Health Sciences

Exponent®

EMF and Health: Review and Update of the Scientific Research

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Acronyms and Abbreviations

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

Introduction

This report has been prepared by Exponent to assess the current status of research regarding the potential for health effects from exposure to electric and magnetic fields (EMF). It serves to update a report filed with the British Columbia Utilities Commission (BCUC) in December 2005, titled "*VITR EMF Health Report Exhibit 1-37 - Response to Evidence Presented by Dr. Magda Havas*" and prepared for BCTC's Vancouver Island Transmission Reinforcement (VITR) Project (Exponent, 2005). When the ILM Application is filed, it will be almost two years since the *VITR EMF Health Report* was filed. This report fulfills the BCUC Directive in the VITR decision to require BCTC to monitor the science and allow residents to keep abreast of major developments in the field of EMF research. Thus, this report serves as an independent evaluation of the recent body of research.

The *VITR EMF Health Report*, hereafter referred to as Exponent 2005, served as an update to reports by the International Commission on Non-ionizing Radiation Protection (ICNIRP) and the International Agency for Research on Cancer (IARC) and reviewed the scientific research published January 1, 2001 through December 5, 2005. The current report systematically evaluates peer-reviewed research and reviews by scientific panels published from December 1, 2005 through August 31, 2007 to determine if there are new developments that would justify changes to conclusions in Exponent 2005 and previous weight-of-evidence reviews.[1] During this 1-1/2 year timeframe, approximately 34 relevant scientific studies were published and 3 scientific organizations issued their evaluations of the scientific evidence. Most important, the World Health Organization (WHO) released an Environmental Health Criteria report in June 2007 following an extensive program to conduct and review research and offer conclusions related to the health effects of EMF and recommendations for policymakers. Since the WHO report is the most recent weight-of-evidence review and it was conducted by an experienced scientific organization that followed standard scientific procedures, this report relies heavily upon its conclusions for research published prior to 2005.

This report follows the same general structure and discusses the same scientific topics as Exponent 2005, with a few modifications and additions. These modifications and additions include an expanded discussion of experimental methods and results (Section 2.4), standards and guidelines (Section 3.2), and the precautionary approach (Section 3.3), in addition to new sections on electromagnetic interference (Section 5), research related to EMF and flora and fauna (Section 6), and other disease outcomes (i.e., neurodegenerative diseases, Section 4.5). The sections outlining basic scientific methods and theory are taken from Exponent 2005 (Section 2), with some modifications, and are repeated in this report for clarity and completeness. A glossary is included at the end of the report, and words that appear in the glossary are shown in ***bold italics*** on their first appearance in the text.

[1] 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, as described in Section 2.4.1 below, such data are supplementary to epidemiology and whole animal studies, and are not directly used by health agencies to assess risk to human health. For that reason, this review systematically addresses epidemiology studies and *in vivo* studies and relies largely on reviews and the conclusions of scientific panels with regard to studies of mechanism (see Section 4.6.3).

Sections 1 and 2 provide a brief background on the nature and sources of EMF and methods for evaluating scientific research. Section 3 summarizes the methods and conclusions of recent weight-of-evidence reviews on EMF, and Section 4 summarizes the recent literature on EMF and health that has been published since December 2005, based on a ***systematic review*** of the literature. Sections 5 and 6 address additional topics relevant to a risk assessment of EMF (electromagnetic interference and possible effects on flora and fauna, respectively).

1 Background: Electric and magnetic fields

EMF are produced by both natural and man-made sources that surround us in our daily lives. In fact, the earth produces a magnetic field—it is this field that is used for compass navigation. Man-made EMF is found wherever electricity is generated, delivered, or used, including power lines, wiring in homes, workplace equipment, electrical appliances, power tools and electric motors. In Canada and the rest of North America, EMF from these sources (often referred to as power-frequency EMF) changes direction and intensity 60 times, or cycles, per second – a frequency of 60 Hertz (Hz).[2]

Electricity is transmitted over considerable distances from generation sources to substations and, finally, to distribution systems that serve our homes and workplaces. Electricity is transmitted as current over power lines to homes, factories and commercial establishments in our neighborhoods.

Electric fields are the result of ***voltages*** applied to electrical conductors and equipment. 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. *Most objects including fences, shrubbery, and buildings easily block electric fields.* Therefore, certain appliances within homes and the workplace are the major source of electric fields indoors, while power lines are the major source of electric fields outdoors.

Magnetic fields are produced by the flow of electric currents; however, unlike electric fields, *most materials do not readily block magnetic fields*. 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.[3] The strength of the magnetic field at any point depends on characteristics of the source, including the arrangement of conductors, the amount of current flow through the source, and its distance from the point of measurement. *The intensity of both electric and magnetic fields diminishes with increasing distance from the source.* Research has focused on magnetic fields because, among other reasons, conductive objects including buildings effectively block electric fields.

Exposure to EMF depends upon where an individual spends time and the sources he or she encounters while at these locations. Electric fields in the home range up to about 0.010 kV/m away from appliances and up to 0.25 kV/m near appliances (WHO, 1984). Electric fields from power lines are higher under the conductors but are much lower as you move away from the conductors, and are almost totally blocked by walls and roofs of buildings.

In most homes, background magnetic field levels average about 1 mG, resulting from wiring within the home, appliances, and power lines outside the home (Zaffanella, 1993). Higher magnetic field levels are measured near distribution and transmission lines. However, since the

[2] EMF from electrical facilities in countries outside North America operate at a frequency of 50-Hz.

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

intensity of magnetic fields diminishes quickly with distance from the source, distance from the power lines reduces the effect on the magnetic field level within the home. In fact, the strongest sources of magnetic fields that are encountered indoors are electrical appliances. Fields near appliances vary over a wide range, from a fraction of a milligauss to a thousand milligauss or more. For example, a study by the U.S. Environmental Protection Agency (EPA) in 1992 reported the median magnetic field at 6 inches from a sampling of appliances was 90 mG (copier), 200 mG (microwave ovens), 600 mG (can opener), 300 mG (hair dryer), 7 mG (color televisions), 9 mG (electric oven), computers (14 mG), and 6 mG (baby monitor).[4]

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

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

[5] The major focus of the review is magnetic field exposure. Research has focused on magnetic fields because, among other reasons, conductive objects shield electric fields.

2 Methods for evaluating scientific research

2.1 Heath risk assessment approach

The standard process for evaluating a body of research to understand the potential health implications of exposure is referred to as health risk assessment.[6] A health risk assessment consists of several, sequential steps. The process starts with systematically evaluating the body of research and identifying any possible risks associated with an exposure (***hazard identification/weight-of-evidence review***).[7] A follow-up to hazard identification is the question, "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 analysis (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 (for example, if a person develops a headache after eating a particular food, he or she may ascribe the headache to the food). Proximity of events or conditions, however, does not guarantee a causal relationship. Scientists use systematic methods to evaluate observations and assess the potential impact of a specific agent on human health.

The scientific process involves looking at *all* the evidence on a particular issue in a systematic and thorough manner (i.e., a weight-of-evidence review or hazard identification). This process 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 all available evidence to advocate or suppress a preconceived idea of an adverse effect. These methods include an assessment of the kind of effect that can be caused by an exposure (hazard identification), as well as an assessment of the levels of exposure that can produce these effects (dose-response assessment). Thus, two steps precede arriving at a weight-of-evidence review: a systematic review to identify the relevant literature and an evaluation of each study to determine its strengths and weaknesses. Once all

[6] Some of the scientific panels that have considered EMF 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).

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

studies have been individually considered, the overall data is then characterized to evaluate whether it provides support for a causal relationship.

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

Epidemiology is the discipline in the health sciences that studies the patterns of disease occurrence in human populations and the factors that influence these patterns. It is, therefore, part of the evidence considered for determining the causes of disease. Epidemiologic studies are observational in that they examine and analyze people in their normal daily life. 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 measure of how things vary together. For example, we may find that people with coronary artery disease eat a diet that is lower in fat compared to people without the disease (i.e., a negative association). Or, we may find 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 help suggest factors that may contribute to the development of disease but they cannot be used as the sole basis for drawing inferences about ***cause-and-effect relationships***. Additional research needs to be considered. Continuing with our example from above, just because one study finds a positive association between high fat diets and coronary artery disease, we cannot conclude that fat (or a component of fat) causes coronary artery disease without further research. This additional research involves studies with *experimental* research designs.

In contrast to epidemiology studies, experimental studies (including both animal studies and studies of tissues and cells) are conducted under controlled laboratory conditions. For example, in animal studies, exposure is precisely measured in the exposed group, and other factors (such as food, housing and temperature) are the same in the exposed and unexposed groups. Experimental studies are designed to test specific hypotheses under controlled conditions and are generally required to establish cause-and-effect relationships. Conversely, the results of experimental studies by themselves may not always be directly extrapolated to predict effects on human populations. It is therefore 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 causality because no individual study is capable of assessing causality independently. Rather, evaluating ***causation*** is an inferential process that is based on a comprehensive assessment of all the

relevant scientific research. The following sections discuss the methods for evaluating epidemiologic (Section 2.3) and experimental research (Section 2.4).

2.3 Evaluating epidemiology

Epidemiology is the science of understanding the causes of disease by enrolling people in studies, asking them questions about their exposures, and correlating their health events with these exposures. Scientists use two major analytic study designs in the field of epidemiology: ***case-control studies*** and ***cohort studies***.[8] A cohort study follows a pre-defined population (e.g., workers at a specific company) over time to see who develops disease. The study examines whether disease rates are different between people who were exposed to a particular agent (i.e., exposed group) and people who were not exposed (i.e., unexposed group). Cohort studies can take a great amount of time and effort to conduct because it takes a long time for diseases to develop and many diseases are rare so only a few cases will occur. Case-control studies were developed to address these limitations and can be thought of as working backwards from a cohort study. A case-control study compares people who have already been diagnosed with a disease (i.e., the cases) to a similar group of people who do not have the disease (i.e., controls). The investigators measure the prevalence and extent of past exposure in both groups to assess whether the cases have a higher exposure level or more frequent exposure than the controls, or vice versa. The goal of a case-control study is, to the extent possible, to enroll a control group that is similar to the cases on all other factors but the presence of disease. Because case-control studies "work backwards," they have more inherent limitations than cohort studies.

2.3.1 Measuring and evaluating an association

The association between a particular disease and exposure is measured quantitatively using an estimate of effect, i.e., either a ***relative risk*** (RR) or an ***odds ratio*** (OR). The general interpretation of an estimate of effect equal to 1.0 is that the exposure has no effect on the incidence of disease. If the estimate of effect is greater than 1.0, the inference is that exposure increases the risk of the disease. On the other hand, if the estimate of effect is less than 1.0, the inference is that exposure reduces the risk of the disease.

- A **relative risk** is the ratio of the rate of disease among persons who are exposed to the rate of disease among persons who are unexposed. For example, in a study of high fat diets and coronary artery disease, a relative risk of 2.0 can be interpreted to mean that persons with a high fat diet (i.e., exposed) are two times more likely to develop coronary artery disease than persons with a low fat diet (i.e., unexposed).

- An **odds ratio** is the ratio of the odds of exposure among persons with a disease to the odds of exposure among persons without a disease. For example, in a study of

[8] An additional study type is discussed in Section 2.3.3.

high fat diets and coronary artery disease, an odds ratio of 2.0 would suggest that persons with coronary artery disease are two times more likely to have had a high fat diet than persons with no coronary artery disease.

The relative risk is the better measure of potential effect since it directly compares the incidence of disease among exposed persons to the incidence of disease among unexposed persons, while the odds ratio is indirect, in that it compares exposure among persons with a disease (i.e., cases) and persons without the disease (i.e., controls). Odds ratios are typically estimated from case-control studies, while relative risks can only be measured in cohort studies.

Confidence intervals (CI) are typically reported along with odds ratios and relatives risk values. A CI 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% CI 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.

The range of the CI is also important for interpreting estimated associations. A very wide CI indicates great uncertainty in the value of the "true" risk estimate. This is usually due to a small number of observations. The larger the number of persons being analyzed in a calculation, the smaller the likelihood that an observed association is due to ***chance***. For this reason, results based on analyses with a large sample size are more easily distinguished from chance or random variation. A narrow CI provides more certainty about where the "true" relative risk estimate lies.

