these outcomes no substantive evidence has been identified by any previous comprehensive reviews. The possible effects of EMF on implantable cardiac devices and fauna/flora are  discussed separately in Sections 5 and 6, respectively. The WHO report continues to remain a good resource for the status of research on these other areas of health research (WHO, 2007).

## 4.1    Cancer

### 4.1.1    Childhood leukemia

Since the late 1970s, numerous epidemiologic studies have evaluated the relationship between childhood leukemia and some proxy of magnetic-field exposure. When independently evaluated, the studies showed mixed and varying results. Some of the largest and most advanced studies did not show a clear relationship between magnetic-field exposure and leukemia (Linet et al., 1997; UKCCS, 2000; McBride et al., 1999). When two, independent pooled analyses combined the data from several of these studies, however, results showed an approximate two-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 two times more likely to have had average

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[19]  PubMed is a service of the U.S. National Library of Medicine that includes over 26 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/).

[20]  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).

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 excess of 3 mG, and 0.4-3.3 percent have time-averaged exposures in excess of 4 mG (WHO, 2007).[21] 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). It also means that it is difficult to draw conclusions about a very small number of children with average magnetic field exposures at or above these levels to any disease as rare as childhood leukemia. A more recent pooled analysis that combined data from studies published between 2000 and 2010 (Kheifets et al., 2010a) reported results comparable to those reported by the earlier pooled analyses (Ahlbom et al., 2000; Greenland et al., 2000), but the reported association in the highest exposure category was weaker than reported previously and no longer statistically significant based on the more recent studies. The studies included in the more recent pooled analysis had limitations similar to those included in the earlier analyses.

The epidemiologic studies of childhood leukemia and EMF were limited in many ways, such that chance, bias, and confounding could not be ruled out as explanations for the association, which has been the overall conclusion of the reviews issued by the IARC (2002), WHO (2007), SCENIHR (2015), and other agencies. 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 chance, due to small numbers of cases with magnetic field exposure above background levels, or some error in some aspects of study design, conduct, or analysis. 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* "*In vivo* studies of carcinogenesis" below), and there was no known mechanism by which magnetic fields cause cancer.

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[21]  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) as noted by Health Canada (2010) .

A number of large case-control studies on EMF and childhood leukemia have been published in recent years from several European countries and from the United States (Sermage-Faure et al., 2013; Bunch et al., 2014, 2015, 2016; Pedersen et al., 2014a, 2014b, 2015; Crespi et al., 2016). These studies, which incorporated large sample sizes and methodological advancements, showed no statistically significant associations between estimates of residential exposure to EMF and childhood leukemia. While these studies provided no further support for an association and somewhat weaken the overall evidence, the previously reported associations remain largely unexplained and the overall conclusion on the epidemiologic data remains that it provides limited evidence for an association. This conclusion also expressed by the most recent reviews by scientific organizations (e.g., SCENIHR, 2015; SSM, 2018).

**Relevant studies 2017-2018**

Several recent publications have presented further analyses on the same study populations used in two of the case-control studies (Bunch et al., 2014; Crespi et al., 2016) summarized in the previous Exponent report (Exponent, 2017). Swanson and Bunch (2018) reanalyzed the same study population used in Bunch et al. (2014)'s study of childhood leukemia in relation to residential proximity to high-voltage power lines in the United Kingdom. In their re-analysis, Swanson and Bunch (2018) used finer categories of distance from power lines (e.g., cut-points of every 50-meter distance) and broader groupings of diagnosis date (e.g., 1960-1979, 1980-1999, and 2000-on) to match the categories used in a recent pooled analysis of childhood leukemia and distance to power lines (Amoon et al., 2018a, summarized below). Swanson and Bunch (2018) reported that no overall associations between distance categories and childhood leukemia were observed for the period including 1980 and later, and that associations for the earlier period (1960-1979) showed no monotonic or consistent pattern with distance. Thus, the authors concluded that their finding *"weakens the evidence that any elevated risks are related to magnetic fields"* (Swanson and Bunch, 2018, p. N30).

Kheifets et al. (2017a) and Amoon et al. (2018b) both conducted additional analyses using the same California Power Line Study (CAPS) population as Crespi et al. (2016). Kheifets et al. (2017a) reported on childhood leukemia and calculated magnetic fields from power lines. Magnetic-field levels at birth address were calculated using geographic information systems,

aerial imagery, historical information on load and phasing, and site visits (Vergara et al., 2015). In the main analyses by Kheifets et al. (2017a), which included 5,788 cases of leukemia and a similar number of primary controls with geocode accuracy, the authors reported no consistent pattern of association. Compared to the lowest exposure category (<1 mG), they reported a slight, statistically non-significant, negative association in the intermediate exposure categories (1 to 2 mG and 2 to 4 mG) and a small, statistically non-significant, positive association in the highest exposure category (≥4 mG). The authors reported similar results in subgroup and sensitivity analyses and commented that all estimates had wide confidence intervals. The authors concluded that their study *"does not in itself provide clear evidence for risk associated with greater exposure to magnetic fields from power lines, but could be viewed as consistent with previous findings of increased risk"* (Kheifets et al., 2017a, p. 1117). Thomas (2018) commented that while the Kheifets et al. (2017a) study had low potential for selection bias due to its record-based methods, the study may be subject to exposure misclassification resulting in bias towards the null because the exposure assessment considered residential proximity only to high-voltage power lines and ignored other sources, including distribution lines.

Amoon et al. (2018b) assessed the potential impact of residential mobility of the study subjects (i.e., moving residences between birth and diagnosis) on the associations reported in Crespi et al. (2016) and Kheifets et al. (2017a). The authors reported that while children that moved tended to be older, lived in housing other than a single-family home, had younger mothers and fewer siblings, and were of lower socioeconomic status, changing residences was not associated with either calculated fields or proximity to ≥200-kV power lines. Thus, the authors concluded that *"[m]obility appears to be an unlikely explanation for the associations observed between power lines [sic] exposure and childhood leukemia"* in the previous California studies (Amoon et al., 2018b, p. 459).

A case-control study in Greece examined the association between parental occupational exposures and childhood acute leukemia at a major pediatric hospital in Athens (Kyriakopoulou et al., 2018). The study included 108 cases of acute leukemia, including lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), under the age of 15, and 108 controls matched on age, gender, and ethnicity. The parents' job titles held during four different exposure periods (1

year before conception, during pregnancy, during breastfeeding, and from birth until diagnosis) were evaluated for exposure (exposed versus unexposed) to four agents (high contact level, chemicals, electromagnetic fields, and ionizing radiation) based on the authors' review of literature and their professional judgment. A total of six cases (5.6%) and six controls (5.6%) were categorized as exposed to electromagnetic[22] fields. Therefore, no statistically significant association was observed between magnetic-field exposure and childhood acute leukemia for any of the four periods of exposure. No associations were observed between childhood acute leukemia and the remaining exposure categories; however, the authors did observe that high birth weight and family history of cancer were associated with children who developed leukemia.

A meta-analysis of epidemiologic studies of residential distance to power lines and childhood leukemia was conducted by Amoon et al. (2018a). The authors pooled the data from 11 studies with record-based assessments of residential distance from high-voltage power lines from 10 countries (Australia, Brazil, Denmark, France, Italy, Norway, Sweden, Switzerland, the United Kingdom, and the United States). In total, 29,049 cases and 68,231 controls were included in the analyses. The authors reported no association when proximity to transmission lines with any voltage was investigated; the adjusted OR for residential distance <50 meters, as compared to distances ≥300 meters, was 1.01 [95% CI, 0.85-1.21]). For power lines with voltages of ≥200 kV, the adjusted OR (1.13) for distances <50 meters also was not statistically significant (95% CI, 0.92-1.93). The reported associations were slightly stronger for leukemia case diagnosed before 5 years of age and in study periods prior to 1980. Adjustment for various potential confounders (e.g., socioeconomic status, dwelling type, residential mobility) had little effect on the estimated associations.

Magne et al. (2017) conducted a national survey of ELF magnetic-field exposure in France, including a representative sample of close to 1,000 children 0 to 14 years of age. The study was purely an exposure assessment study and the authors did not investigate any health outcome in relation to magnetic-field exposure. The authors conducted 24-hour measurements of ELF magnetic-fields of the included children and reported that 3.1% of the study participants had a

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[22]  In this context, "electromagnetic fields" is used to refer to ELF magnetic fields.

24-hour average exposure >0.4 µT (4 mG). Only 0.8% of the children, however, had 24-hour average exposure >0.4 µT (>4 mG) when exposure from alarm clocks was excluded. The authors also reported that none of the children with 24-hour average exposure >0.4 µT (>4 mG) lived within 125 meters of a 225-kV transmission line or within 200 meters of a 400-kV transmission line.

Kheifets et al. (2017b) conducted a comparative analysis of epidemiologic studies of childhood leukemia that investigated the association between childhood leukemia and ionizing radiation (i.e., radon or gamma radiation) or non-ionizing radiation (i.e., ELF EMF), or both, in an attempt to evaluate to what extent bias, confounding, and other methodological issues might be responsible for the reported associations. The authors reported that while they found some indication of bias, they found little evidence that confounding has a substantial influence on results.

In summary, the results of recent studies do not change the classification of the epidemiologic data as limited. While most of the recently published studies showed no statistically significant associations between estimates of exposures from power lines, and the most recent pooled analyses indicated weaker and statistically non-significant associations (Amoon et al., 2018a), the association between childhood leukemia and magnetic fields observed in some earlier studies remains unexplained.