Another way of interpreting the CI is as follows: if the 95% CI does not include 1.0, the probability of an association being due to chance alone is 5% or lower and the result is considered ***statistically significant***. As discussed elsewhere, however, statistical significance is a measure of random variability, and other factors, including study quality and completeness, must be considered to determine whether or not a statistically significant association reflects a causal relationship.

For example, a hypothetical study of fat intake and coronary artery disease reported a relative risk of 1.9 (95% CI = 1.2-3.9). This is a statistically significant but weak positive association. The data suggests that the risk of coronary artery disease is 90% higher among persons with a high fat intake compared to persons with a low fat intake, although the increase in risk could plausibly be as low as 20%, or as high as 290%, or anywhere in between, based on the 95% CI. In summary, there are three things to consider when assessing whether an estimate of effect truly represents an association between the exposure and disease being studied:

1) The *probability* that the association is not attributable to chance based on a 95% CI that does not contain 1.0. The use of the CI provides more information than the statement "statistically significant."

2) The *magnitude* of the effect estimate, which is often referred to as its strength (i.e., strong vs. weak). Smaller estimates of effect are more likely to be affected by factors

such as ***bias*** and ***confounding***, as described below. Therefore, there is less certainty that a smaller estimate of effect represents a real statistical association.

3) The *precision* of the effect estimate, as measured by the range of values reported in the 95% CI. If the CI is narrow, there is less random variability.

In addition, it is necessary to evaluate whether the observed association is likely to be produced by bias or confounding. Bias refers to any systematic error in the design, implementation or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease. For example, if a proxy or surrogate is used to estimate exposure in place of a true exposure measurement (e.g., if a job title is used to estimate exposure to a particular agent rather than actually measuring the agent), there is the potential to introduce error into the study's findings. A confounder is something that is related to both the disease under study and the exposure of interest such that we cannot be sure what causes the observed association - the confounder or the exposure of interest.[9] If care is not taken to evaluate the role of chance and minimize bias and confounding in the design and analysis of a study, these factors can distort the study's findings.

2.3.2 Association vs. causation

An association is a relationship between two events, a finding that they occur together more often than expected by chance. A reported association between a particular exposure and disease 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. For example, we may find in a particular study that children with respiratory infections are significantly more likely to have eaten ice cream than children without respiratory infections; in other words, there is a positive association between exposure to ice cream and respiratory infections that is not likely to be due to chance. However, based upon this information alone we obviously could not conclude that ice cream is a cause of respiratory infections.

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

[9] 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 (Kelsey et al, 1996). In this example, smoking confounded the relationship between coffee drinking and low birth weight.

remain. 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 meant to be an inflexible set of rules; rather, they serve as guidance for weighing the evidence to reach a decision about the plausibility of a cause-and-effect relationship. The more firmly these criteria are met by the data, the more convincing the evidence. For example, the presence of a dose-response relationship provides weight in support of a cause-and-effect relationship; however, it does not, in and of itself indicate a cause-and-effect relationship. Referring to the hypothetical example discussed above, the totality of the evidence would more strongly suggest that ice cream may be a cause of respiratory infections if: 1) strong associations were also found in other epidemiologic studies and these associations showed a dose-response relationship; 2) animals with high ice cream intake also had an increased incidence of respiratory infections; and 3) an organism was isolated from the ice cream that could cause the infection.

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

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

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

2.3.3 Meta- and pooled analyses

In scientific research, the results of smaller studies may be 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 altogether. These methods are valuable because they increase the number of individuals in the analysis, which allows for a more robust and stable estimate of association. Meta- and pooled analyses are also an important tool for qualitatively synthesizing the results of a large group of studies.

The disadvantage of meta- and pooled analyses is that they can convey a false sense of consistency across studies if *only* the combined estimate of effect is considered (Rothman and Greenland, 1998). These analyses typically combine data from studies with different study populations, methods for measuring and defining exposure, and definitions of disease. This is particularly true for analyses that combine data from case-control studies, which often use very different methods for the selection of cases and controls and exposure assessment. Therefore, in addition to the synthesis or combining of data, meta- and pooled analyses are used to understand what factors cause the results of the studies analyzed to vary, and how these factors

affect the associations calculated from the data of all the studies (Rothman and Greenland, 1998). For example, Greenland et al. (2000) performed analyses to assess how excluding particular studies from the group impacted the results of the analysis. In summary, meta- and pooled analyses are a valuable technique in epidemiology; however, in addition to calculating a summary relative risk, meta- and pooled analyses should analyze the factors that contribute to any heterogeneity between the studies.

2.3.4 Exposure estimation for EMF

One of the most crucial aspects in the review of any epidemiology study is an evaluation of how exposure was measured. A good exposure metric should measure the element that is believed to cause the disease at the appropriate time in the disease process. Estimating exposure to EMF is difficult since: 1) EMF is ubiquitous; 2) exposure is often estimated retrospectively; and 3) there is currently no accepted biological mechanism for carcinogenicity or any other disease process, so the appropriate exposure metric and timing is unknown. In the absence of substantive knowledge about a specific mechanism by which magnetic fields could affect normal cells, the focus on long-term exposures is based upon the standard assumption that exposures that affect the development of cancer require repeated exposures 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 magnetic field measurements to estimate a person's long-term average exposure, i.e., their ***time-weighted average (TWA)*** exposure. One method of estimating a person's TWA exposure is to sum all magnetic field exposures encountered during the day (e.g., while at work or school, at home, at a grocery store, shopping, etc.), weight each estimate by the number of hours in that environment, and divide that value by the total number of hours.

Exposure to magnetic fields has been quantitatively estimated in studies using a variety of methods, including:

1) Categories of exposure based on the number and thickness of power line conductors and their distance to nearby residences (***wire code categories***);

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

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

4) Calculations of fields from nearby transmission lines using information on loading, height, configuration, etc.

In general, studies that estimate long-term exposure using personal magnetic field measurements are preferred. In a recent analysis of children from 5 Canadian provinces, the children wore personal exposure meters, which took single readings each minute for 48 hours to estimate the child's 48-hour average magnetic field exposure (Armstrong et al., 2001). Since this type of measurement may be cost prohibitive in some locations, the investigators

evaluated what proxy exposure measures might best predict the child's 48-hour average magnetic field exposure. 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 were not found to be an accurate predictor of a child's exposure.

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

2.4 Evaluating experimental research

2.4.1 General research methods

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

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

In Vivo animal 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 (USEPA, 2005; USEPA, 2002; IARC, 2002 preamble; Health Canada, 1994; WHO, 1994). From a public health perspective, long-term (chronic) studies in which animals undergo exposure over most of their lifetime, or during their entire pregnancy, are of high importance in assessing potential risks of cancer and other adverse effects. In these long-term studies, researchers examine a large number of anatomical sites to assess changes and adverse effects in body organs, cells, and tissues.

These data are used in the hazard identification step of the risk assessment process by agencies to determine whether an environmental exposure is likely to produce cancer or damage organs and tissues. Health Canada specifies 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 EPA recently stated, "…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" (page 2-22, USEPA, 2005).

In Vitro cellular studies

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

Additional information on experimental research methods specific for cancer and developmental effects is discussed below.

2.4.2 Experimental methods for cancer

Cancer research in the laboratory includes specific types of studies to assess the 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. This is also known as ***initiation*** or induction. Other steps, or stages, must occur for a cancerous cell to develop into a tumor, and one of these stages is often referred to as ***promotion***. Some exposures affect both of these stages, and are known as complete carcinogens. Other types of exposures affect only initiation, or only promotion. 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.

In vitro assays isolate specific cells or microorganisms in glassware in the laboratory to assess the likelihood that exposure to the agent can cause mutations, a step necessary in the initiation of cancer. Initiation tests have also been developed in animals, in which scientists expose them for less than lifetime periods to determine whether an exposure causes changes typical for early 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 cellular changes typical of initiation have already occurred. Studies of promotion include two steps: first, exposing the experimental animals to a chemical known to initiate cancer, and second, exposing the animals to the agent to be tested as a promoter. The occurrence of cancer in the animals exposed in both steps is compared to the occurrence of cancer that develops in animals exposed only to the initiator.

2.4.3 Experimental methods for developmental toxicity

Studies in animals are also used to assess whether an exposure can pose 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 animal studies are used by regulatory agencies to assess risk and help set human exposure limits (USEPA, 1991; USEPA, 1998; NTP, 2007).

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, or further exposure to the animal after it 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 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 animal 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 3 different dose groups. One of these dose groups is a high level 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 in the analysis of results 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 considered 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. Again, 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	The 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.

3 Conclusions of weight-of-evidence reviews on EMF

Scientists, scientific organizations, and regulatory agencies use the weight-of-evidence approach worldwide to assess the health risk associated with exposures. These expert groups have included many scientists with diverse skills that reflect the different research approaches required to answer questions about health. Using a weight-of-evidence approach as an analytic framework, each group has provided its scientific consensus based on a review of the evidence. In this assessment, we focus on the weight-of-evidence reviews published December 1, 2005 – August 31, 2007 by the national and international scientific panels that have considered this issue (SCENIHR, 2007; SSI, 2007; WHO, 2007).[10] We also make reference to weight-of-evidence reviews that were published by scientific organizations prior to 2005, the full details of which can be found in Exponent 2005. While some of these reviews are not explicitly referred to as "weight-of-evidence reviews," each of these panels consisted of a group of scientists that used a structured and systematic process to weigh both the laboratory and epidemiologic evidence and provide a conclusion about causality. In particular, this assessment focuses on the conclusions of the scientific panel assembled by the WHO, because it is the most recent.

In an earlier report, the WHO provided insight as to why reviews by reputable scientific organizations are important to weighing 30 years of literature on a single topic:

> Science is a powerful tool and has earned its credibility by being predictive. However, its usefulness depends on the quality of the data, which is related to the quality and credibility of the scientists. It is important to verify the knowledge and integrity of so called "experts," who may look and sound extremely convincing but hold unorthodox views that the media feel justified in airing "in the interests of balance." In fact giving weight to these unorthodox views can disproportionately influence public opinion. For the public, often the best sources of information are from panels of independent experts who periodically provide summaries of the current state of knowledge. (WHO, 2002)

3.1 Recent weight-of-evidence reviews

Overall, the conclusions of scientific review panels have been consistent. None of the panels concluded that magnetic fields are a known or likely cause of any long-term adverse health

[10] We are aware of other summaries of the EMF research that have been published over the past 1-1/2 years. In particular, with an increase in transmission infrastructure development and the advent of the Internet, various reviews and summaries are being released on an ongoing basis. 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, which do not follow this approach are not addressed because they do not assist in making science-based risk assessments and conclusions.

effect and, as a result, no standards or guidelines have been recommended for magnetic fields at the strengths normally encountered in our environment. Most of the uncertainty and controversy surrounding magnetic fields is still 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 the 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 exposures greater than 3-4 mG (Ahlbom et al., 2000; Greenland et al., 2000). These calculations, referred to here as pooled 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 not considered to provide strong epidemiologic support for a causal relationship. 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, panels issuing conclusions following the publication of the pooled analyses characterized **magnetic** fields as a *possible* cause of childhood leukemia (NRPB, 2001a; IARC, 2002; ICNIRP, 2003; HCN, 2004). 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.

The IARC classified electric fields as "not classifiable as to their carcinogenicity to humans" (p. 338). More studies have focused on magnetic field exposures because, among other reasons, conductive objects block electric fields. The epidemiologic studies that estimated electric field exposure also have not produced suggestive associations, although the IARC concluded that the epidemiologic evidence related to electric fields is "inadequate" because of major qualitative or quantitative limitations in the data.

The recent evaluations of the latest research have concluded that the classification of "possible carcinogen" for magnetic fields remains appropriate (SCENIHR, 2007; SSI, 2007; WHO, 2007). These views have stressed the importance of reconciling the epidemiologic data on childhood leukemia and the lack of evidence from experimental studies through innovative research. Just like any other cancer, researchers believe that the development of childhood leukemia is influenced by a multitude of different factors, e.g., genetics, environmental exposures, and infectious agents (Buffler et al., 2005; McNally et al., 2006).