**Table 4.   Studies of childhood leukemia (2017-2018)**

| Authors | Year | Study |
| --- | --- | --- |
| Amoon et al. | 2018a | Proximity to overhead power lines and childhood leukaemia: an international pooled analysis. |
| Amoon et al. | 2018b | Residential mobility and childhood leukemia. |
| Kheifets et al. | 2017a | Residential magnetic fields exposure and childhood leukemia: a population-based case-control study in California. |
| Kheifets et al. | 2017b | Comparative analyses of studies of childhood leukemia and magnetic fields, radon and gamma radiation. |
| Kyriakopoulou et al. | 2018 | Parental occupational exposures and risk of childhood acute leukemia. |
| Magne et al. | 2017 | Exposure of children to extremely low frequency magnetic fields in France: Results of the EXPERS study. |
| Swanson and Bunch | 2018 | Reanalysis of risks of childhood leukaemia with distance from overhead power lines in the UK. |

| Authors | Year | Study |
|---|---|---|
| **Comment on Kheifets et al. (2017a)** | | |
| Thomas | 2018 | Re: Kheifets et al. (2017): Residential magnetic fields exposure and childhood leukemia: a population-based case-control study in California. |

## 4.1.2 Childhood brain cancer

Compared to the research on magnetic fields and childhood leukemia, there have been fewer studies of childhood brain cancer and the evidence linking magnetic fields to childhood brain cancer is considerably weaker. No consistent association has been found, although studies are limited by the small number of participants (since childhood brain cancer is rare). To address the issue of small numbers, both a meta-analysis (Mezei et al., 2008) and a pooled analysis (Kheifets et al., 2010b) were conducted. Overall, no association was reported in the meta-analysis, but a sub-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) (Mezei et al., 2008). 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.

Kheifets et al. (2010b), in direct response to a recommendation by the WHO, pooled data from 10 studies on childhood brain cancer and residential magnetic-field exposure. Similar to the pooled analysis of childhood leukemia (Kheifets et al., 2010a), there were few cases in the upper exposure categories; however, contrary to the childhood leukemia results, no consistent associations were reported for childhood brain cancer (Kheifets et al., 2010b). While some elevated ORs were observed, 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.

Subsequent studies have not reported any consistent associations between EMF and childhood brain tumors and thus did not warrant any change in the classification of the epidemiologic evidence as *inadequate*.

**Relevant studies 2017-2018**

Only one major study has been published on childhood brain cancer since the previous Exponent report (Exponent, 2017). Su et al. (2018) conducted a meta-analysis of epidemiologic studies that investigated the association between parental occupational exposure to ELF magnetic fields and childhood nervous system tumors. The authors included a total of 22 studies (of which 21 were case-control studies) published as of December 2017 in their analysis. For central nervous system (CNS) tumors, they reported no statistically significant association for paternal exposure to ELF magnetic fields but reported a weak statistically significant association (OR = 1.16, 95% CI 1.06, 1.26) for maternal exposure based on a subset of eight studies. For neuroblastoma, the authors reported no association with either maternal or paternal exposure to ELF magnetic fields. The authors also reported the results of several subgroup analyses. Study quality, as assessed by the authors, had inconsistent effects on the associations reported for maternal and paternal exposure. The authors noted that, when based on higher quality studies, observed associations were stronger for maternal exposure but weaker for paternal exposure. In addition, it is noteworthy that associations for CNS tumors were statistically significant only when studies using non-quantitative exposure assessment methods (i.e., relying on job titles only) were pooled; however, no associations were reported based on studies with a quantitative exposure assessment. Limitations of the analysis include the fact that the majority of included studies did not classify the histological subtype of CNS tumor and that several of the studies included persons with tumors diagnosed up to 30 years of age. The authors also reported evidence for publication bias.

In summary, the weight-of-evidence continues to not support an association between magnetic-field exposures and the development of childhood brain cancer.

**Table 5.  Studies of childhood brain cancer (2017-2018)**

| Authors | Year | Study |
|---------|------|-------|
| Su et al. | 2018 | Association between parental occupational exposure to extremely low frequency magnetic fields and childhood nervous system tumors risk: A meta-analysis. |

## 4.1.3    Breast cancer

Early studies conducted on breast cancer and electric blanket use and residential and occupational magnetic-field exposure reported inconsistent findings. More recent studies, published around and after 2000, however, tended to be methodologically more advanced and, overall, reported no consistent associations. The WHO, in its 2007 report, concluded that the body of research they reviewed was higher in quality compared with the early studies, and that there was strong support for consensus statements that magnetic-field exposure does not influence the risk of breast cancer.[23] The WHO recommended no further research with respect to breast cancer and magnetic-field exposure, even though the epidemiologic evidence was still classified as *inadequate*.

More recently published large epidemiologic studies have overall reported no consistent or statistically significant associations between EMF and breast cancer among either men or women. Recently published reviews also conclude that the evidence does not suggest a risk (SCENIHR, 2015; SSM, 2016, 2018). The most recently published annual reports by the Swedish Scientific Council on EMF and Health concluded that, with respect to female breast cancer, *"now it is fairly certain that there is no causal relation with exposure to ELF magnetic fields"* (SSM, 2016; p. 7), and with respect to male breast cancer, *"[t]o date, there is no established link between ELF-MF exposure and breast cancer in men."* (SSM, 2018; p. 49).

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[23] 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).

**Relevant studies 2017-2018**

There have been no new epidemiology studies published on breast cancer and EMF exposure since Exponent's previous report (Exponent, 2017). Therefore, the previous assessment that EMF is not causally linked to breast cancer remains appropriate.

### 4.1.4    Other adult cancers

In general, scientific panels have concluded that the scientific evidence is inadequate to establish a causal link between other adult cancers and exposure to magnetic fields, but due to the inherent nature of scientific research, the possibility cannot be entirely ruled out (IARC, 2002; WHO 2007). Most epidemiologic studies of EMF and adult cancers (in addition to breast cancer) examined leukemia, lymphoma, and brain cancer, and studies of these outcomes will be discussed in detail below. Fewer studies have been conducted on adult cancers other than leukemia, lymphoma, and cancers of the brain and breast , and no consistently replicated findings were identified by any of the expert panels. Since studies with improved exposure assessment methods do not report stronger or more consistent findings, scientific panels concluded that the evidence for an association 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 job-exposure matrix). The latter method, while representing a methodological advancement, still has some important limitations as highlighted 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.

### 4.1.4.1    Adult brain cancer

Epidemiologic studies on EMF and adult brain cancer published following the WHO assessment provided no additional consistent evidence for an association (e.g., Johansen et al., 2007; Coble et al., 2009; Baldi et al., 2011; Marcilio et al., 2011). In a meta-analysis of occupational EMF exposure and leukemia and brain cancer (Khefeits et al., 2008), a small but 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, the authors reported a weaker association in the more recent studies than the observed association in their previous meta-analysis (Kheifets et al., 1995), 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 that "the lack of a clear pattern of EMF exposure and outcome risk does not support a hypothesis that these exposures are responsible for the observed excess risk" (Kheifets et al., 1995, p. 677).

Overall, the epidemiologic studies that have been reviewed in our previous reports predominantly support no association between adult brain cancer and residential or occupational EMF exposure. However, an association could not be ruled out *entirely* due to limitations in exposure assessment methods and insufficient data available on specific brain cancer subtypes.

**Relevant studies 2017-2018**

Carlberg et al. (2017, 2018) published the results of two case-control epidemiologic studies of occupational exposure to ELF EMF and brain cancer. Both studies relied on data from previously published case-control studies in Sweden (Hardell et al., 2006, 2013; Carlberg et al., 2013, 2015). Carlberg et al. (2017) included 1,346 living glioma cases diagnosed between the periods of 1997 to 2003 and 2007 to 2009 and 3,485 controls, ascertained from the Swedish Population Registry, who were matched to cases on sex and 5-year age group. Average and

cumulative occupational exposure to ELF EMF was assessed from self-reported questionnaires on lifetime occupational history and a previously developed job-exposure matrix (Turner et al., 2014). Overall, the authors observed no associations with cumulative exposure to ELF EMF and a weak statistical association in the highest average exposure category (>0.27 µT [2.7 mG]). Statistically signification associations were reported for grade IV astrocytoma and cumulative and average exposure when restricted to exposure experienced during the more recent exposure periods (1 to 14 years prior to diagnosis). The authors reported no association, however, with more distant exposure periods (15 to 20+ years), and observed no associations for other tumor grades. The authors hypothesized that the observed association for grade IV astrocytoma in the recent exposure periods may be the result of a potential late effect on cancer promotion. Because deceased subjects were excluded from the analyses, and the reported association was limited to tumors of the highest grade (with the highest mortality rate), there is a high likelihood that the reported pattern of results arose due to differential exclusion of rapidly fatal cases among patients with the highest-grade tumors.

Carlberg et al. (2018) included 1,592 meningioma cases and 3,485 controls. The investigators used a similar approach and methods as in the glioma study (Carlberg et al., 2017). The authors reported no trend or association between meningioma development and any of the investigated metrics of occupational exposure to ELF EMF (i.e., average occupational exposure, highest exposed job, or cumulative exposure) regardless of the time windows investigated (i.e., exposure during 1 to 14 years prior to diagnosis, or exposure more than 15 years prior to diagnosis). The authors concluded that occupational ELF-EMF was not associated with an increased risk for meningioma (Carlberg et al., 2018).

Turner et al. (2017) investigated the potential interaction between occupational exposure to ELF magnetic fields and 29 chemical agents – including cadmium, chromium, iron, nickel, solvents, benzo(a)pyrene, polycyclic aromatic hydrocarbons, and environmental tobacco smoke – on brain cancer development within the INTEROCC case-control study. The study included 1,939 glioma and 1,822 meningioma cases, along with 5,404 controls, matched on sex and age. Occupational exposure to both ELF magnetic fields and the chemicals of interest were assessed using job-exposure matrices. The authors reported that there was *"no clear evidence"* for an

interaction between occupational exposure to ELF magnetic fields and occupational exposure to any of the included chemicals for either glioma or meningioma (p. 802).

In summary, recent studies do not provide support for an association between exposure to magnetic fields and brain cancer development. The data remains inadequate (EFHRAN, 2012; SCENIHR, 2015).

**Table 6.    Studies of adult brain cancer (2017-2018)**

| Authors | Year | Study |
|---|---|---|
| Carlberg et al. | 2017 | Case-control study on occupational exposure to extremely low-frequency electromagnetic fields and glioma risk. |
| Carlberg et al. | 2018 | Case-control study on occupational exposure to extremely low-frequency electromagnetic fields and the association with meningioma. |
| Turner et al. | 2017 | Occupational exposure to extremely low frequency magnetic fields and brain tumor risks in the INTEROCC study. |

### 4.1.4.2    Adult leukemia and lymphoma

Similar to adult brain cancer, the WHO classified the epidemiologic evidence with regard to adult leukemia as *"inadequate"* (WHO 2007). Epidemiologic studies of adult leukemia and lymphoma published subsequent to the WHO report (2007) provided no consistent support for an association (e.g., Johansen et al., 2007; Wong et al., 2010; Marcilio et al., 2011). As described above, a small and statistically significant increase of leukemia in relation to the highest estimate of magnetic-field exposure reported in the meta-analysis by Kheifets et al. (2008), but the authors concluded that the overall pattern of results (e.g., there was no consistency in findings by leukemia subtype) did not support a causal relationship between EMF and leukemia.

More recent studies did not provide substantive new evidence in support of an association between EMF exposure and leukemia and lymphoma in adults. Because of scientific uncertain due to study limitations, the scientific body of studies provided inadequate evidence for an association (EFHRAN, 2012; SCENIHR, 2015).

**Relevant studies 2017-2018**

One large study has been published on adult leukemia and lymphoma since the previous Exponent report (Exponent, 2017). Huss et al. (2018a) conducted a census-based, retrospective cohort study examining exposure to ELF magnetic fields and death from several types of hematopoietic malignancies within the Swiss National Cohort. The study included a total of 3.1 million economically active individuals between 30 and 65 years of age (for men) or 62 years of age (for women) who participated in the Swiss 1990 or 2000 census, or both. The authors evaluated mortality from different malignant neoplasms of the lymphoid and hematopoietic tissue (i.e., various types of acute and chronic leukemias and lymphomas) from 1990 to 2008. Occupational exposure to ELF magnetic fields was assessed using the study subjects' reported job title at the time of the census and a job-exposure matrix that assigned exposure levels of low, medium, or high. None of the hematopoietic cancer types included in the main analyses were statistically associated with medium or high exposure to ELF magnetic fields in the fully-adjusted models. Adjustment for other occupational exposures, including solvents, pesticides, herbicides, metals, and electric shocks, had a very small effect on the risk estimates.

The authors reported statistically significant associations for myeloid leukemia among men who were ever highly exposed at the time of both censuses (HR: 1.31, 95%: 1.02-1.67) and for acute myeloid leukemia among men ever highly exposed at the time of both censuses and additionally during their vocational training (HR: 2.75; 95%: 1.11-6.83). Both estimates were based on a very small number of cases (n = 6 and 5, respectively). Lung cancer mortality, included as an outcome unlikely to be caused by EMF, showed statistically significant associations and a clear exposure-response pattern with exposure to ELF magnetic fields. The authors hypothesized *a priori* that lung cancer was not associated with exposure to ELF magnetic fields (Huss et al., 2018a, p. 468). Thus, this finding clearly indicates that confounding by smoking, which is a well-established cause of both lung cancer and leukemias/lymphomas, remains a major weakness of the study, and may explain the association reported in some of the sub-analyses. The authors concluded that their analysis *"provided no convincing evidence for an increased risk of death"* from hematopoietic cancers in workers occupationally exposed to ELF magnetic fields (Huss et al., 2018a, p. 467).

In the same publication, Huss et al. (2018a) also reported a meta-analysis of 28 epidemiologic studies of occupational exposure to ELF magnetic fields and acute myeloid leukemia published up to September 2017. The authors reported a weak overall association with acute myeloid leukemia, with a summary RR of 1.21 (95% CI: 1.08, 1.37). The authors noted that studies evaluating cumulative exposure were more likely to observe increase risks of acute myeloid leukemia; in the subset of studies that evaluated cumulative exposure (n=4), the summary RR was 1.51 (95% CI: 1.06, 1.37). The authors concluded that their findings were in line with previous meta-analysis results and stated that if any risk of hematopoietic cancers exists from occupational magnetic field exposure *"it appears to be small"* (Huss et al., 2018a, p. 474). In summary, recent results did not provide substantial new evidence for a consistent association between EMF and leukemia overall, leukemia sub-types, or lymphoma in adults that would alter previous conclusions. While some scientific uncertainty remains on a potential relationship between adult lymphohematopoietic malignancies and magnetic-field exposure because of continued deficiencies in study methods, the current database of studies provides inadequate evidence for an association (EFHRAN, 2012; SCENIHR, 2015).

**Table 7.    Studies of adult leukemia/lymphoma (2017-2018)**

| Authors | Year | Study |
| --- | --- | --- |
| Huss et al. | 2018a | Occupational extremely low frequency magnetic fields (ELF-MF) exposure and hematolymphopoietic cancers - Swiss National Cohort analysis and updated meta-analysis. |

## 4.1.5    *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 also have been shown to cause cancer in laboratory animals and such studies are better suited to determining causation than epidemiology studies (IARC, 2002).

*Magnetic field bioassays*

The major focus of interest is on chronic bioassay studies in which animals, including those with a particular genetic susceptibility to cancer, are exposed at high levels over their entire

lifespan (or a large part of it) and tissue evaluations are performed to assess the incidence of tumors in many organs. These studies are judged to be one of the gold standards for identifying carcinogenic agents and are often considered when establishing regulatory actions.

The 2007 WHO review described four large-scale, long-term studies of rodents exposed to magnetic fields over the course of their lifetime that did not report increases in any type of cancer (Mandeville et al., 1997; Yasui et al., 1997; McCormick et al., 1999; Boorman et al., 1999a, 1999b). Fam and Mikhail (1996) reported that some animals developed a type of lymphoma similar to childhood ALL, but other studies that exposed transgenic mice predisposed to develop leukemias to ELF magnetic fields did not show an increased incidence of this lymphoma type (Harris et al., 1998; McCormick et al., 1999; Sommer and Lerchl, 2004). More recent studies also do not report effects of chronic magnetic field exposure at levels from 20 mG to 10,000 mG on the incidence of lymphomas or other cancer types (Qi et al., 2015; Soffritti et al., 2016a, 2016b).

*Magnetic field exposure + known carcinogens*

Other studies test whether the exposure of interest, in combination with a known carcinogen, produces a promotional or co-carcinogenetic effect, or whether the exposure in combination with a known carcinogen and a known promoter produces a co-promotional effect. These types of studies can be problematic in their interpretation because of the sometimes limited nature of the interaction of treatments with particular tissues and because of the complexity of the study designs and conditions.

Most studies reviewed by the WHO did not find evidence that magnetic-field exposure, when combined with chemical carcinogens, affected the development of tumors in skin, liver, etc. For over a decade, however, one laboratory in Germany has reported that the incidence of mammary tumors caused by 7, 12-dimethylbenz[a]anthracene (DMBA) was generally, but inconsistently, increased by 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). The reported influence of magnetic fields on the carcinogenic effects of DMBA as reported by the German laboratory could not be replicated in studies from laboratories supported by the U.S. National Toxicology Program (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 and/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, most studies published subsequently have investigated the potential promotional or co-carcinogenic effects of magnetic-field exposure. These studies show that long-term exposure to magnetic fields does not alter the incidence of brain tumors or leukemia/lymphoma in rats and mice treated with the chemical initiators DMBA (Negishi et al., 2008), ethylnitrosourea (Chung et al., 2008), or n-butylnitrosourea (Bernard et al., 2008) or the cancer incidence rates or survival time in a strain of mice genetically predisposed to develop leukemia (Chung et al., 2010). The German laboratory continues to report findings similar to earlier work and have explored potential associations of magnetic-field exposure with the expression of certain genes and proteins in the mammary tissue of different rat strains (Fedrowitz and Löscher, 2008, 2012). Other studies have looked for effects of chronic magnetic fields exposure in combination with exposure to ionizing radiation such as x-rays (Soffritti et al., 2016a) or the carcinogen formaldehyde (Soffritti et al. 2016b), but because of multiple flaws in the design and analysis of the data, the results are insufficient to support an interaction between magnetic fields and known carcinogens.

In other studies investigating the therapeutic applications of magnetic fields, much higher level exposures to magnetic fields in combination with cancer treatments have been reported to reduce tumor size or increase the survival of animals injected with tumors (Berg et al., 2010; Wen et al., 2011; El-Bialy and Rageh, 2013; Mahna et al., 2014) or to reduce the development of pre-neoplastic lesions in the livers of rats initiated via chemicals and surgery (Jiménez-Garcia et al., 2010). Such anti-tumor effects are reported for magnetic field exposures greater than 70,000 mG.