Both the IARC and ICNIRP concluded that the epidemiologic evidence does not support a cause-and-effect relationship between magnetic fields and adult leukemia/lymphoma or brain cancer; recent studies have not altered that conclusion (SCENIHR, 2007; WHO, 2007). Breast cancer has received more attention because of some initial epidemiologic and experimental findings suggesting that magnetic fields may alter levels of the hormone melatonin, leading to the development of breast cancer (i.e., the melatonin hypothesis). An additional review by the Health Protection Agency (HPA) of Great Britain in 2006 concluded that the evidence to date

did not support the hypothesis that exposure to magnetic fields affects melatonin levels, or the risk of breast cancer (HPA, 2006).[11] The SCENIHR and WHO reviews concluded that recent studies added support to the conclusion that magnetic fields are not associated with breast cancer (SCENIHR, 2007; WHO, 2007). With regard to miscarriage, two epidemiologic studies reported a statistical association between peak magnetic field exposure and miscarriage (Lee et al. 2002; Li et al. 2002), although a serious bias in how these studies were conducted was identified and various scientific panels concluded that these biases preclude making any conclusions about the effect of magnetic fields on miscarriage (HCN, 2004; NRPB, 2004; WHO, 2007).

Some epidemiologic studies on neurodegenerative diseases (including Alzheimer's disease and Amyotrophic Lateral Sclerosis [ALS]) have reported associations with estimates of occupational magnetic field exposure. The scientific panels have recommended more research in this area, particularly with regard to ALS, as the initial studies were of relatively low quality (NRPB, 2001b; SCENIHR, 2007; WHO, 2007).

In summary, reviews of the research published over the last few years concluded that the cumulative body of research to date does not support the idea that magnetic fields cause any long-term adverse health effects at the levels we encounter in our everyday environments.

For additional reference, the sections below provide a more detailed summary of each scientific panel, the methods they employed to review the evidence, and their scientific conclusions.

3.1.1 The World Health Organization (WHO)

The World Health Organization is a scientific organization within the United Nations system whose mandate includes providing leadership on global health matters, shaping the health research agenda, and setting norms and standards. WHO established the International EMF Project in 1996, in response to public concerns about exposures to EMF and possible adverse health effects. The Project's membership includes 8 international organizations, 8 collaborating institutions and over 54 national authorities. The overall purpose of the project is to assess health and environmental effects of exposure to static and time varying EMF in the frequency range 0-300 GigaHertz (GHz). A key objective of the Project is to evaluate the scientific literature and make a status report on health effects, to be used as the basis for a coherent international response, including the identification of important research gaps and the development of internationally acceptable standards for EMF exposure. The WHO's weight-of-evidence review was published in June 2007 as part of their Environmental Health Criteria (EHC) Programme.

The WHO used standard scientific procedures to conduct its health risk assessment. The Task Group responsible for the report's overall conclusions consisted of 21 scientists from around the world with expertise in a wide range of disciplines. The Task Group relied on the

[11] The National Radiation Protection Board of Great Britain (NRPB) merged with the HPA in April 2005 to form its new Radiation Protection Division.

conclusions of previous weight-of-evidence reviews, where possible, and (with regard to cancer) mainly focused on evaluating studies published after the IARC review in 2002. Specific terms were used by the Task Group to describe the strength of the evidence in support of causality. *Limited evidence* was used to describe a body of research where the findings are inconsistent or there are outstanding questions about study design or other methodological issues that preclude making strong conclusions. *Inadequate evidence* describes a body of research where it is unclear whether the data is supportive or unsupportive of causation because there is a lack of data or there are major quantitative or qualitative issues. The WHO also used the IARC method for categorizing exposures based on their likely carcinogenicity. Categories include (from highest to lowest risk): carcinogenic to humans, probably carcinogenic to humans, possibly carcinogenic to humans, unclassifiable, and probably not carcinogenic to humans. These categories are intentionally meant to err on the side of caution, giving more weight to the possibility that the exposure is truly carcinogenic and less weight to the possibility that the exposure is not carcinogenic. The category "possibly carcinogenic to humans" denotes exposures for which there is limited evidence of carcinogenicity in epidemiology studies and less than sufficient evidence of carcinogenicity in studies of experimental animals.

The WHO Report provided the following conclusions:[12]

> New human, animal, and in vitro studies published since the 2002 IARC Monograph, 2002 [sic] do not change the overall classification of ELF as a possible human carcinogen (p. 347).

> Acute biological effects [i.e., short-term, transient health effects such as a small shock (see Section 3.2)] have been established for exposure to ELF electric and magnetic fields in the frequency range up to 100 kHz that may have adverse consequences on health. Therefore, exposure limits are needed. International guidelines exist that have addressed this issue. Compliance with these guidelines provides adequate protection. Consistent epidemiological evidence suggests that chronic low-intensity ELF magnetic field exposure is associated with an increased risk of childhood leukaemia. However, the evidence for a causal relationship is limited, therefore exposure limits based upon epidemiological evidence are not recommended, but some precautionary measures are warranted (p. 355).

3.1.2 Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

The SCENIHR is a committee that provides advice to the European Commission (EC) on issues of public health. The Working Group responsible for the report on EMF consisted of

[12] More specific conclusions from the WHO report are provided in discussions of specific outcomes in the literature update (Section 4).

nine persons with expertise in various fields. The SCENIHR issued their first report on EMF in March 2007 as an update to a report released in 2001 to the Health Directorate of the EC (CSTEE, 2001).[13] The purpose of the 2007 report was not to provide an exhaustive review, but to note new findings since 2001 and characterize risks.

The report provided the following conclusion on ELF-EMF:

> The previous opinion came to a similar conclusion regarding carcinogenicity of ELF fields as IARC's evaluation, namely that ELF magnetic fields are possibly carcinogenic. This conclusion was mainly based on epidemiologic results indicating that exposure to EMF fields might be a cause of childhood leukemia. This assessment is still valid. The fact that epidemiological results for childhood leukemia have little support from known mechanisms or experimental studies is intriguing and it is a high priority to reconcile these data.
>
> For some other diseases, notably breast cancer and cardiovascular disease, later research has indicated that an association is unlikely. For yet some other diseases, such as neurodegenerative disease and brain cancer, the issue of an association to ELF fields remains open and more research is called for. A relation between ELF fields and symptoms has not been demonstrated (p. 37).

3.1.3 Swedish Radiation Protection Authority (SSI)

The SSI is an "international independent expert group for electromagnetic fields and health" consisting of eight scientists. Using other major scientific reviews as a starting point, the SSI has evaluated recent studies in consecutive annual reports.[14] The report released in 2007 was their fourth annual report.

The report concluded that recently published studies on childhood leukemia are in line with previous findings and that recently published animal and *in vitro* studies on genotoxicity have not provided evidence that ELF magnetic fields can damage DNA. They also identified no new plausible biological mechanisms to explain the statistical association between childhood leukemia and magnetic fields.

[13] The 2001 report of the Scientific Committee on Toxicity, Ecotoxicity, and the Environment (CSTEE) was not included in the Exponent 2005 report because priority was given in that report to scientific organizations that, at one time, had published a full weight-of-evidence review of the published literature, rather than reports that reviewed the research in separate documents periodically as it became available.

[14] Previous SSI reports were not mentioned in the Exponent 2005 report because priority was given in that report to scientific organizations that, at one time, had published a full weight-of-evidence review of the published literature, rather than reports that reviewed the research in separate documents periodically as it became available.

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. These guidelines set limits at high field levels to protect against the direct, acute health effects (i.e., stimulation of nerves and muscles, a shock-like effect) that can occur at these high field levels. Although the ICNIRP and ICES have the same objectives[15] and used similar methods, the recommended limits for exposure of the general public to EMF at the frequencies used to transmit electricity differ, as seen in Table 3. Exposure standards are set based on acute effects – those that occur from short-term exposure to high levels – because both organizations judged that evidence for effects from long-term exposure to ELF-EMF was insufficient for setting exposure standards.

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

Organization Recommending Limit	Magnetic Fields [a]	Electric Fields [a]
ICNIRP Restriction Level	833 mG	4.2 kV /m
ICES Maximum permissible exposure (MPE)	9,040 mG	5 kV/m 10 kV/m [b]

a. Both organizations judged that evidence for effects from long-term exposure was insufficient for setting exposure standards.

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

The ICNIRP recommends a residential exposure limit to magnetic fields of 833 mG and an occupational exposure limit of 4,200 mG (ICNIRP, 1998). The ICES recommends that magnetic field exposures be limited to 9,040 mG (ICES, 2002). Magnetic field levels in ordinary environments are far too low to cause acute effects.

As Table 3 shows, there is some difference between in the electric field limits of ICNIRP and ICES. The ICNIRP guideline for general public exposure is 4.2 kV/m, and the ICES guideline for general public exposure is 5 kV/m. These guidelines are the same as those reported in Exponent 2005 and remain unchanged despite additional research and reviews.

[15] The scope of ICES is the "Development of standards for the safe use of electromagnetic energy in the range of 0 Hz to 300 GHz relative to the hazards of exposure to man … to such energy." ICES encourages balanced international volunteer participation of the public, the scientific and engineering community, agencies of governments, producers, and users. ICNIRP is an independent group of approximately 40 experts assembled from around the world. It is the formally recognized, non-governmental organization charged with developing safety guidance for non-ionizing radiation for the WHO, the International Labour Organization, and the European Union.

The discussion in this section of the biological basis for the standard focuses mainly on electric fields, because exposure to magnetic fields can induce or conduct electric fields into the body. Thus, limits on internal levels of electric fields are the basis of both the electric and magnetic field standards**.**

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

> At present, there are no Canadian government guidelines for exposure to EMFs at ELF. Health Canada does not consider guidelines necessary because the scientific evidence is not strong enough to conclude that typical exposures cause health problems. (Health Canada, 2004)

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

3.2.2 Similarities between ICES and ICNIRP guidelines

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

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

The ICNIRP and ICES basic restrictions are set well below the value at which an adverse effect was observed in experiments, therefore these exposure limits are conservative.[16] This is because they incorporate dose reduction factors, known as ***safety factors*** to account for potential sources of uncertainty. For example, both groups consider the potentially higher sensitivity in vulnerable groups as a reason for using a safety factor.

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

3.2.3 Differences between the two guidelines

While both the ICNIRP and ICES standards are designed to protect against short-term reactions to electrostimulation of nerve and muscle, they are based on different aspects of the data (Reilly, 2005). ICES estimates an internal field that would lead to a 1-percent reaction level in the most sensitive tissue, and then applies a safety factor of 3, whereas ICNIRP identified an adverse effect level that is 28 times higher than ICES, does not specify the probability of effect on any specific tissue, and applies a safety factor of 50. Table 4 shows the main factors responsible for the differences in electric field limits between the two standards.[17] These differences also affect the magnetic fields limits.[18]

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

[17] The WHO (2007) acknowledges that the guidance recommended by ICNIRP is more restrictive than that recommended by ICES. As the WHO (2007) notes "The major factor responsible for this difference [between the standards] is the cut-off frequency … at which thresholds for electric field strength and induced current density begin to rise."

[18] The derivation of the magnetic field standard is not further addressed in this report other than the note above that the standard is based on short-term effects due to the inadequate evidence for long-term effects. The exposures of the public to magnetic fields from transmission lines are more than 10 – 100 fold lower than the ICNIRP limit.

Table 4. Scientific basis of exposure limits for the general public at 60-Hz

Organization Recommending Exposure Limit	Health and Scientific Basis	Threshold Estimate for Internal Electric field (E-field) [a]	Safety Factor
ICNIRP Restriction Level	Effect level, not a threshold, for acute changes in central nervous system excitability. Applies to head and torso.	500 mV/m[c]	50[b]
ICES Maximum permissible exposure (MPE)	Threshold for median (50%) probability of changes in synaptic response in brain, the most sensitive tissue, reduced 3-fold to estimate threshold for a 1% response level. Applies only to head	5.9 mV/m	3

a. The standard is based on the internal or *in situ* E-field, called a basic restriction in both of the guidelines. The actual exposure limits, expressed in kV/m, are based on the measured environmental level deemed likely to lead to that internal E-field.

b. 50-fold safety factor based on a 10-fold reduction to reduce it to a level deemed unlikely to cause effects, and an additional 5-fold for general public exposure. (ICNIRP, 1998 p. 509)

c. The ICNIRP basic restriction or the general public is 2 mA/m^2, but has been transformed to mV/m to facilitate comparison with the ICES level.