*Damage to DNA and oxidative stress*

Another focus of animal research is on the potential for magnetic fields to damage the DNA directly or in combination with known carcinogenic chemicals or x-rays (Lai and Singh, 2004). Studies have continued to look for evidence of DNA damage with mixed results from magnetic-field exposure alone (Mariucci et al., 2010; Okudan et al., 2010; Alcaraz et al., 2014; Villarini et al., 2013; Wilson et al., 2015; Korr et al., 2014) or in combination with radiation (Miyakoshi et al., 2012; Saha et al., 2014; Woodbine et al., 2015 ). Where small effects are reported, they are not convincing given that the reported changes in DNA damage markers appear to be unrelated to the strength of the magnetic field.

Without good evidence that either cancer or DNA damage is caused by magnetic-field exposures, a number of studies have investigated the role of magnetic-field exposures on indicators of tissue oxidative stress on the premise that oxidative stress is the mechanism that connects magnetic-field exposure to cancer. However, these studies typically have been of low quality, and not designed to establish any direct relevance of their findings to cancer (Seifirad et al., 2014; Glinka et al., 2013; Hassan and Abdelkawi, 2014; Deng et al., 2013; Cui et al., 2012; Duan et al., 2013; Manikonda et al., 2014; Martínez-Sámano et al., 2012; Akdag et al., 2013; Kiray et al., 2013).

**Relevant studies 2017-2018**

The research themes that have been pursued in animal studies of cancer and biological processes possibly related to cancer before 2017 have continued to be addressed in more recent *in vivo* studies.

*Magnetic field bioassay*

The Ramazinni laboratory that previously investigated the combined effects of magnetic fields and x-rays or formaldehyde in chronic exposure bioassays recently reported on the effects of life-long exposure to magnetic fields alone from levels of 200 mG to 10,000 mG (Bua et al., 2018).

Bua et al. (2018) reported no effect of magnetic-field exposure on the incidence of total tumors in any group exposed to magnetic fields or on food and water consumption, body weight, or survival. The incidences of the specific types of malignancies reported, specifically mammary gland tumors, Schwannomas of the heart, thyroid C-cell carcinomas, and hemolymphoreticular neoplasia (HLRN) also were not increased by magnetic field exposure. Unexpectedly, Bua et al (2018) reported a statistically significant 8.4% decrease in malignant tumors in male rats following lifelong exposure to a 1,000 mG magnetic field. Based on these data, Bua et al. concluded that the study "provided no evidence of any carcinogenic effect related to the exposure of ELF EMF alone" (p. 274)  This result is consistent with a previous report from this same laboratory (Soffritti, 2010). Contrary to good experimental practice, the control group in this study was the same as used in other studies from this laboratory (Soffritti, 2010; Soffritti et al., 2016a). Further, this study suffers from the same flaws in design and data analyses as the other studies from ,the Ramazinni laboratory, including the failure to analyze the results by cage rather than per individual animal.

*Magnetic field exposure + known carcinogens*

As noted previously, several investigators have investigated the capability of very strong magnetic fields to enhance the anti-tumor effects of compounds used to treat cancer.

Only one study was recently reported in this category. Yuan et al. (2018) injected G401 nephroblastoma cells into nude mice (that have an impaired immune system due to a genetic mutation that causes deterioration of the thymus gland). With the immune system partially deactivated in the nude mice, tumors grow rapidly from the injected kidney cells. On the 7th day after injection of cells, groups of 8 mice were treated for 15 days with: 1) 50-Hz AC magnetic fields (intensity varying from 10,000 mG to 25,000 mG combined with DC magnetic fields (intensity between 30-40,000 mG), 2) the magnetic field with the anti-tumor drug, cisplatin – 3x/week, 3) just cisplatin – 3x/week, or 4) sham-exposure to the magnetic field and cisplatin (control). Exposures each day consisted of 3-4 treatment sessions. In each session, magnetic field exposure consisted of 8rounds (combinations of AC and DC magnetic fields of varying intensity) lasting 10 minutes each.

Yuan et al. (2018) reported that neither the magnetic field nor cisplatin treatments alone affected the weight of the tumors. However, when the mice were treated with both magnetic fields and cisplatin, the average weight of the tumors decreased by about 40%. The effects of the treatments on kidney and liver enzymes released into blood were measured to monitor organ toxicity. A statistically increase in levels of AST and ALT was observed in mice with the combined treatment (described as a "trivial" side effect). None of the treatments affected the weight of the mice measured 3 days after the last treatments.

M*arkers of immune function and oxidative stress*

Various short-term studies have been conducted to investigate potential mechanisms related to carcinogenesis, including immune-function changes and oxidative stress.

The immune system is thought to play an important role in the immunosurveillance against cancer cells. Further, ALL, one of the cancers of concern for EMF exposures in children, arises in cells of the immune system. Thus, there is an interest in the potential effects of EMF exposures on immune function. Because most cancers elicit a response from the immune system, blood levels of certain chemokines (important to inducing immune system functions) are reported to increase when various types of cancer occur. Li et al. (2018) investigated the chemokine response of Balb/c mice (100 per group) exposed to 50-Hz magnetic fields at levels of 0 (sham controls), 1,000 mG, 5,000 mG, and 25,000 mG for <1, 1, 10, 30, or 90 days. At each time point, blood was drawn from four mice and the average value reported. The investigators analyzed the samples for nine different chemokines that affect the immune response by promoting pro-inflammatory functions and recruiting immune cells to sites of infection.

The investigators reported that exposure to magnetic fields over 90 days did not affect the body weight of the mice. Nor did the level of magnetic-field exposure have a significant effect on the chemokine levels in blood measured by immunoassay, with two exceptions: MCP-1 and EOTAXIN-1. The change in these chemokines was confirmed by ELISA assay and the clearest increase in levels was at 5,000 mG; magnetic field exposure at the higher level of 25,000 mG reduced the increase in these chemokines. The authors reported that they did not see the

expected dose-dependent rise in chemokines. The study had serious limitations in the experimental design and procedures, including small numbers of mice from each group evaluated at any single timepoint and for any specific chemokine, the failure to randomly allocate animals to treatment groups or to analyze the cage, not the individual animals in the statistical analyses. It is not clear that the differences reported are attributable to magnetic-field exposure *per se*. Further, because chemokines are important in eliciting immune reactions, an increase in chemokine levels may be indicative of a protective effect rather than increased susceptibility to cancer.

Oxidative stress is a condition in which oxygen free radical levels in tissues are elevated and is one mechanism by which DNA damage, as well as other forms of cellular damage, may occur. While there is general agreement that oxidative stress from endogenous cellular processes are an overwhelming source of damage to DNA and other cellular components (de Bont and Larebeke, 2004), whether such mechanisms are activated by magnetic fields is under investigation. Previous in vivo studies that have evaluated whether magnetic-field exposure may be associated with oxidative stress provided mixed results.

Luo et al. (2016) investigated the potential effects of magnetic-field exposure on a variety of physiologic measures related to cellular oxidative processes. This study was predicated upon the theory that prolonged, uncompensated, high levels of oxidative products might contribute to cancer and neurodegenerative disease. The WHO (2007) and SCENIHR (2015) previously reviewed similar studies. Luo et al. (2016) suggested that a decline in superoxide dismutase (SOD) and a rise in malondialdehyde (MDA) in blood and the brain cortex are indicative of oxidative stress in cells.

Luo et al. (2016) randomly assigned male ICR mice in groups of 12 to 50-Hz, 40,000 mG, 60,000 mG, 80,000 mG, or 100,000 mG magnetic fields, or sham-exposure (control) conditions for 4 hours per day and assayed the blood and brain for SOD and MDA levels after 7, 14, 21 and 28 days. The authors observed noticeable and statistically significant changes in these two indicators in the predicted directions with exposures at or above 80,000 mG. The design of the study and the effects reported are similar to those reported in a previous study from this laboratory (Duan et al., 2013.

In the Luo et al. (2016) study, other groups of mice exposed to 80,000 mG magnetic fields also were orally administered 60, 90, or 120 mg of an antioxidant (lotus seedpod procyanidins [LSPC]) for 15 days before magnetic-field exposure and daily thereafter with magnetic-field exposure for an additional 28 days. The highest LSPC dose reversed the changes in SOD activity and MDA levels in the blood and brain cortex compared to mice exposed to magnetic fields only; changes in other oxidative indicators, including catalase, glutathione peroxidase, glutathione reductase, and glutathione-S-transferase, were also reversed. A strength of the study is that the authors tested for effects of magnetic fields at multiple exposure levels and randomized the mice to the experimental groups, which minimizes systematic bias. Yet, while the study was reported in detail, the analysis of the data was not performed blind, the authors reported no controls on noise and vibration from the magnetic-field coils and power supply, and like Bua et al. (2018), the authors did not properly account for the multiple animals exposed in each cage in the statistical analyses.

Zhang et al. (2016b) compared a group of males who worked in 110-410 kilovolt substations to other administrative staff with the utility with insignificant exposure on their urine levels of oxidative stress markers (isoprostane and 8-OHdG) in a simple cross-sectional study. In addition, subjects within each group were given capsules of green tea extract or a placebo twice a day for 12 months. The authors suggested that the higher levels of oxidation products in the urine of the substation workers were related to magnetic field exposure, as the substation and administrative workers did not differ with respect to multiple other factors. Treatment with green tea extract reduced the levels of oxidation products among substation workers, but not administrative workers; the levels increased again after stopping green tea extract treatment.