3.2.4 Implications for human health

The underlying question for people who make decisions about public health and safety is whether the ICNIRP reference value (4.2 kV/m) implies greater safety simply because it is lower and includes a larger "safety factor." In developing public health standards, safety factors are used when uncertainty is recognized, and the general rule is that smaller safety factors are needed as the relevant information on risk to humans is improved. As can be seen in Table 4, although ICNIRP uses a larger safety factor, it applies that factor to a higher level of exposure as the 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 like these that have a threshold, the goal of the standard setting process is to set the exposure limit where no effects will occur in the population. Therefore, further lowering of the exposure limit is not expected to have any health benefit. For additional perspective on the question of the safety of exceeding ICNRIP exposure limits up to the level of the ICES limits, consider that ICNIRP states that EMF guidelines are conservative,[19] and that the ICNIRP recommended limit for occupational exposure is 8.3 kV/m (ICNIRP, 1998).

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

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, precautionary measures may be taken that are proportional to the perceived level of risk, with science as the basis for measuring 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 reduce the level of adverse effects in the population.

The EC prepared a report to clarify what became known as "the precautionary principle" because it had been subject to controversy and variability in interpretation.[20] The EC report explained that the implementation of the precautionary principle should be science based, starting with a complete scientific evaluation, and the range of actions taken should depend on the extent of the risk and the degree of uncertainty surrounding the occurrence of adverse effects. The EC provided guidelines for the application of the precautionary principle or other risk management measures as five general principles: proportionality, non-discrimination, consistency, examination of costs and benefits of actions, and examination of scientific developments.[21]

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).

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[20] 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]

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

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

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

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

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

3.3.2 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).

3.3.3 WHO recommendations regarding precautionary measures for EMF

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

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

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

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

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

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

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

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

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

- Government and industry should promote research programs to reduce the uncertainty of the scientific evidence on the health effects of ELF field exposure. (adapted from pp. 372-373, WHO 2007)

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 (p. 367).

4 Evaluation of recent EMF research

This section summarizes an up-to-date assessment of the current literature to determine whether recent findings are consistent with the conclusions of the scientific panels presented in Section 3. Exponent 2005 reviewed the literature through December 2005; therefore, this assessment reviews literature published December 1, 2005 through August 31, 2007. Childhood leukemia, adult leukemias and lymphomas, brain cancer, breast cancer, reproductive and developmental outcomes, and neurodegenerative diseases are considered.

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 is carried out using a weight-of-evidence approach with standard epidemiologic principles and Hill's guidelines as an analytic foundation. All relevant research as identified below is taken into consideration and more weight is assigned to studies that are well designed and 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, as described in Section 2.4.1 above, such data are supplementary to epidemiology and whole animal studies, and are not directly used by health agencies to assess risk to human health. For that reason, this review systematically addresses epidemiology studies and *in vivo* studies, but relies largely on reviews and the conclusions of scientific panels with regard to studies of mechanism (see Section 4.6.3).

4.1 Details of the literature search process

A standard literature review begins with a search for relevant literature. A structured literature search was conducted according to published, standard criteria (Stroup et al., 2000) using PubMed, a search engine provided by the National Library of Medicine and the National Institutes of Health that includes over 15 million up-to-date citations from MEDLINE and other life science journals for biomedical articles dating back to the 1950s (http://www.pubmed.gov). A well-defined search strategy was used to identify epidemiologic publications between December 1, 2005 and August 31, 2007, as detailed in Figure 1 of the Appendix. Only published, peer-reviewed studies were considered. The literature review was supplemented by hand searching the reference lists of retrieved articles.

All fields (title, abstract, etc.) were searched for a term that referenced the exposure of interest (EMF, magnetic fields, electric fields, or electromagnetic) *and* the outcome of interest: cancer (cancer, leukemia, or lymphoma), neurodegenerative disease (neurodegenerative disease, Alzheimer's disease, amyotrophic lateral sclerosis, or Lou Gehrig's disease), or reproduction (miscarriage, reproduction or development). An epidemiologist reviewed the titles and abstracts of these publications, 49 of which were epidemiology-related publications on 50/60-Hz[22] alternating current (AC) ELF-EMF and health effects. Of these 49 publications, 27 original studies and 1 pooled analysis were identified. For each disease outcome discussed below (i.e., childhood leukemia [7 studies], adult leukemia/lymphoma [5 studies], brain cancer [4 studies], breast cancer [6 studies], reproductive outcomes [3 studies], and neurodegenerative diseases [3 studies]), the full-text of the retrieved studies was evaluated to assess the relevance of the study and the adequacy of its design for assessing whether exposure to EMF was associated with the adverse health outcome. The following additional inclusion criteria were applied to the retrieved epidemiologic studies:

1. Only case-control and cohort studies were included. ***Case-series*** or case reports and analyses of perceived cancer ***clusters*** were excluded. These study designs lack a control group, and generally include a small sample size, which provides little information for assessing causation; rather, these studies are typically only helpful for hypothesis generation**.**

2. Included studies must address the following hypothesis in some capacity: is exposure to magnetic or electric fields associated with the adverse health outcome being studied?

3. Included studies must assess EMF exposure beyond a self-reported job title.[23]

The remaining studies were considered, in concert with the review panels' conclusions, in a weight-of-evidence review. When considering all of the epidemiologic reports together, causality is more likely if high-quality studies report dose-response patterns and consistent results across many different populations and study designs. After weighing the evidence from each study, Hill's criteria were used as an analytic guide for deriving a conclusion with regard the interpretation of reported associations. As discussed in Section 2, a weight-of-evidence review assigns more weight to studies with a better design. While there are many factors involved in the critical analysis of epidemiology studies, a few important tenets are recognized in the analytic framework of several of the major reviews and are worth mentioning (FPTRPC,

[22] The frequency associated with the transmission and distribution of electricity outside of the United States and Canada is typically 50-Hz. One study (Roosli et al., 2007) examined exposure to 16.7-Hz magnetic fields among railway workers, but was still considered given that this frequency is within the ELF range.

[23] 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).

2005; IARC, 2002). First, the authors should clearly define the study population and the disease and exposure under study. Second, it is vital to assess the impact of bias, confounding and chance on the study's results. Methodologically sound studies include those that are large (to decrease the role of chance and increase precision), test for relevant confounders and use methods that reduce the possibility of ***bias***. Finally, the methods and data upon which the conclusions of the study are based should be clearly reported and based on accepted techniques.

4.2 Leukemia and lymphomas

4.2.1 Childhood leukemia

Childhood leukemia was the first disease investigators examined to understand its possible relation to magnetic field exposures in epidemiologic studies, and it remains the most controversial because of suggestive (but methodologically limited) epidemiologic results that conflict with experimental findings. Since the first investigation in 1979, approximately 25 epidemiologic studies have been conducted of varying methods and designs and by different investigators in the United States (US), Canada, Germany, the United Kingdom (UK), New Zealand, Denmark, Finland, Norway and Sweden that have addressed the possible association between childhood leukemia and magnetic fields in some facet. When the data was combined from a subset of these studies into one analysis, a 1.7- to 2-fold association was reported among the few children exposed to long-term, average magnetic field levels greater than 3-4 mG; no association was reported in the lower exposure categories (Ahlbom et al., 2000; Greenland et al., 2000).

After considering this body of research, multidisciplinary scientific panels concluded that long-term exposure to magnetic fields at levels above 3-4 mG is a *possible* cause of childhood leukemia. The panels did not conclude that magnetic fields are a *known* cause of childhood leukemia because, while the observed association does not appear to be a chance occurrence, they could not rule out that errors in the way these studies were conducted or the lack of control for unknown confounding variables are a cause of some, or all, of the observed association. More importantly, the data remain unconvincing for a causal association because studies conducted in animals have not reported consistent increases in the incidence of cancer among highly exposed animals, nor have investigators identified a mechanism at the cellular level which could explain how magnetic fields would initiate or promote carcinogenesis, or any other disease process. This is reflected in the conclusion on childhood leukemia from the Exponent 2005 report:

> In summary, recent studies do not alter the conclusion that there is no consistent or convincing evidence that exposure to magnetic fields is a cause of childhood leukemia. The current body of evidence for a causal relationship is weak, at best. Researchers are increasingly focusing on new hypotheses as to what could cause childhood leukemia, including

> whether exposure to viruses or bacteria may promote cancer (McNally and Eden, 2004). (p. 36)

The WHO reached a similar conclusion in its June 2007 report. The report listed a causal relationship as one of several alternative interpretations of the association observed in epidemiologic studies. The other possible explanations included random variation or chance, systematic errors (including ***selection bias*** and misclassification bias) and other factors that could confound the association. The issue remains unresolved, and research to assess the role of these factors is considered important. The WHO, as well as other scientific panels, recommended that future research use novel and sound methods to understand what is causing the observed statistical association (i.e., bias, confounding, or a real causal relationship).

Recent studies have followed-up on this recommendation by asking tangential questions:

- Do magnetic fields contribute to the higher rate of childhood leukemia among genetically susceptible children? (Mejia-Arangure et al., 2007)
- Do magnetic fields contribute to a worse prognosis among those already diagnosed with childhood leukemia? (Foliart et al., 2006, 2007; Svendson et al., 2007)
- Is the association more strongly influenced by nighttime magnetic field exposures? (Schüz et al., 2007)
- Do trends in the incidence of childhood leukemia correlate with trends in average population magnetic field exposures? (Kheifets et al., 2006)

The recent literature also includes two case-control studies that were conducted in non-Western countries, i.e., Iran and Japan (Feizi and Arabi, 2007; Kabuto et al., 2006, respectively).[24]

[24] Lowenthal et al. (2007) also included cases of leukemia among children, although most cases were among adults so this study is included in the adult leukemia section (Section 4.2.2).

Case-control studies

In the case-control study by Feizi and Arabi (2007), interviews were conducted with the mothers of 60 children with leukemia and 59 children without leukemia to determine the distance from their home to any nearby power lines. The study recruited cases and controls from hospitals, which may introduce bias.[25] The investigators reported that children with leukemia were more likely to reside in homes within 500 meters of a transmission line compared to the children selected for the control group (OR=8.76, 95% CI=1.74-58.4); cases were also more likely to have estimated magnetic field exposures greater than 4.5 mG (OR=3.60, 95% CI=1.11-12.39), using standard formulas to calculate exposures from power lines.

This study was based on consecutively diagnosed cases from hospitals in one city. Its ***validity*** is significantly limited by its small size, possible selection bias, and lack of assessment of confounding variables (such as socioeconomic status and mobility), and reliance upon distance as a proxy for exposure. The results are similar to, but much more limited than, the much larger study by Draper et al. in 2005, which reported that birth addresses of leukemia cases were more likely to be within 600 meters of a high-voltage transmission line. A much higher percentage of children with leukemia lived in close proximity to transmission lines in the study by Feizi and Arabi compared with the study by Draper et al. (2005), which (according to the authors) is a result of housing conditions in some developing countries, including Iran. The WHO concluded the following, with respect to the Draper et al. findings:

> [the] observation of the excess risk so far from the power lines, both noted by the authors and others, is surprising. Furthermore, distance is known to be a very poor predictor of magnetic field exposure, and therefore, results of this material based on calculated magnetic fields, when completed, should be much more informative. (p. 270)

The same conclusions apply to Feizi and Arabi (2007).

Kabuto et al. conducted a larger case-control study in Japan that measured the average weekly magnetic field level in the bedrooms of 312 children with leukemia and 603 children without leukemia. The investigators reported that children with leukemia were more likely to have average magnetic field levels >4 mG, compared to children without leukemia. The association was statistically significant (i.e., unlikely to be due to chance) when acute lymphocytic leukemia (ALL) was considered alone and no confounding variables were controlled for in the risk estimate (OR=4.67, 95% CI=1.15-19.0). This study's strength is its exposure assessment in that measurements were taken continuously over a weeklong period approximately one year after a diagnosis of leukemia. There are several shortcomings of this study, however, that limit its overall weight in this assessment. The intent of the study was to include all leukemia cases identified between 1999 and 2001 from five urban regions in Japan; however, nearly half of the leukemia cases declined to participate, the lowest ***participation rate*** ever reported in a case-

[25] Studies that use hospital-recruited cases and controls (as opposed to study subjects recruited from the general population) are typically more prone to bias because it is difficult to identify the true source population and the control group is also diagnosed with conditions and illnesses, which may be related to the exposure of interest.

control study of childhood leukemia and EMF. The participation rate for controls was also extremely low (16%). Low participation is a significant source of bias because the association may be distorted if there are important differences between the children who participated in the study and those that did not (i.e., selection bias).[26] Another limitation of this study was its small sample size in the highest exposure category (6 ALL cases and 3 controls had an average exposure >4 mG). A small sample size makes the reported results unstable – if a few children are classified in the wrong exposure category, the results can change. This is a common limitation of studies of childhood leukemia, in which the association depends upon the exposures of a few children at the upper end of the population distribution of exposure.