The subject population could not have been randomly allocated to the substation and administrative groups as claimed and there was no validation of the exposure differences between groups with respect to magnetic fields or other occupational exposures. Further, a substantial number of the study participants (546 or 63%) dropped out of the study before its completion. While the Zhang et al. study provided no evidence to link magnetic fields to higher levels of oxidation products in urine (apart from some other unmeasured factor), it does,

however, provide a reasonable basis to suggest that a daily ingestion of green tea extract may reduce urinary measures of oxidative stress.[24]

Overall, it is hard to draw any firm conclusions from these studies. Although markers of oxidative stress were generally increased with higher rather than lower magnetic-field exposures, it is not known if this effect is reversible or even biologically relevant. Independent replication of the findings in studies with greater sample sizes and blinded analyses is needed. Moreover, without studies that are specifically designed to quantitatively assess the relationship between markers of oxidative stress and measurements of DNA damage in an established model animal system, any relationship to a carcinogenic process is based on speculation rather than scientific evidence.

In summary, the *in vivo* studies published since the last update do not alter the previous conclusion of the WHO that there is inadequate evidence of carcinogenicity due to ELF EMF exposure.

**Reviews of *in vivo* research**

Reviews of *in vivo* research, including studies on carcinogenesis by SSM (2013, 2014, 2015) and SCENIHR (2015) cover a good deal of the research published after 2012. The relevant conclusions are:

**SSM (2013):**

> Other studies indicated increased oxidative stress, again mostly by exposures at levels well above the current exposure limits. One study showed indications for tumour growth inhibition by a 100 mT [1,000,000 mG] field, but with only small numbers of animals. Replication is necessary to obtain more insight. In general, the latest animal studies do not contribute to understanding a mechanism that could explain the association found in epidemiological studies between long term exposure to ELF magnetic fields below 1 μT [10 mG] and an increased risk of

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[24]  A very similar study from this same laboratory also reported that another antioxidant, resveratrol, had similar effects in lowering elevated levels of urinary isoprostane and 8-OHdG in power plant workers with average estimated exposures of 1.4 kV/m and 200 mG for more than 20 years but not in control workers (Zhang et al., 2017).

childhood leukaemia. Hence, there is still a need for dedicated studies in this area using new animal models (pp. 28-29).

**SSM (2014):**

> In general, the results of the studies are not very consistent. In some studies a function may be increased and in others decreased, while dose-responses cannot be derived. Most of the results are from single studies that need to be replicated in order to establish whether the observed effects are real or not. Also the large variety of exposure schedules used does not add to get a unified picture. Finally, none of these studies provide information that can be used in the interpretation of the association found in epidemiology studies between ELF magnetic field exposure and an increased risk of childhood leukaemia (p. 36).

**SSM (2015):**

> With the exception of single studies, the quality of the experiments and their description did not substantially improve compared to the previous years …Furthermore, referring to direct DNA-damage due to "low doses" of ELF-MF or presenting "dose-dependencies" using two groups only is somehow doubtful. Overall and similar to the previous SSM report, the results of the described studies are not very consistent (p. 9).

**SCENIHR (2015):**

> Previously SCENIHR (2009) concluded that animal studies did not provide evidence that exposure to magnetic fields alone caused tumours or enhanced the growth of implanted tumours. The inclusion of more recent studies does not alter that assessment. In addition, these studies do not provide further insight into how magnetic fields could contribute to an increased risk of childhood leukaemia (p. 161).

Based on *in vivo* research published after these reviews and evaluated in this report , these conclusions are still appropriate.[25]

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[25] A review of human cytogenetic studies involving exposure to ELF-EMF magnetic fields (most involving occupational exposures) also has drawn the conclusion that *"no firm conclusion can be drawn with respect to alleged ELF-EMF induce genetic effects"* (Maes and Verschaeve, 2016, p. 2347).

**Table 8. Studies of in vivo carcinogenesis (2017-2018)**

| Authors | Year | Study |
|---------|------|-------|
| Bua, L., et al | 2018 | Results of lifespan exposure to continuous and intermittent extremely low frequency electromagnetic fields (ELFEMF) administered alone to Sprague Dawley rats. |
| Li, H., et al. | 2018 | Eotaxin1 and MCP1 serve as circulating indicators in response to power frequency electromagnetic field exposure in mice |
| Luo, X., et al. | 2016 | Chemoprotective action of lotus seedpod procyanidins on oxidative stress in mice induced by extremely low-frequency electromagnetic field exposure |
| Yuan et al. | 2018 | The antitumor effect of static and extremely low frequency magnetic fields against nephroblastoma and neuroblastoma. |
| Zhang et al. | 2016 | Effects of dietary green tea polyphenol supplementation on the health of workers exposed to high-voltage power lines. |
| Zhang et al. | 2017 | Resveratrol may reverse the effects of long-term occupational exposure to electromagnetic fields on workers of a power plant. |

## 4.2 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), but no consistent findings emerged.

In 2002, 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). In an accompanying editorial to these two papers, a well-known epidemiologist proposed a hypothesis that the observed association may be the result of behavioral differences between women with healthy pregnancies (i.e., less physically active) and women who miscarried (i.e., more physically active), as opposed to a causal relationship between EMF and miscarriage (Savitz, 2002). Savitz proposed that physical activity is associated with higher likelihood of peak magnetic-field exposures at any given cut-points, and nausea commonly experienced in early, healthy pregnancies and the cumbersomeness of late, healthy pregnancies would reduce

physical activity levels, thereby decreasing the opportunity for exposure to peak magnetic fields. Later studies that reported consistent associations between activity (mobility during the day) and peak magnetic-field exposure metrics (Mezei et al., 2006; Savitz et al., 2006; Lewis et al., 2015) provided empirical support to the notion that the associations observed in Lee et al. (2002) and Li et al. (2002) were not due to a causal relationship but were likely due to behavioral differences between cases and non-cases. Other criticisms of the two studies also considered the timing of EMF measurements of the study subjects. In the Li et al. (2002) study, nearly half of women who had miscarriages in the cohort had their magnetic-field measurements taken after the miscarriage occurred, when changes in physical activity may have already occurred; in the Lee et al. study (2002), all measurements occurred after the miscarriage.

The scientific panels that have considered these two studies concluded that the possibility of bias in the studies precludes making any conclusions about the effect of magnetic fields on miscarriage (NRPB, 2004; FPTRPC, 2005; WHO, 2007). With respect to epidemiologic studies, the WHO concluded that *"On the whole, epidemiological studies have not shown an association between adverse human reproductive outcomes and maternal or paternal exposure to ELF fields. There is some evidence for an increased risk of miscarriage associated with maternal magnetic field exposure, but this evidence is inadequate"* (WHO, 2007, pp. 8-9). The WHO also concluded that, in general, experimental studies provide no consistent or convincing evidence in support of a potential adverse effect of EMF on human reproductive and developmental outcomes, and concluded that *"Overall, the evidence for developmental and reproductive effects is inadequate"* (WHO, 2007, p. 9).

Epidemiologic studies on pregnancy and reproductive outcomes that were reviewed in the previous Exponent reports provided little new insight in this research area and did not change the classification of the data from earlier assessments as inadequate.

**Relevant studies 2017-2018**

Several epidemiologic studies investigated the potential association between ELF magnetic-field exposure and miscarriage (Li et al., 2017; Sadeghi et al., 2017) or birth outcomes (Migault et al. 2018). Li et al. (2017) examined the association between magnetic-field exposure and miscarriage in a cohort of 913 pregnant women in California. Exposure was assessed using 24-

hour personal magnetic-field measurements collected on a single day during pregnancy, and the 99th percentile value observed during the 24-hour measurement period was used as the exposure of interest by the authors. Participants were also asked to keep a diary of their activities on the day of measurement. The authors reported an increased risk of miscarriage in women with high magnetic-field exposure (i.e., the 99th percentile value during the 24-hour measurement of ≥2.5 mG) compared to women with low magnetic-field exposure (<2.5 mG) when measurements were collected on a typical day (defined as a day reflecting participants' typical pattern of work and leisure activities during pregnancy). They reported no association, however, among those women whose magnetic-field exposure was measured on a non-typical day, and no trend was observed for miscarriage risk with increasing magnetic-field exposures >2.5 mG. The authors did not report the overall TWA for the 24-hours of exposure that could be compared to previous studies.

While personal exposure measurements are an improvement in exposure assessment over some of the earlier studies, the collection of only one measurement over a single 24-hour period during pregnancy is a limitation of the Li et al. (2017) study, as day-to-day changes in exposure cannot be captured. No information was provided in the paper on the exact timing of the measurement (i.e., whether the measurement day preceded or followed the occurrence of miscarriage among cases); this is a substantial limitation, as measurements taken following miscarriage in a substantial fraction of cases, was a major criticism of the previous study by the same research team (Li et al., 2002). Li et al. (2017) also failed to measure mobility during the measurement day, a potential major source of confounding in the study (e.g., Savitz, 2002; Mezei et al., 2006; Savitz et al., 2006). Varying levels of mobility between women with healthy pregnancies and women who suffer a miscarriage remain a viable alternative explanation for the findings in both the previous and the current studies.

Iranian scientists (Sadeghi et al., 2017) conducted a case-control analysis of preterm birth and residential distance to high-voltage overhead power lines. The researchers identified 135 cases of live spontaneous preterm birth in an Iranian hospital between 2013 and 2014 and compared their estimated exposure to 150 controls with term live births selected using randomized-digit dialing. The nearest linear distance from the high voltage power lines to the maternal residence

during pregnancy was measured using geographical information system software. Exposure was categorized using distance from power lines (<600 meters vs. ≥ 600 meters). The authors reported no statistically significant associations between preterm birth or birth defects and the mothers' residential distance from power lines. One of the main limitations of the study is the reliance on maternal address within 600 meters to high-voltage power lines as a surrogate for exposure. No elevation of ELF EMF levels can be expected for distances from approximately 100 to 600 meters in that zone; thus, no valid conclusions can be drawn from the study with respect to exposure to EMF.