The WHO considered the Kabuto et al. study in its 2007 review concluding, "The low response rate was a limitation of this study. Thus the addition of this study to the database will not add much as far as the overall results are concerned" (p. 269).

Both the recent Iranian and Japanese case-control studies reported results that are consistent with the previously observed association between magnetic field exposures greater than 3-4 mG and childhood leukemia. When these studies are examined individually for methodological soundness, however, and then evaluated in the context of the entire body of literature, neither study provides evidence to change the conclusion that the observed association provides limited support for a causal relationship. The uncertainty surrounding the impact of selection bias in Kabuto et al. and the small study size and crude methods for estimating exposure in Feizi and Arabi suggest that less weight should be placed on these studies relative to studies of magnetic fields and childhood leukemia that were population based and also had good exposure assessments, but did not have low participation rates (e.g., Linet et al., 1997; McBride et al., 1999; UKCCS et al., 2000).

Nighttime exposures

Schüz et al. conducted a pooled analysis of a subset of studies to test whether the association observed in the previous pooled analyses is the result of magnetic field exposures occurring during the nighttime hours, as reported in an earlier study by Schüz et al. (2001) in Germany. The analysis pooled results from studies that reported average 24- or 48-hour magnetic field exposure levels, including studies conducted in Canada (McBride et al., 1999), the US (Linet et al., 1997), Germany (Michaelis et al., 1997; Michaelis et al., 1998; Schüz et al., 2001), and the UK (UKCCS, 1999). The pooled ORs reported for average 24-hour exposure levels were similar to those reported for average nighttime exposure levels in the categories 1-2 mG, 2-4 mG, and >4 mG. When analyzed alone, the only study reporting an association for nighttime exposures was the German study by Schüz et al. in 2001. Thus, the authors concluded that nighttime exposures do not explain the observed association between exposure to high, average

[26] For example, if the parents of a child with leukemia were informed that the study was investigating magnetic field exposure and they resided close to a transmission line, they may be more likely to participate than a family that lived far from a transmission line. As a result, children with leukemia that lived closer to transmission lines (and with a presumably higher magnetic field exposure) would be over-represented in the study population compared to the source population. In this scenario, the study may report that children with leukemia are more likely to have higher magnetic field exposure when, if the entire ***source population*** of leukemia cases had participated, there would be no difference in the exposure levels between leukemia cases and controls.

magnetic field levels and childhood leukemia. A recent experimental study in mice predisposed to develop lymphoma also reported that mice exposed to magnetic fields only at night exhibit no increased risk of cancer (Sommer and Lerchl, 2006).

Magnetic fields and leukemia survival

Foliart and colleagues tested a new hypothesis: among children already diagnosed with ALL, is exposure to higher, average magnetic field levels associated with a worse prognosis (i.e., a shorter survival time or more relapses, secondary malignancies, or treatment failures)? Magnetic field exposure was assessed in 386 children diagnosed with ALL, using a personal monitor for a 24-hour period shortly after diagnosis. Increasing exposure was not associated with more events (death, relapse, secondary malignancy, or treatment failure), overall. There was a statistically significant ***hazard ratio***, however, for magnetic field exposure ≥3 mG and death (from any cause) compared to ≥1 mG, but the result was based on only four deaths and there was only borderline evidence for a dose-response relationship in ***multivariate analyses*** (p=0.06). A subsequent publication on the same study population reported that magnetic field exposure ≥3 mG was not associated with markers of poorer ALL prognosis (e.g., particular chromosomal rearrangements, clinical factors such as platelet counts, etc.), suggesting that the association observed in the earlier study is not caused by a magnetic-field effect on these variables (Foliart et al., 2007). The studies were limited by a very low participation rate (29%), small numbers in the highest exposure categories, and the lack of prospective information on magnetic field levels among residentially mobile children. After noting these limitations, the authors concluded:

> Although we report poorer survival among children with the highest MF exposure category, clinical inferences are limited, with results possibly attributable to chance alone. Independent confirmation is needed, as our study is the first to look at relapse and survival and thus our findings can be viewed only as hypothesis generating (p. 164).

Shortly after the publication of the studies by Foliart et al., Svendsen et al. (2007) evaluated the same hypothesis on a group of 486 German children with ALL assembled from previous case-control studies conducted in Lower Saxony, Berlin, and the former West Germany (Michaelis et al., 1997; Michaelis et al., 1998; Schüz et al., 2001, respectively). Svendsen et al. used the same general methods as Foliart et al., although exposure was based on measurements taken in the child's bedroom up to a few years after diagnosis. The results from this study were generally consistent with those reported by Foliart et al.; an elevated hazard ratio for overall survival (and not event-free survival) was reported for persons exposed to >3 mG (OR=2.8, 95% CI=0.4-20.6, based on 1 death). Associations were also reported for the exposure categories 1-2 mG (OR=2.8, 95% CI=1.2-6.2, based on 7 deaths) and ≥2 mG (OR=3.0, 95% CI=0.9-9.8, based on 3 deaths).

The interpretation of these results, similar to Foliart et al., is limited by low participation rates, small numbers in the highest exposure categories, and the lack of relevant and prospective information on magnetic field exposures (measurements were made in the house where the

child lived the longest *before* diagnosis). Furthermore, the associations reported in this analysis are puzzling because magnetic field exposures in the range of 1-2 mG are common.

Other childhood leukemia studies

Mejia-Arangure and colleagues conducted a series of studies in Mexico City to investigate what environmental factors (including maternal smoking, maternal drinking, or residential magnetic field exposure) might contribute to the development of childhood leukemia in children with Down's syndrome (Mejia-Arangure et al., 2003; 2007). Children with Down's syndrome are 10-20 times more likely to develop childhood leukemia (Hitzler and Zipursky, 2005; Ross et al., 2005). Thus, the intent of these analyses was to determine whether there is an association between magnetic field exposure and childhood leukemia among a population that is believed to be genetically susceptible. The small case-control study compared spot measurements taken at the front door of the homes of children who had both Down's syndrome and leukemia (N=42) with similar measurements taken at the homes of children with only Down's syndrome (N=124). The 42 children with Down's syndrome who developed leukemia were more likely to have spot measurements greater than 6 mG, although no association was observed for the lower magnetic field exposure categories >1-3.99 mG and 4.00-5.99 mG. The authors concluded that these results suggest, "genetic susceptibility to leukemia may modify an effect of magnetic fields" (p. 160). As noted by the investigators, however, the study's weaknesses include its small size and crude exposure assessment.

Some investigators have cited parallel increases in the incidence of childhood leukemia and electric consumption over time to support an association between magnetic fields and childhood leukemia (Milham and Ossiander, 2001). This is referred to as an ecological study, in which an association is estimated using variables measured on populations and not individuals (i.e., average energy consumption and annual leukemia incidence rates). Kheifets et al. (2006) re-examined this question using ecological data for the US and the UK. The investigators concluded that, while there has been a parallel increase, changes in other suspect causes of childhood leukemia and patterns in the reporting and diagnosis of leukemia, as well as the many assumptions involved with estimating changes in magnetic field exposure, preclude any definitive conclusions. The inability of ecological data to be directly extrapolated to individuals is a well known limitation of this type of data (i.e., ecologic fallacy), and, for this reason, epidemiologists give individual-level data much more weight than data collected from populations.

Conclusion

The recently published studies reported an association between childhood leukemia and residence within 500 meters of a transmission line and magnetic field levels greater than approximately 4 mG, but there was no dose-response relationship and small numbers in the upper exposure categories limit inferences. New studies also suggest that there may be an association between overall survival after a diagnosis of leukemia and average magnetic field levels greater than 4 mG, although no associations were observed between clinical indices of poorer survival and magnetic field exposure. None of these recent studies, however, are sufficiently strong methodologically to alter previous conclusions that the epidemiologic evidence on magnetic fields and childhood

leukemia is limited. Chance, confounding, and several sources of bias cannot be ruled out.

It is also important to recognize these studies address just one of the many exposures being studied with respect to the etiology of childhood leukemia, including pesticides, benzene, paternal alcohol consumption, ionizing radiation and infections (McNally and Parker, 2006).

4.2.2 Adult leukemias and lymphomas

The epidemiologic findings for leukemia in adults are quite different from those observed in children. A large number of studies have been conducted on adult leukemia of varying quality and with varying exposure metrics, study designs and sources of exposure. Some older studies reported positive associations, although (as noted by the ICNIRP in 2001) there was no pattern between higher quality studies being more or less likely to report a positive association. Thus, review panels concluded that the evidence in support of an association between adult leukemia and magnetic fields was "weak" (ICNIRP, 2001) and "inadequate" (IARC, 2002). The group of studies published from 2001 to 2005 and considered in Exponent 2005 found no evidence to support an association; the report concluded that "the consistent absence of an association between adult leukemia and magnetic field exposure in studies published since 2001 adds support to the earlier conclusions of review panels that there is weak evidence for an association" (p. 38). Considering nearly the same body of studies and updating the IARC 2002 report, the WHO concluded,

> In the case of adult brain cancer and leukaemia, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF and the risk of these diseases remains inadequate [Note: *Inadequate evidence* describes a body of research where it is unclear whether the data is supportive or unsupportive of causation because there is a lack of data or there are major quantitative or qualitative issues]. (p. 307)[27]

Five studies have been published since 2005 that report on exposure to magnetic fields in relation to adult leukemia (Johansen et al., 2007; Lowenthal et al., 2007; Roosli et al., 2007) or lymphomas (Karipidis et al., 2007a; Mester et al., 2006; Roosli et al., 2007).[28] Mester et al. (2006) was excluded from this review because exposure was based solely on self-reported occupation and industry. Three of the remaining studies assessed occupational magnetic field exposure in cohort studies of electrical utility workers (Johansen et al., 2007) and railway workers (Roosli et al., 2007) and in a case-control study of non-Hodgkin's lymphoma (NHL) (Karipidis et al., 2007a). All three studies utilized a job-exposure matrix to estimate occupational magnetic field exposure. Lowenthal et al. addressed residential exposure, using

[27] The WHO (2007) review offers no conclusions specific to lymphoma.

[28] Lymphomas and leukemias are together considered lymphohematopoietic cancers (i.e., cancers of the lymph and blood-forming organs). Exponent 2005 did not consider lymphomas separately; however, they are considered in this report as a separate disease entity for completeness.

distance as a surrogate for magnetic field exposure. The study grouped cases of some types of leukemias and lymphomas as 'lymphoproliferative disorders' and groups of other types of leukemia and diagnoses as 'myeloproliferative disorders.'

The two cohort studies are updates of previously published studies.[29] Roosli et al. extended follow-up of a cohort of 20,000 Swedish railway workers by nine years. Each of the 20,000 men in this cohort was assigned a cumulative magnetic field exposure by linking the cohort member's occupational history with exposures based on measurements and modeling. Also, leukemia and lymphoma mortality was compared between stationmasters (who spent most of their time in the station and on the platforms) and train attendants (who were exposed to magnetic fields from the 16.7-Hz AC engines). It was assumed that, if magnetic fields were associated with disease, higher mortality would be observed among the train attendants compared to the stationmasters. The previous publication on this cohort provided some evidence to support an association between leukemia mortality and increased magnetic field exposure (Minder and Pfluger, 2001). The current study, however, which was based on 29 additional deaths due to leukemia, did not report an association between overall leukemia mortality and increasing magnetic field exposure. Increased hazard ratios were reported for myeloid leukemias with some features of a dose-response relationship, however, chance could not be ruled out as an explanation for this finding. The second cohort update reported on approximately 28,000 workers employed by utility companies in Denmark (Johansen et al., 2007). These workers were followed for the incidence of cancer and classified into magnetic field exposure categories (high, medium and background) based on their first reported job title. The authors reported that male employees in high exposure jobs were no more likely to be diagnosed with leukemia than persons in medium or background exposure jobs.