Migault et al. (2018) studied the relationship between maternal cumulative exposure to ELF EMF and two pregnancy outcomes (moderate prematurity and being small for gestational age) within a prospective birth cohort in France. The study included 18,329 infants born at 33 weeks of gestation or more during 2011 and follows the children until 20 years of age. Cumulative exposure to both occupational and residential ELF EMF during pregnancy was assessed using the mothers' self-reported occupation and a job-exposure matrix. The job-exposure matrix included exposure estimates for five non-professional categories (e.g., housewife, student, and unemployed) that were used to estimate residential exposure. The authors observed no statistically significant association between maternal cumulative exposure and moderate prematurity or small for gestational age. The authors noted that the ability to consider both occupational and residential exposures in their cumulative estimates is a strength of the study but suggested that the small sample size in the high exposure categories limited the study's power to detect a potential association.

Using data from the Danish National Birth Cohort, Sudan et al. (2017) conducted a follow-up study to a previously reported association between intrauterine exposure to magnetic fields and childhood asthma (Li et al., 2011). The researchers examined 92,675 children born to 91,661 mothers who were pregnant between 1996 and 2002, and assessed intrauterine exposure of the children using distance from the residence of the mother during pregnancy to the nearest power line. They observed no association between magnetic-field exposure estimated by distance from power lines and asthma development, regardless of how the asthma diagnosis was defined. The authors noted, however, that the majority of mothers and children in the dataset had no

residential exposure from power lines (i.e., lived in a home that was located outside a specified distance to the nearest power line), thus limiting the ability to make firm conclusions. In addition, potential errors in the estimation of distances to power lines, which were used in the calculations of magnetic-field levels, are a limitation of the study's method of exposure assessment (Chang et al., 2014).

In summary, the recent epidemiologic studies evaluated do not provide substantial new evidence in support of an association between EMF and reproductive or developmental outcomes. The classification of the data as inadequate remains appropriate, as studies in this research area still suffer from limitations in study design, sample size, and exposure assessment method.

**Table 9.   Studies of reproductive and developmental effects (2017-2018)**

| Authors | Year | Study |
|---|---|---|
| Li et al. | 2017 | Exposure to magnetic field non-ionizing radiation and the risk of miscarriage: a prospective cohort study. |
| Migault et al. | 2018 | Maternal cumulative exposure to extremely low frequency electromagnetic fields and pregnancy outcomes in the Elfe cohort. |
| Sadeghi et al. | 2017 | Preterm birth among women living within 600 meters of high voltage overhead Power Lines: a case-control study. |
| Sudan et al. | 2017 | Re-examining the association between residential exposure to magnetic fields from power lines and childhood asthma in the Danish National Birth Cohort. |

## 4.3    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 ALS, which is also known as Lou Gehrig's disease. Based on the initial findings on the Alzheimer's disease the NRPB concluded in 2001 that there was *"only very weak evidence to suggest that it [ELF magnetic fields] could cause Alzheimer's disease"* (NRPB, 2001b, p. 21). Early studies on ALS also reported an association between ALS mortality among workers with certain 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.

Also including more recent studies, the WHO panel concluded that there is *"inadequate"* data in support of an association between magnetic fields and Alzheimer's disease or ALS. They stated that *"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"* (WHO 2007, p. 194). While a subsequent meta-analysis also reported an association between occupational EMF exposure and Alzheimer's disease (Garcia et al., 2008), its conclusion was necessarily limited by the quality of the studies included in the analysis. A Swiss study that was the first to examine residential proximity to high-voltage power lines and neurodegenerative disease, reported an increase in Alzheimer's disease mortality among people living with 50 meters of transmission lines, but observed no association for ALS, Parkinson's disease, and multiple sclerosis (Huss et al., 2009) spurred interest in research on Alzheimer's disease. Based on a review of the evidence that also considered these studies, the Health Council of the Netherlands EFHRAN review still considered the evidence as "inadequate" for all forms of neurodegenerative diseases (EFHRAN, 2012).

Following the research recommendations of the WHO, scientists conducted epidemiologic research that studied exposure to ELF EMF and development of neurodegenerative diseases. Overall, these studies did not provide consistent and convincing support for an association. Several meta-analyses of these studies reported weak to no evidence of an association between occupational exposure to ELF magnetic fields and neurodegenerative disease (Zhou et al., 2012; Vergara et al., 2013). The authors of these meta-analyses concluded that potential within-study biases, evidence of publication bias, and uncertainties in the various exposure assessments greatly limit the ability to infer an association, if any, between occupational exposure to magnetic fields and neurodegenerative disease.

**Relevant studies 2017-2018**

Two case-control studies (Koeman et al., 2017; Vinceti et al., 2017) and two meta-analyses (Huss et al., 2018b; Röösli and Jalilian, 2018) have been recently published regarding EMF exposure and ALS. Koeman et al. (2017) conducted a nested case-control analysis within the Netherlands Cohort Study that assessed various occupational exposures, including solvents, pesticides, metals, ELF magnetic fields and electric shocks, and ALS mortality in a cohort of

more than 120,000 men and women. The analysis included 136 ALS cases and a random subset (n=4,344) of the cohort study population. Information on occupational history and potential confounders were assessed using self-administered questionnaires at enrollment. Exposure to various agents in the occupational environment was assessed using job-exposure matrices. The authors reported a statistically significant association among men who were ever highly exposed; however, this was based on a small number of cases (n=9) in the high exposure category. In addition, they reported a statistically significant association between the ALS mortality among men for those with the highest 30 percent or more of cumulative ELF magnetic-field exposure in the cohort; this association was no longer statistically significant when adjusted for the effects of other occupational exposures, including insecticides. They reported no statistically significant associations for other occupational exposures investigated in the study and that due to the overall low number of exposed women, risk analyses for women were *"largely uninformative."*

Vinceti et al. (2017) conducted a population-based, case-control study of magnetic fields from high-voltage power lines and ALS within Italy. The authors included 703 ALS cases, diagnosed between 1998 and 2011, and a sample of 2,737 randomly selected controls from the same provinces. The authors used information on the residential addresses of the cases and controls and geodata on high-voltage power lines (with voltages between 132 and 380 kV) to model magnetic-field exposure at the study subjects' residences. The authors reported no statistically significant associations between ALS and calculated magnetic-field levels, and they observed no exposure-response trend. The authors concluded that their findings *"appear to confirm"* that exposure to magnetic fields from power lines occurring in the general population is not associated with an increased risk of ALS (Vincente et al., 2017, p. 583).

Huss et al. (2018b) conducted a meta-analysis combining data from 20 studies of occupational exposure to ELF magnetic fields and ALS. Overall, the authors reported a weak association with borderline statistical significance for ALS and estimated ELF magnetic-field levels (summary RR 1.14; 95% CI, 1.00-1.30) and a somewhat stronger association in a subset of six studies with full occupational history compared to studies where occupation was available only at certain time points. The authors also reported substantial heterogeneity among studies, evidence for

publication bias, and the lack of a clear exposure-response relationship between estimates of ELF magnetic fields and ALS. Röösli and Jalilian (2018) combined data from five epidemiologic studies that examined residential exposure to ELF magnetic fields from high-voltage power lines and ALS. The authors reported no statistically significant associations; the pooled RR for the most exposed populations (either <200 meters from high-voltage lines or >0.1 µT [>1 mG]) was 0.71 (95% CI, 0.48-1.07).

Pedersen et al. (2017) updated a prior cohort study (Johansen, 2000) of occupational exposure to ELF magnetic fields and CNS disease, including dementia, motor neuron disease, Parkinson's disease, multiple sclerosis, and epilepsy, among more than 32,000 male electric utility workers in Denmark. The authors identified cases within the occupational cohort of electric utility workers from the Danish National Patient Registry diagnosed from 1982 to 2010. They estimated exposure to ELF magnetic fields using a JEM and company records of job title and area of work, and classified into three categories (<0.1 µT [<1 mG], 0.1-0.99 µT [1-9.9 mG], and ≥1.0 µT [≥10 mG]).

Pederson et al. compared disease incidence of exposed worker within the cohort to: 1) disease incidence in the general population of Danish men (external comparison); and 2) to disease incidence among unexposed workers to account for the potential healthy-worker effect (internal comparison). No consistent pattern of disease association was reported by the authors for any of the investigated outcomes. While the external comparison indicated statistically significant associations for all types of dementia in the highest exposure category of ELF magnetic fields, the internal comparison, which is the more appropriate comparison, reported no such associations. The authors reported no statistically significant increases with exposure to ELF-magnetic fields for motor neuron disease, Parkinson's disease, multiple sclerosis, or epilepsy in either external or internal comparisons.