Roosli et al. was limited by the use of death certificate data[30] and small numbers, while Johansen et al. was based on a relatively large number of incident cancer cases. Neither cohort controlled for possible confounding factors. Both cohorts, however, had a long period of follow-up and consisted of persons who were occupationally exposed to high levels of magnetic fields.

Lowenthal et al. grouped cases in five cancer diagnostic categories (including ALL) as lymphoproliferative disorders (LPD), and cases of three diseases (including some types of leukemia) as myeloproliferative disorders (MPD). These groups included both adults and children of all ages. They estimated exposure by obtaining a lifetime residential history and assessing distance of the residences from any of three types of power lines (88 kV, 110 kV, or 220 kV). An individual's exposure was based on the closest distance ever having lived from a power line, grouped in categories of 0-50 meters, 51-300 meters, and >300 meters. They reported elevated ORs for those who lived within 50 meters of any of these power lines, and an

[29] Extending follow-up in a cohort study means that the cohort is followed for an additional period of time beyond the last publication. Cohort updates provide valuable information because the longer a cohort is followed, the more follow-up time and events are available, resulting in increased ***power*** and larger numbers.

[30] Death certificates may not always contain the diagnosis of interest because they may only report immediate, and not underlying, causes of death. Furthermore, survival is increasing for many cancers and lymphomas. Thus, if a person survives their cancer, the cancer diagnosis will not be listed on their death certificate. Both of these limitations result in an under-ascertainment of cases, which could bias risk estimates toward 1.0.

indication of decreasing ORs with increasing distance. However, the numbers were small and the results were imprecise (i.e., wide CIs). Chance could not be ruled out as a factor in any of these results. They also reported an increased OR when only considering exposures that occurred up to the age of 15; the authors presented the concept of a possible effect of childhood exposure on long-term disease risk as a "novel finding" deserving further study.

This study of LPD and MPD included many limitations that may introduce bias, reduce validity and detract from its findings (Lowenthal et al., 2007). For example, data was obtained from cases by interview, using trained interviewers, but information was obtained from controls by postal questionnaires, thus breaking a cardinal rule in epidemiology that information from cases and controls should be obtained in the same manner. The distance measure, a poor surrogate for residential magnetic fields exposure, is further reduced in value because the power lines in question were at three different voltages. If, as is likely, these lines carried different loads, then magnetic fields at any given distance would differ among the lines.

As the discussions above and previous sections illustrate, epidemiologic studies typically evaluate each different type of cancer individually. There are many reasons why studies of EMF have not combined different types of cancer, or adults and children, together as Lowenthal et al. have done. This is because differences among cancers in patterns of age at diagnosis, cell type, rate of growth and response to different treatments illustrate the unique aspect of each cancer diagnosis. Therefore, studies of possible causes are studied separately for each type of cancer because each cancer has a distinct etiology. The reported findings from Lowenthal et al. are based on combined disease types and age groups, whereas adults and children typically have different patterns of leukemia. The combination of different diseases and age groups, the highly imprecise exposure surrogate, the different methods for evaluating cases and controls, and the role of chance diminish the implications of the findings from this study.

In conclusion, the recently published updates of large cohorts occupationally exposed to magnetic fields are in line with the previous summary conclusions from IARC, ICNIRP, WHO, and Exponent 2005. The cumulative body of evidence does not support an epidemiologic association between magnetic fields and adult leukemia. Lowenthal et al. reported findings for distance from power lines that cannot be distinguished from a chance finding. The reported association between early exposure and later cancer cannot be evaluated without additional testing.

Roosli et al. also reported on lymphoma mortality, including Hodgkin's disease and NHL. Increased hazard ratios were reported for Hodgkin's disease with some features of a dose-response relationship, however chance could not be ruled out as an explanation for this finding, as the results were based on only 15 deaths spread among the 5 occupational groups.

The case-control analysis by Karipidis et al. enrolled persons diagnosed with NHL in New South Wales and a similar group of persons randomly selected from electoral rolls. Most eligible persons participated and cumulative occupational magnetic field exposure was estimated from a job-exposure matrix. NHL patients were slightly more likely to have the highest cumulative magnetic field exposure (OR=1.48, 95% CI=1.02-2.16). Overall, this study was well conducted, with its most significant limitation being the possibility of uncontrolled

confounding because little is known about the causes of NHL. This is one of the first population-based studies examining an association between NHL and magnetic field exposure using calculated exposure estimates. Therefore, it is still a hypothesis-generating study,[31] and further research is required before any conclusions can be provided.

4.3 Other cancers

4.3.1 Brain cancer

Some early studies reported associations between magnetic field exposures and brain cancers, although consistent results were not reported and no patterns were identified between positive studies, causing the panels to conclude that the evidence is weak and inadequate (IARC 2002; ICNIRP 2003). Exponent 2005 concluded that the recent body of literature at that time provided no convincing evidence of an association. Several, large cohort studies with good exposure assessment techniques reported no increased risks (Sorahan et al., 2001; Hakansson et al., 2002), and where an association was found, it was reported only for a particular sub-group with small numbers. Exponent 2005 concluded, "recent research supports the consensus that there is no cause-and-effect relationship between magnetic field exposure and brain cancer" (p. 40). Similarly, the WHO concluded,

> In the case of adult brain cancer …, the new studies published after the IARC monograph do not change the conclusion that the overall evidence for an association between ELF and the risk of these diseases remains inadequate [Note: *Inadequate evidence* describes a body of research where it is unclear whether the data is supportive or unsupportive of causation because there is a lack of data or there are major quantitative or qualitative issues] (p. 307).

Four studies have been published since 2005 that report on exposure to magnetic fields in relation to adult brain cancer, including the two cohort updates described above (Johansen et al., 2007; Roosli et al., 2007) and two case-control studies of specific brain cancer types, gliomas and acoustic neuromas (Forssén et al., 2006; Karipidis et al., 2007b, respectively). All four studies examined occupational magnetic field exposure using a job-exposure matrix.

No association was reported between brain cancer incidence or mortality and high magnetic field exposures encountered as a utility worker or railway worker in the two recent cohort updates (Johansen et al., 2007; Roosli et al., 2007). Details of these studies are reported above in the adult leukemia/lymphoma section.

[31] Studies generate and test scientific questions, or hypotheses. The first studies reporting results on a specific scientific question are called hypothesis-generating to highlight that there is little available data with which to compare the results. In addition, certain study designs are useful for screening different hypotheses but are not specific enough to produce results definitive enough for assessing cause-and-effect. Therefore, hypothesis-generating studies cannot provide strong conclusions because the questions being considered require further study.

In a case-control study of gliomas in Australia, Karipidis et al. used three different techniques to estimate exposure among glioma cases and controls: self-reported exposure, industrial hygienist interpretation, and a job-exposure matrix. No significant differences in exposures estimated through self-report and ***job exposure matrices*** were reported between cases and controls; however, cases were more likely to be classified in the highest exposure category for exposures rated by an industrial hygienist, but the association was not statistically significant. This study had a number of significant limitations (low participation rates and a high percentage of proxy interviews among cases) that may have influenced the findings.

Forssén et al. is the first case-control study to report on the association between magnetic field exposure and acoustic neuroma, a benign (non-cancerous) and rare brain tumor for which causes are unknown. The large study consisted of all diagnoses of acoustic neuroma in Sweden over a 12-year period (N=793) and controls randomly selected from the entire Swedish population (N=101,762). Magnetic field exposure was estimated by the average fields in the person's occupation, and occupation was the one listed on the country's census forms. The authors did not find any evidence that magnetic field exposure increases the risk of acoustic neuroma, regardless of the exposure level or the time period considered. This study was advanced because selection bias, recall bias, and participation bias were not an issue; however, incomplete occupational data was an important limitation.

The recently published studies do not support a role for magnetic fields in the etiology of brain cancer. Thus, recent studies add support to the previous weight-of-evidence review conclusions that the data does not indicate a cause-and-effect relationship between magnetic fields and brain cancer.

4.3.2 Breast cancer

Since December 2005, two case-control studies have estimated the association between magnetic field exposure and breast cancer, both of which focused on *occupational* magnetic field exposures (McElroy et al., 2007; Ray et al., 2007).[32] Two additional studies evaluated occupational magnetic field exposure, but are not considered further in this report because the exposure assessment did not extend beyond job titles. The excluded studies include a brief report of a proportionate mortality analysis conducted on a select group of occupational titles the authors believed to be associated with electric typewriter use (Milham and Ossiander 2007) and a case-control study of female breast cancer reporting associations for a wide range of occupations and industries (Peplonska et al., 2007).

Questions about the effect of job-related exposures on breast cancer risk were first addressed among men in electrical occupations. Occupational exposures among women were initially more challenging to study given the rarity of females employed in electrical occupations and the lack of magnetic field exposure data collected specifically for female occupations. Some of

[32] An additional case-control study was published post-2005 that examined residential magnetic field exposure and breast cancer (Davis and Mirick, 2007), although it was not fully evaluated in this report because it was a re-analysis of a study published by the same investigators in 2001 (Davis et al., 2001a) with the addition of a few variables.

the initial studies reported a weak association; however, the association was often restricted to a particular sub-group but showed no consistent pattern across studies. These initial analyses were limited by incomplete occupational histories and crude estimates of magnetic field exposure (e.g., job title from a death certificate). As noted in Exponent 2005 and in the recent reviews by the WHO and SCENIHR, later studies were more methodologically sound and did not provide evidence in support of an association between occupational magnetic field exposure and breast cancer (Labreche et al., 2003; Kliukiene et al. 2004; Forssén et al., 2005). In particular, scientific review panels have placed more weight on the large study by Forssén et al. in 2005 because it was the first and only study to estimate magnetic field exposure using 24-hour measurements in a representative sample of female occupations (SCENIHR, 2007; WHO, 2007). This conclusion was summarized in Exponent 2005 as follows:

> This recent body of research was higher in quality compared with previous studies, and, for that reason, provides strong support to previous consensus statements that magnetic field exposure does not appear to influence the risk of breast cancer. (p. 41)

In 2007, McElroy et al. evaluated whether occupational exposures to high, low, medium, or background EMF levels (estimated qualitatively by an industrial hygienist) were different between a large number of breast cancer cases and controls. The authors reported increasing risk with increasing categories of exposure (low, medium and high), but the ORs were very small and not statistically significant (1.05, 1.11, and 1.17, respectively). Given the limitations of this analysis, these results do not provide strong support for an association.

Ray et al. (2007) was a ***nested case-control study*** in a cohort of approximately 250,000 textile workers in China followed for breast cancer incidence; breast cancer cases were no more likely than the women in the cohort who did not develop breast cancer to have EMF-exposed jobs. The strength of the study was its large size and nested design, but, as noted by the authors, "duration of employment in EMF-exposed jobs was too crude a dose metric to detect a weak to modest association" (p. 390). According to the authors, research will continue on this Chinese cohort to estimate exposure quantitatively.

Melatonin Hypothesis

The mechanism hypothesized by some investigators to explain a relationship between breast cancer and magnetic field exposure involves a decrease in the production of a hormone called melatonin induced by magnetic fields, which (according to the theory) could result in cancer because of melatonin's putative anti-carcinogenic effects and its regulatory control of reproductive hormones such as estrogen. This idea was proposed in the late 1980s and is now referred to as the "melatonin hypothesis." The hypothesis has received considerable attention with regard to *in vitro, in vivo*, and epidemiologic investigations into whether 1) magnetic fields could decrease melatonin levels, and 2) a decrease in melatonin levels could lead to cancer. The HPA published an extensive weight-of-evidence review in 2006 that evaluated the available experimental and epidemiologic evidence related to the melatonin hypothesis (HPA, 2006). The review concluded that there is no consistent evidence in experimental or epidemiologic studies to suggest that magnetic fields can alter melatonin levels. *In vitro* and *in vivo* studies have suggested that melatonin can limit growth of cancer cells, however,

epidemiologic data linking reduced melatonin levels to subsequent breast cancer risk is limited. Consistent with our evaluation and the reports from other review panels, the review also concluded that the epidemiologic evidence does not support an association between magnetic fields and breast cancer. Taking all of this evidence together, the review concluded the following:

> In aggregate, the evidence to date does not support the hypothesis that exposure to power frequency EMFs affects melatonin levels or risk of breast cancer. (p. 161).