Checkoway et al. (2018) investigated the association between Parkinsonism[26] and occupational exposure to several agents, including endotoxin, solvents, shift work, and magnetic fields,

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[26] Parkinsonism is defined by Checkoway et al. (2018) as "a syndrome whose cardinal clinical features are bradykinesia, rest tremor, muscle rigidity, and postural instability. Parkinson disease is the most common neurodegenerative form of parkinsonism" (p. 887).

among female Shanghai textile workers. The study included 537 retired cotton factory workers who were at least 50 years of age, and 286 age-matched controls who were retired cotton factory workers not exposed to cotton dust (which was used to define endotoxin exposure). Exposure to magnetic fields was assessed using a JEM. The authors reported no statistically significant associations between occupational exposure to magnetic fields and parkinsonism. In addition, the authors, did not observe statistically significant associations with endotoxin, shift work, or solvent exposure. Huss et al. (2015) conducted a meta-analysis of 11 studies of occupational exposure to ELF magnetic fields and Parkinson's disease. The authors observed no statistically significant association (summary RR 1.05, 95% CI 0.98-1.13) and they reported that overall, there was *"no evidence that the exposure to ELF-MF [magnetic fields] increases the risk of Parkinson's disease"* (Huss et al., 2015, p. 7348).

Jalilian et al. (2018) conducted a meta-analysis of 20 epidemiologic studies of occupational exposure to ELF magnetic fields and Alzheimer's disease. The authors reported a moderate, but statistically significant overall association for Alzheimer's disease (summary RR 1.63; 95% CI, 1.35-1.96), with weaker associations in cohort studies than in case-control studies. The authors also reported substantial heterogeneity among studies, and evidence for publication bias. Pooling results from studies with *"higher risk"* of bias, as assessed by the authors, resulted in stronger associations, suggesting that bias in the studies likely contributed to the reported associations.

In summary, many of the recent studies on neurodegenerative diseases have represented methodological improvements (e.g., increased sample size, improved exposure assessment, inclusion of incidence cases) compared to previous studies. In spite of these improvements, the overall evidence from these studies do not materially change the assessment that there is no consistent or convincing support for a causal association between EMF exposure and neurodegenerative diseases.

**Table 10. Studies of neurodegenerative diseases (2017-2018)**

| Authors | Year | Study |
| --- | --- | --- |
| Checkoway et al. | 2018 | Occupational exposures and parkinsonism among Shanghai women textile workers. |

| Authors | Year | Study |
|---|---|---|
| Huss et al. | 2018b | Occupational exposure to extremely low-frequency magnetic fields and the risk of ALS: A systematic review and meta-analysis. |
| Jalilian et al. | 2018 | Occupational exposure to extremely low frequency magnetic fields and risk of Alzheimer disease: A systematic review and meta-analysis. |
| Koeman et al. | 2017 | Occupational exposure and amyotrophic lateral sclerosis in a prospective cohort. |
| Pedersen et al. | 2017 | Occupational exposure to extremely low-frequency magnetic fields and risk for central nervous system disease: an update of a Danish cohort study among utility workers. |
| Röösli and Jililian | 2018 | A meta-analysis on residential exposure to magnetic fields and the risk of amyotrophic lateral sclerosis. |
| Vinceti et al. | 2017 | Magnetic fields exposure from high-voltage power lines and risk of amyotrophic lateral sclerosis in two Italian populations. |

## 4.4    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. Based on double-blind studies of human volunteers, office workers, and self-reported hypersensitive individuals, however, the WHO review concluded that the perception of EMF and health complaints are not related to exposure. Neither healthy volunteers nor self-identified hypersensitive individuals can reliably distinguish field exposure from sham-exposure. Also, no exposure-related differences were observed in levels of stress hormones or inflammatory mediators. 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).

Studies published following the WHO review, overall, supported the conclusion that ELF EMF is not detected by self-identified 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.

The 2012 EFHRAN report also concluded that the available evidence suggests the lack of an effect on people with "electrical hypersensitivity" (EFHRAN, 2012).

Subsequent studies continue to report that persons who identify as having electromagnetic sensitivity are unable to detect exposure to EMF better than chance (Van Moorselaar et al., 2016). Other reports indicate detection of 50-Hz magnetic fields to *"some extent"* or to *"small extent,"* but reporting of symptoms by these individuals were related to perceived exposure (Köteles et al., 2013; Szemerszky et al., 2015).

The 2015 SCENIHR review concluded *"The studies published since the 2009 Opinion show discordant results. However, observational studies suffered from weaknesses and do not provide convincing evidence of an effect of ELF exposure on symptoms in the general population and most experimental evidence also points to the absence of any causal effect."* (p. 184)

**Relevant studies 2017-2018**

Most recent research on IEI attributable to EMF (IEI-EMF) has focused on addressing the prevalence of self-reported IEI symptoms in populations and their psychological characteristics (Andrianome et al., 2017; Dömötör et al., 2017; Slottje et al., 207; Claeson et al., 2018; Gruber et al., 2018; Karvala et al., 2018; Huang et al., 2018a,b; Vuokko et al., 2018). Another focus of recent research is on reports that mere perception of exposure to EMF even when no exposure is present can influence feelings of well-being among both persons who do and don't identify as IEI (Boehmert et al., 2018; Eltiti et al., 2018; Verrender et al., 2018)). The attribution of the reported symptoms to a  perceived exposure  is called the *"nocebo"* effect (i.e., symptoms explained by unconscious psychological reaction as a result of the expectation of an effect, rather than the effect of the exposure itself).

The only new experimental study of the responses of subjects actually exposed to magnetic fields (Van Moorselaar et al., 2017) is a follow-up to a previous double-blind randomized controlled trial that found subjects with self-identified electromagnetic hypersensitivity were not able to detect exposure to EMF better than chance (van Moorselaar et al., 2016).

Some IEI persons had criticized previous studies because they were conducted in laboratories which necessitated travel from home and this source of stress hampered their response to test exposures and that the test exposures did not match what they believed to be the source of their symptom (van Moorselaar et al. 2017). To address these concerns, van Moorselaar et al. (2017) devised a sophisticated and extremely well-controlled study. They visited members of an IEI self-help group at their homes and with the assistance of each volunteer determined what exposure ELF-EMF, RF, etc. they responded to. Then, volunteers were exposed to the type of electromagnetic field that they said they could detect within 15 minutes of exposure onset. Questionnaires were administered immediately before and after testing and after two or four months after testing. Of the 40 participants, only 4 stated that they could detect ELF-EMF. These volunteers were then exposed to magnetic field at levels they had selected ranging from 1.5 to 66 mG or no-field conditions in a double-blind randomized series of tests. None of the participants could reliably detect the presence of ELF-magnetic fields under blinded testing conditions although in the unblinded pre-test they asserted that they could. Similarly, other participants also were found to be unable to detect electromagnetic field at other frequencies and characteristics.

In summary, recent studies did not provide new sufficient evidence to change the overall conclusion that either self-identified individuals with electromagnetic hypersensitivity or members of the general populations can detect EMF exposure encountered in our environment, or that general non-specific symptoms are related to EMF exposure. The recent SCENIHR review stated that *"Overall, existing studies do not provide convincing evidence for a causal relationship between ELF MF exposure and self-reported symptoms"* (SCENIHR, 2015, p. 7).

**Table 11.  Studies of electromagnetic hypersensitivity (2017-2018)**

| Authors | Year | Study |
|---|---|---|
| van Moorselaar et al. | 2017 | Effects of personalised exposure on self-rated electromagnetic hypersensitivity and sensibility - A double-blind randomised controlled trial. |

# 5    Possible Effects of ELF Electric and Magnetic Fields on Implantable Cardiac Devices

The sensing system of pacemakers and implantable cardioverter-defibrillators (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 implantable 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 parameters (e.g., strength, frequency, duty cycle) of the interfering 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. Modern devices incorporate various technological safeguards (e.g., shielding by titanium casing and electrical filtering) to minimize the potential for EMI (Dyrda and Khairy, 2008). Experimental research has been conducted to assess whether interference may occur when currents are induced in the patient's body by environmental electric fields and magnetic fields.

In the absence of specific recommendations from medical device manufacturers, the American Conference of Governmental Industrial Hygienists (ACGIH) suggested exposure levels to prevent pacemaker EMI. For electric fields, the ACGIH suggested keeping exposures below 1 kV/m, and for magnetic fields, they recommended exposure not exceed 1 G (ACGIH, 2015). These recommendations are general in nature and do not address that classes of pacemakers from some manufacturers are quite immune to interference even at levels much greater than these recommended guidelines. The ACGIH also recommended that patients consult their physicians and the respective pacemaker manufacturers before following any organizations' guidelines.

Manufacturers of pacemakers and other implantable devices will typically follow the AAMI PC69:2007 or ANSI/AAMI/ISO 14117:2012 (North America) or EN 45502-2-1:2003 / IEC 45502-2-2:2003 (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 peak-to-peak signal applied to the sensing electrodes. This test verifies immunity of a cardiac device[27] of at least 0.83 G (root-mean-square magnetic field) at 60 Hz. At 60 Hz, the reference levels in EC 519/99 (also known as 1999/519/EC) are 0.83 G and 4.167 kV/m—the standard assumes that only an electric or magnetic field is present at any time (CEU, 1999).

Moreover, the standard procedure (EN 50527-1:2010) 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" (CENELEC, 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.

Previous studies indicated occurrence of pacing abnormalities at magnetic-field levels that are much higher than the levels a person would encounter on a daily basis. While electric fields did produce interference at levels that can be produced by certain electrical sources (Toivonen et al., 1991; Astridge et al., 1993; Scholten and Silny, 2001; Joosten et al., 2009), most pacemakers were not affected by high levels of electric fields (up to 20 kV/m) and did not exhibit any pacing abnormalities. Joosten et al. (2009) showed that the most sensitive unipolar pacemakers may be affected by electric-field levels between 4.3 kV/m and 6.2 kV/m; however, most modern pacemakers are bipolar devices, which are designed specifically to reduce the potential for EMI. Joosten et al. (2009), for example, found that in Germany in 2007, only 6% of the pacemakers in use had a unipolar sensing system. The conclusions of other researchers are similar (Tiikkaja et al., 2013a,b; Napp et al., 2014; Korpinen et al., 2014; von Olshausen et al., 2016) regarding the

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[27]   The magnetic-field value is calculated using an average area (225 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.

relative rarity of interference, especially below ICNIRP reference levels, and that interference from use of specific devices is relatively common whilst interference from power lines or substations is not reported.