The HPA review included a series of studies related to the role of melatonin in the etiology of breast cancer conducted by a group of investigators in Seattle (Davis and Mirick, 2006). The initial case-control study by these investigators reported no association between residential magnetic field exposure and breast cancer (Davis et al., 2001a), but an extension of this study reported that urinary levels of a melatonin metabolite (6-sulfatoxymelatonin) were reduced in persons with higher magnetic field measurements in the bedroom, although the results were only statistically significant when considered among persons taking medications known to reduce melatonin levels (Davis et al., 2001b).[33] To explore this result further, a re-analysis of the 2001 case-control study evaluated whether the association between breast cancer and residential magnetic field exposure was more pronounced among persons reporting medication use; no significant association was reported when medication users were considered alone (Davis and Mirick, 2007). A cross-over experiment, however, by the same group of investigators reported statistically lower urinary levels of 6-sulfatoxymelatonin in women exposed to controlled magnetic field levels over the course of five consecutive nights (Davis et al., 2006). The latter investigations were not considered in the HPA review, although when considered with the entire body of research, they do not provide sufficient evidence to alter the conclusion that neither epidemiologic nor experimental data support a role for melatonin in the etiology of breast cancer.

Thus, recent studies do not provide strong evidence to support the conclusion that magnetic fields experienced in the workplace cause breast cancer (McElroy et al., 2007; Ray et al., 2007) or that magnetic fields cause breast cancer through a melatonin-driven pathway (Davis and Mirick, 2007; Davis et al., 2006). The conclusion from Exponent 2005 remains: "the weight of the available epidemiologic evidence to date does not support the hypothesis that EMF is a cause of breast cancer" (p. 45).

[33] The HPA review considered these results in their evaluation, along with other epidemiologic investigations correlating magnetic field exposure and 6-sulfatoxymelatonin, noting that the evidence is not strong because associations were only reported in specific sub-groups (i.e.., medication users).

This conclusion is consistent with a recently published review of the literature by Feychting and Forssén (2006) in Sweden, which concluded the following:

> … considering the results of the latest well designed studies performed specifically to test the hypothesis that ELF magnetic field exposure increase breast cancer risk, one must conclude that the weight of the evidence available today suggest that power frequency magnetic field exposure most likely is not a risk factor for breast cancer development. (p. 557)

4.4 Reproductive and developmental outcomes

With regard to reproductive and developmental outcomes, Exponent 2005 focused on two studies that received considerable attention because of a reported association between peak magnetic field exposure and miscarriage, a prospective cohort study of women in early pregnancy (Lee et al., 2002) and a nested case-control study of women who miscarried compared to their late-pregnancy counterparts (Li et al., 2002). The authors focused on a statistical association with peak exposures, although no association was found for average exposures.

These two studies improved on the existing body of literature because average exposure among the pregnant women was assessed using 24-hour personal magnetic field measurements (early studies on the potential effect of magnetic fields on miscarriage were limited because they used surrogate measures of exposure, including visual display terminal use, electric blanket use or wire code data). Following the publication of these two studies, however, a hypothesis was put forth that the observed association may be the result of behavioral differences between women with healthy pregnancies (less physically active) and women who miscarried (more physically active) (Savitz et al., 2002). It was proposed that physical activity is associated with an increased opportunity for peak magnetic field exposures, and the nausea 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. The scientific panels that have considered these studies concluded that the possibility of this bias precludes making any conclusions about the effect of magnetic fields on miscarriage (NRPB, 2004; FPTRPC, 2005; WHO, 2007). The WHO concluded, "There is some evidence for increased risk of miscarriage associated with measured maternal magnetic field exposure, but this evidence is inadequate" (p. 254). Similarly, Exponent 2005 concluded, "no strong research has been published post-2001 in support of a cause-and-effect relationship between magnetic field exposure and miscarriage" (p. 46).

It is not possible to directly "test" for the effects of this bias in the original studies, but two recent analyses examined whether reduced physical activity was associated with a lower probability of encountering peak magnetic fields (Mezei et al., 2006; Savitz et al., 2006;). In a study of seven-day personal magnetic field measurements in 100 pregnant women, Savitz et al. reported that active women were more likely to encounter peak magnetic fields. This finding supports the hypothesis that reduced activity among women in early pregnancies because of

nausea and later pregnancies because of cumbersomeness may explain the observed association between peak magnetic fields and miscarriage. In addition, an analysis by Mezei et al. of pre-existing databases of magnetic field measurements also found that increased activity levels were associated with peak magnetic fields (Mezei et al., 2006).

Thus, these two recently published studies support Savitz's hypothesis that the associations observed in Lee et al. and Li et al. were due to a bias and there is no convincing epidemiologic evidence linking magnetic field exposure to the risk of miscarriage. Furthermore, there remains no biological basis to indicate that magnetic field exposure increases the risk of miscarriage (see Section 4.6.2).

An additional study was recently published related to developmental outcomes. Fadel et al. (2006) conducted a cross-sectional study in Egypt of 390 children 0-12 years of age living in an area within 50 meters of an electrical power line and 390 children 0-12 years of age living in a region with no power lines in close proximity. Measurements were taken as proxies of growth retardation, and radiological assessments were performed on carpal bones. The authors reported that children living in the region near power lines had a statistically significant lower weight at birth and a reduced head and chest circumference and height at all ages. The authors concluded that "exposure to low frequency electromagnetic fields emerged (sic) from high voltage electric power lines increases the incidence of growth retardation among children" (p. 211). However, this conclusion fails to adequately take into account the many limitations of their cross-sectional analysis (namely, inadequate control for the possible confounding effects of nutritional and socioeconomic status) and the pre-existing body of literature, which does not support such an association (WHO, 2007). The WHO concluded in 2007 that "Overall the evidence for developmental effects and for reproductive effects is inadequate" (p. 254). Furthermore, this study does not provide sufficient evidence to alter that conclusion. Recent studies of animals *in vivo,* summarized in Section 4.6, also do not provide evidence to change the conclusions expressed by the WHO.

4.5 Neurodegenerative diseases

Neurodegenerative diseases were not systematically evaluated in Exponent 2005 because the report was primarily structured as a rebuttal to another expert's opinions, which did not include any statements regarding neurodegenerative disease. For completeness, the epidemiologic literature related to neurodegenerative diseases and magnetic field exposure is evaluated in this section.

Research into the possible effects of magnetic fields on the development of neurodegenerative diseases began around 1995, and the majority of research since then has focused on Alzheimer's disease and a specific type of motor neuron disease called ALS or Lou Gehrig's disease.[34] The WHO evaluated this body of research in their 2007 report; in addition, the National Radiation Protection Board of Great Britain (NRPB) published a report in 2001 that specifically addressed neurodegenerative diseases. The conclusions of the WHO and NRPB reports were used to summarize and evaluate the body of literature published pre-2005; three epidemiologic studies were identified in the literature search post-2005 (Davanipour et al., 2007; Seidler et al., 2007; Sorahan and Kheifets, 2007), and these studies are evaluated to determine whether they are consistent with the conclusions of previous weight-of-evidence reviews.

Alzheimer's disease

The WHO classified the evidence in support of an association between magnetic field exposure and Alzheimer's disease as "inadequate" (p. 206, WHO, 2007). The NRPB noted the inconsistency of the studies and concluded that there is "only weak evidence to suggest that it [i.e., ELF magnetic fields] could cause Alzheimer's disease" (p. 20, NRPB, 2001b). The first studies to generate the hypothesis of a link with Alzheimer's disease reported a 2-fold association between Alzheimer's disease and persons thought to be highly exposed in their occupations. This series of studies, however, was limited by a number of important biases including possible selection bias, lack of validation of exposure, and the use of proxy respondents to ascertain occupational history (Sobel et al., 1995; Sobel et al., 1996).

Subsequent studies did not consistently support an association between occupational magnetic field exposure and Alzheimer's disease, although these studies continued to have significant methodological limitations that make them difficult to interpret. The onset of Alzheimer's disease occurs late in life and is difficult to define precisely because it is preceded by a period of dementia that is difficult to distinguish from other etiologies, such as cerebrovascular disease. Since magnetic field exposure occurs throughout a person's life, it is a challenge to design studies that ascertain lifetime exposure accurately and at the ***etiologically*** relevant time period (Brown et al., 2005). A large portion of these studies relied on crude estimates of exposure such as occupational titles reported on death certificates (Savitz et al., 1998a), occupational titles from census data (Feychting et al., 2003; Hakansson et al., 2003), and proxy respondents (Feychting et al., 1998; Qiu et al., 2004). An additional complication is that a number of these studies used death certificates to ascertain cases (Savitz et al., 1998a,b; Johansen and Olsen, 1998; Feychting et al., 2003). Use of death certificates or other mortality data is likely to result in a large number of missed cases, and therefore possible bias, because a large percentage of elderly Alzheimer's patients die from other causes and Alzheimer's disease

[34] A few epidemiologic studies have also been conducted on Parkinson's disease and multiple sclerosis, although since initial studies did not report suggestive results, subsequent publications focused on Alzheimer's disease and ALS. The WHO concluded the following with respect to Parkinson's disease and multiple sclerosis: "No study has provided clear evidence of an association with above-average exposure to extremely low frequency EMFs and, in the absence of laboratory evidence to the contrary, it seems unlikely that such field are involved in the disease." (p. 203)

may not be mentioned on the death certificate (Brown et al., 2005). Furthermore, none of these studies estimated residential exposure and most did not control for the possible confounding effect of other risk factors for Alzheimer's disease (increasing age, family history, Down's syndrome, and a genetic predisposition). After considering the entire body of literature and its limitations, the WHO report concluded,

> When evaluated across all the studies, there is only very limited evidence of an association between estimated ELF exposure and [Alzheimer's] disease risk (p. 194).

ALS

Early studies on ALS, which had no obvious biases and were generally well conducted, reported some suggestive findings. The review panels, however, were hesitant to conclude that the associations provided strong support for a causal relationship between ALS and occupational magnetic field exposure. Rather, the reviewers felt that an alternative explanation (i.e., electric shocks) may be the source of the observed association. The NRPB concluded: "In summary, the epidemiologic evidence suggests that employment in electrical occupations may increase the risk of ALS, possibly, however, as a result of the increased risk of receiving an electric shock rather than from the increased exposure to electromagnetic fields" (p. 20, NRPB, 2001b). The WHO reported a similar conclusion, specifically recommending that additional work be carried out to clarify the role of magnetic fields and/or electrical shocks in the etiology of ALS.

Recent studies

Three studies were published following the studies reviewed by the WHO report. Davanipour et al. extended the early hypothesis-generating study by Sobel et al. by collecting cases from eight California Alzheimer's Disease Diagnostic and Treatment Centers (Sobel et al. examined the 9th Center in 1996). Occupational information was collected from verified diagnoses of Alzheimer's disease and compared to occupational information collected from persons diagnosed with other dementia-related problems at the Centers. The results of this study were consistent with the previous studies by Sobel et al.; cases were approximately twice as likely to be classified as having medium/high exposures, compared with controls. The strengths of this study included its large size and that disease status was based on expert diagnosis. The main limitation was that the exposure assessment only considered a person's primary occupation, classified as low, medium or high exposure. The WHO noted other limitations of the 1996 publication that are relevant to this publication as well, including the use of controls with dementia (which some studies found had an increased risk of Alzheimer's disease) and the classification of seamstresses, dressmakers and tailors as "high exposure" occupations which drives the increase in risk. Seidler et al. conducted a similar case-control study in Germany, except cases included all types of dementia (55% of which had Alzheimer's disease). Cumulative magnetic field exposure was estimated from occupational histories taken from proxy respondents, and no difference was reported between cases of dementia or probable Alzheimer's disease and controls (although an association was reported among electrical and

electronics workers). The authors reported that exposure misclassification was likely to be a significant problem, and concluded that their results indicate a strong effect of low-dose EMF is "rather improbable." (p. 114)

Sorahan and Kheifets followed a cohort of approximately 84,000 electrical and generation workers in the UK for deaths attributed to neurodegenerative disease on death certificates. Cumulative magnetic field exposure was calculated for each worker, using job and facility information. The authors reported that the cohort did not have a significantly greater number of deaths due to Alzheimer's disease or motor neuron disease, compared to the general UK population. They also reported that persons with higher estimated magnetic field exposures did not have a consistently greater risk of Alzheimer's disease or motor neuron disease. A statistically significant excess of Parkinson's disease was observed in the cohort, although there was no association between calculated magnetic field exposure and Parkinson's disease. The authors concluded "our results provide no convincing evidence for an association between occupational exposure to magnetic fields and neurodegenerative disease" (p. 14). This result is consistent with two other Alzheimer's mortality follow-up studies of electric utility workers in the US (Savitz et al., 1998) and Denmark (Johansen and Olsen 1998). The findings may be limited by the use of death certificate data, but are strengthened by the detailed exposure assessment.