**Relevant studies 2017-2018**

Some recent medical case reports describe interference with pacemakers and other implantable cardiac devices produced by electrical currents are conducted from a mechanical heart implanted in the chest (Ahmed et al., 2017), faulting wiring in pump in a swimming pool (Roberto et al., 2017), or hot tub (Shenasa et al., 2018) to an implanted cardioverter defibrillator (ICD). Other studies have tested typical dental devices for potential EMF interference to ICDs without finding cause for concern (Dadalti et al., 2017), or reviewed studies of the application of electrical currents to teeth, if general precautions are followed (AlRahabi and Ghabbani, 2018). While some of these reports indicate the possibility of interference in certain scenarios with these equipment devices, these interference scenarios are not relevant to the exposure to EMF in electric utility environments due to differences in many factors, including, most importantly, the proximity of the interfering sources and the intensity and frequency of the interfering electromagnetic fields.

As in past reviews, there are reports that exposure of ICDs and pacemakers to EMF at sufficient intensities can affect device operation. This was demonstrated by Seckler et al. (2017) who stimulated the hearts of 160 patients in the University Hospital in Aachen, Germany with ICDs to determine what role the position and orientation of the leads from the device to the heard had on thresholds for interference. The maximum 50-Hz electric and magnetic field exposures tested were 30 kV/m and 25,500 mG, respectively. The researchers recommended that the orientation and position of the lead tips be optimized and the appropriate sensitivity of the pacemaker be set at the time of implant as these procedures could effectively minimize interference.

Stunder et al. (2017), also at the University Hospital in Aachen, measured the thresholds for interference from 50-Hz electric and magnetic fields for 119 patients with implanted pacemakers under conditions that were most likely to result in interference. At nominal sensitivity settings the threshold for 5 unipolar pacemakers was 9.6 kV/m or 2000 mG for

electric and magnetic fields, respectively, or 3 kV/m and 1,500 mG when exposed to electric or magnetic fields simultaneously. For 114 bipolar lead devices at nominal sensitivity settings, the lowest interference thresholds were 11.9 kV/m and 3,000 mG for electric and magnetic fields, respectively, or 5.2 kV/m and 2,550 mG when exposed to electric or magnetic fields simultaneously. When these pacemakers were set to their maximum sensitivity the thresholds were far lower, as would be expected. Since the general public would rarely, if ever, encounter a magnetic field from under transmission line or other utility source close to the threshold for interference of any of the devices tested (400 mG) set to maximum sensitivity, pacemaker interference is highly unlikely. On the other hand, when set to maximum sensitivity, about 35% of pacemakers tested in this study would be affected by an electric field of 10 kV/m, a value similar to the electric field (8-12 kV/m) under 765 kV transmission line (Tell et al., 1977). At maximum sensitivity the threshold drops to levels that could be found under some lower voltage lines. The authors place these results in practical context by comparing the theoretical rate of interference for pacemakers at nominal sensitivity for combined electric and magnetic field exposures at reference levels under the ICNIRP and ICES standards as 0-4.4 %, respectively. This compares to 16% of the pacemakers predicted to exhibit interference for a person using a hand drill.

De Rotte et al. (2017) placed ICDs from four different manufacturers in a human phantom dummy within a Piper Dakota single-engine plane to record electromagnetic interference that would be detected as tachycardia (R- or P-waves) or inappropriate defibrillation discharge. The devices were set at maximum sensitivity. No interference was detected during 11, 932 minutes of the testing. No measurements of EMF were made to assess the intensity or frequency of the EMF within the plane.

Lennerz et al. (2018) randomly assigned 108 volunteers with ICDs to sit within 4 of the most popular electric cars in Europe while the car was 'bench-driven' to achieve maximum electromagnetic field generation. Two cardiologists blindly reviewed the volunteers' electrocardiograms for abnormal device function, tachyarrhythmia, or other spurious functioning. The magnetic fields during operation on the test bench and during driving were measured as 301-1165 mG during charging. Fields measured in front seats 5 cm from the

implanted device when the cars were not charging were much lower (20-36 mG). The authors
indicated that these values were lower than measurements of about 200 mG made in the back
seat in a sample of gasoline-powered cars (Halgamuge et al., 2010). No evidence of
electromagnetic field interference with the performance of the ICDs was reported in this study.

**Table 12.  Studies of EMI (2017-2018)**

| Authors | Year | Study |
|---------|------|-------|
| De Rotte et al. | 2017 | Electromagnetic interference in implantable defibrillators in single-engine fixed-wing aircraft |
| Lennerz et al. | 2018 | Electric cars and electromagnetic interference with cardiac implantable electronic devices; a cross-sectional evaluation |
| Seckler et al. | 2017 | Effect of lead position and orientation on electromagnetic interference in patients with bipolar cardiovascular implantable electronic devices. |
| Strunder et al. | 2017 | In vivo study of electromagnetic interference with pacemakers caused by everyday electric and magnetic fields |

# 6 Fauna and Flora Research

## 6.1 Fauna

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.

**Relevant studies 2017-2018**

In this period, only one relevant study was identified. Shepherd et al. (2018) reported an exquisitely designed study of magnetic fields on the behavior of honey bees which was appropriately analyzed but unfortunately the investigators failed to control for confounding effects of vibration from the coils that produced the magnetic field.

The investigators performed three experiments. First, they attached the bees to plate with adhesive tape and then taught the bees to expect a sugar-water reward after delivery of a flower odor on 5 trials of the pairing of sugar water with the scent. After each of the 5 trials, bees were exposed to 200 mG, 1000 mG, 10,000 mG or no magnetic field for one minute after each trial. Evidence of learning was indicated by the bee extending it tongue-like proboscis (proboscis extension response [PER]) during the 10-second presentation of the odor stimulus before the sugar water was presented. A lower percentage of bees exposed to 200, 1,000 and 10,000 mG magnetic field displayed PER but the reduction was not significantly greater at the higher of these two field levels. Only bees from five of the six hives showed this response. All bees were tested one hour after training but no differences between the PER response at the end of training and the memory test one hour later were observed in any of the groups of bees.

In the second experiment the bees were attached to the plate with a light tether and the frequency of wing beats were measured from analyses of videotapes of exposure to magnetic fields or no magnetic field. Magnetic fields at 7,000 mG significantly increased wing-beat from about 2.5 to 6 beats per second.

The third experiment observed the effect of the 1,000 mG magnetic field on free-flying bees from 6 hives. A netting-enclosed passage from the hive led to a feeding station 1.4 meters away. To get to the feeding station the bees had to fly through the magnetic field generated by 2 wire coils. Over a 15 minute observation period the average number of bees leaving the hive increased and reaching the feeding station increased by 5 bees above pre-study baseline while the average number of bees exposed to 1,000 mG magnetic field declined by 3 bees. Having reached the feeding station (and not turning around *en route*), the number of bees returning to the hive was the same for bees exposed to the magnetic field or not.

While the researchers suggested that bees might encounter the highest levels of magnetic fields investigated in the study from 400 kV transmission lines, their calculations show that highest field levels are found only about 1 m from the phase conductors. As their calculations document, the magnetic fields at ground level where bees are visiting flowers are at least 50-fold lower. As for the observed responses of the bees, there is a real question as to whether the bees were responding just to the magnetic field. Apparently the researchers were unaware that the magnetic coils they used to generate the magnetic field also produce noise and vibration at a frequency of 120 Hz in the same way that the electromagnet in audio speakers cause vibration and sound. Researchers in the field of magnetobiology know this and have urged others to take precautions against confounding effects of noise and vibration in magnetic field studies (IARC, 2002; Makinistian et al., 2018). In particular, it is surprising that the researchers did not design their magnetic field coils to minimize noise and vibration because that was a very specific concern of the researchers decades ago who started research on bees and magnetic fields and who design their magnetic field coils to solve this problem (Kirschvink, 1992; Kirschvink et al., 1997). In addition, the electricity flowing through the coils are a source of electric fields which should have been blocked by shielding. As for the bees, they don't have ears but they do have sensory cells that can detect vibration by mechanical contact or through the air by sound up to about 500 Hz and their ability to perceive even the very weak vibrations during honey bee waggle dances and other behaviors as part of normal bee communications has been explored in recent years ( Wenner, 1964; Tsujiuchi et al., 2007; Collison, 2016).

In short, this study describes some interesting observations of bees during their experiments but does not clearly identify whether the response of the bees is caused by the magnetic field or

vibrations and noise, or an electric field from the exposure system. Furthermore, it is unclear whether the behavior described in the unusual conditions of this study would occur in the real world where if the bees found locations of high magnetic field to be disturbing they could fly away from those regions an option not available to the captive bees in this study. This very option was mentioned by the researchers "*Moreover, the effects cause by EMF on flight could serve as an aversive stimulus that bees could avoid. There are therefore many questions remaining to be addressed to fully understand how EMFs could impact on bees.*" (p. 6).

Results of studies published since 2012 have not provided substantive new evidence that would alter previous conclusions.

## 6.2    Flora

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 peer review studies published since 2012 added substantial new information to our knowledge about effects of EMF on flora that would be relevant to transmission lines.

# 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.

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