In conclusion, the WHO stated that there is inadequate data in support of an association between magnetic fields and Alzheimer's disease or ALS; the recent studies do not alter this conclusion. While some studies reported an association between occupational magnetic field exposure and Alzheimer's disease or ALS, the studies are weak in design, meaning the data in support of a causal relationship is still limited. Furthermore, there are no consistent biological data that would support the plausibility of such an association. The WHO panel highly recommended that further studies be conducted with regard to neurodegenerative diseases, particularly studies where the association between magnetic fields and ALS is estimated while controlling for the possible confounding effect of electric shocks.

4.6 Experimental research

This section reviews the recent studies of cancerous tumors and developmental effects in whole animals to update the previous report. The literature search described in Section 4.1 identified seven *in vivo* studies (Al-Akhras et al. 2006; Anselmo et al., 2006; Jelenkovic et al., 2006; Juutilainen et al., 2006; Sommer and Lerchl, 2006; Udroiu et al, 2006; Yamaguchi et al., 2006) and one additional study was identified by hand-searching reference lists (Okundan et al. 2006). Original research studies of whole animals using 50-60-Hz AC fields were the focus, and reviews were omitted (Juutilainen et al., 2006) as well as studies of other EMF frequencies (Yamaguchi et al., 2006). Studies of effects on cellular processes and hypothesized mechanisms were omitted as they were beyond the scope of this update (Jelenkovic et al., 2006; Udroiu et al, 2006).

4.6.1 Studies related to cancer

The results of these experimental animal studies regarding cancer were consistent with the previous review of the literature through 2005 and did not report evidence that magnetic fields cause, enhance, or promote the development of cancer overall, or of leukemia and lymphoma specifically (Exponent, 2005). Likewise, the WHO report (2007) concluded that large-scale long-term studies in rodents have not shown any consistent increase in any type of cancer, including leukemia, lymphoma, mammary, brain and skin tumors. No animal studies provide evidence that exposure to EMF at these low frequencies causes tumors (p. 322).

These conclusions were based on a number of *in vivo* studies, including two large-scale studies that completed the National Toxicology Program (NTP) protocol of testing in both sexes, two species, three exposure concentrations, two years of exposure, and comprehensive histopathology (Boorman, et al. 1999; McCormick, et al. 1999; NTP, 2006). In these studies, lifetime magnetic field exposure did not increase leukemia or lymphoma rates, or cancers of the breast, brain, or any other site. In addition, studies specifically designed to test cancer promotion have not found evidence that magnetic fields promote cancer. For example, using mice prone to lymphoma, Babbitt et al (2000) evaluated possible *promotional and co-promotional* effects of chronic exposure to power-frequency magnetic fields. The study used a large number of animals (2,600 mice) genetically predisposed to develop leukemia/lymphoma. To study promotion, lymphoma was first induced by ionizing radiation (gamma or X-irradiation), then animals were exposed to either 1.4 mT (14,000 mG) or no magnetic field for the duration of the study. The occurrence of cancer was similar in magnetic field-exposed and unexposed mice that received the same pre-treatment with ionizing radiation. This study indicated that magnetic fields do not promote (i.e., increase the incidence of) radiation-induced leukemia/lymphoma.

The literature search located one experimental *in vivo* study of cancer (Sommer and Lerchl, 2006). The possible effects of exposure to 50-Hz magnetic fields were studied in a strain of mice that carry a virus that predisposes them to develop a type of lymphoma (Sommer and Lerchl, 2004, 2006). In the first study of chronic exposure the animals were exposed to 1 and 100 μT (10 and 1,000 mG) for 24 hours every day for 32 weeks. As noted in the WHO review (2007), this prolonged exposure to mice predisposed to develop cancer did not increase the incidence of cancer in the exposed groups (Sommer and Lerchl, 2004). In the follow-up study, the exposure was increased to 1 mT (1,000 μT or 10,000 mG), and some of the animals were exposed only 12 hours at night, to test the hypothesis that nighttime exposure may have a stronger effect than continuous exposure (Sommer and Lerchl, 2006). There was no influence of exposure on body weight, time to tumor, cancer incidence, or survival time. This new study is consistent with and reinforces previous conclusions that exposure to magnetic fields does not increase the incidence of cancer, even in animals predisposed to cancer.

4.6.2 Studies related to developmental and reproductive outcomes

Exponent 2005 noted that, despite years of research, there is no biological basis to indicate that magnetic fields increase the risk of miscarriage. Large studies of laboratory animals exposed

to pure 60-Hz magnetic fields have shown no increase in birth defects, no multigenerational effects, and no changes that would indicate an increase in miscarriage or loss of fertility. The WHO concluded that exposure of animals up to 20 mT (200,000 mG) did not result in gross external, visceral, or skeletal malformation, but subtle effects on skeletal development cannot be ruled out (based on some findings in chick embryos). However, the WHO noted that studies in mammalian species carry more weight that those in non-mammalian experimental models.

The literature search found three *in vivo* studies related to pregnancy or fetal development and exposure to magnetic (Al-Akhras et al., 2006; Anselmo et al., 2006) or electric fields (Okundan et al., 2006). In a study designed to assess the effect of magnetic field exposure on the development of motor reflexes, researchers exposed pregnant females to 3 μT (30 mG) for two hours daily during pregnancy (Anselmo et al., 2006). The study reported that development of 6 of the 7 reflexes was delayed in the first 21 days among male pups born to female rats that were fed a diet deficient in several nutrients during pregnancy. In newborn rats born to females exposed to magnetic fields, but with an adequate diet during pregnancy, delay was observed in 4 of the 7 reflexes. For example, the auditory startle reflex occurred at day 10.5 in the control group, but at day 12 in the offspring of exposed maternal rats.

Al-Akhras et al. (2006) reported that exposures of adult male rats to 50-Hz magnetic fields at 250 mG for 18 weeks produced no effect on testes weight, but reduced the weight of seminal vesicles, sperm count, and preputal gland. Lower levels of testosterone were found at 6 and 12 weeks compared to controls, but not at 18 weeks. Changes in organ weights and hormone levels are indirect measures of reproductive effects (changes in fertility are direct measures of reproductive function). As summarized in Exponent 2005:

> Large studies of laboratory animals exposed to pure 60-Hz magnetic fields have shown no increase in … loss of fertility (e.g., Ryan et al., 1996; Ryan et al., 1999; Ryan et al., 2000; Ohnishi et al., 2002; Chung et al., 2003; Juutilainen et al., 2003; Elbetieha et al., 2002) (p. 43).

This study provides no convincing evidence of biologically significant changes in fertility, and is unlikely to change the WHO's conclusion that the evidence is inadequate to support the hypothesis that ELF-EMF causes adverse reproductive effects

Most *in vivo* studies have exposed animals to magnetic fields, because buildings and vegetation shield residents from electric fields. One study of electric field exposures examined effects on fetal development. Okundan et al. (2006) studied the effect of exposure to 50-Hz electric fields *in utero* and 14 days after birth on rat bones. The investigators exposed one pregnant female rat (and her pups) to 50-Hz electric fields at 10 kV/m, and another to 0-Hz (static) at 10 kV/m. A third pregnant female was not exposed to the fields but was otherwise maintained under the same conditions for the duration of the experiment. After the 28-day experiment, bone mineral content and density was assessed overall, and in femoral and lumbar bones. Whole body bone mineral content and bone mineral density was lower and tested statistically significant in the female and pups exposed to 50-Hz electric fields compared to controls. The most serious limitation of this study is the use of only one pregnant rat in each group; therefore, there is no way to separate results related to the exposure from those that arose from inherent differences

among the three adult female rats. The interpretation of this study is limited for several other reasons: results were not consistent among bone types, there was no long-term follow-up of the offspring to see if these differences were permanent, and no information to assess whether these differences were of biological significance.

Weaknesses in study design limit the interpretation of the study of effects of electric fields on rat bone development (Okundan et al., 2006) and of magnetic fields on fertility (Al-Akras et al, 2006). Few studies exist to compare the results of the study on maternal magnetic field exposure on reflexes in newborn rats. Previous studies, however, of function and behavior in the offspring of rats exposed to higher levels of magnetic fields for longer periods have not shown clear behavioral or functional deficiencies (Sienkowitz, et al., 1996; Chung, et al., 2004).

4.6.3 *In vitro* studies

There has been no consistent or strong evidence to explain how EMF exposure could affect biological processes in cells and tissues. In addition, as described in Section 2.4.1 above, such data are supplementary to epidemiology and whole animal studies, and are not directly used by health agencies to assess risk to human health. For that reason, this review relies largely on reviews and the conclusions of scientific panels with regard to studies of mechanism.

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

4.7 Summary of recent literature

Approximately 27 epidemiologic and 7 *in vivo* studies have been published since the Exponent report to the BCUC in 2005. Overall, very few of these studies used high quality methods, meaning there is little evidence available from these new studies that could alter previous

conclusions. Many of the recent epidemiologic studies still used proxy measures for exposure and suffered from significant study design limitations. A few epidemiologic studies tested new hypotheses that require further study, such as the reported statistical association between magnetic fields and childhood leukemia survival and the incidence of childhood leukemia in Down's syndrome patients.

The weak statistical association between high, average magnetic fields and childhood leukemia remains unexplained. Recent research (which focused largely on occupational exposures) supports the conclusion that there is no association between magnetic fields and adult leukemia/lymphoma, brain cancer and breast cancer. Recent studies suggest that the observed association between peak magnetic field exposure and miscarriage is due to a bias in the collection of the data, although future studies still need to confirm some components of this hypothesis. Although the current body of evidence does not provide strong evidence in support of causal relationship, further research is required on Alzheimer's disease and ALS to clarify the association observed in some studies. In conclusion, the recent studies do not provide evidence to alter the conclusion that the body of research does not suggest that electric or magnetic fields are the cause of cancer or any other disease process at the levels we encounter in our everyday environment.

5 Pacemakers and ICDs

The heart's rhythm is controlled naturally by electrical signals. When there is a disturbance to this rhythm, a pacemaker or an implantable cardiac defibrillator (ICD) is implanted to restore normal cardiac function. Pacemakers and ICDs have two distinct systems – a system that senses the heart's rhythm and a system that provides electrical signals to the heart based on the input it receives. Because the sensing system of these devices is naturally responsive to the heart's electrical signal, other electrical signals can interfere with the normal functioning of pacemakers and ICDs, a phenomenon called electromagnetic interference (EMI). Most sources of EMF are too weak to affect a pacemaker or ICD; however, EMF from certain sources, e.g., some appliances and industrial equipment, may cause interference. Other potential sources of EMI include cellular telephones, anti-theft devices in stores, MRI machines, slot machines, and certain medical procedures (e.g., radiation therapy, electrocautery and defibrillation).

Pacemakers are specially designed to reject signals outside of the frequency range of the heart's electrical signal. If the external signal is the right frequency, but the wrong modulation or shape, the pacemaker identifies the signal as noise and reverts to the "asynchronous mode." In this mode, the pacemaker delivers a regular electrical signal to the heart without responding to the heart's natural rhythm. This mode was specifically designed to prevent interference, and research suggests that it presents little risk to the patient. Potentially more serious health effects can occur if the external signal has the same characteristics as the heart's signal. In this case, triggering or inhibition of the pacemaker's output can occur. This can be a serious problem if prolonged inhibition occurs and the patient is completely dependent on a pacemaker for normal cardiac functioning.

Experimental tests have been conducted to determine the threshold level for interference in implanted cardiac pacemakers (Butrous et al., 1982; Butrous et al., 1983; Kaye et al., 1988; Moss and Carstensen 1985; Toivonen et al., 1991; Astridge et al., 1993; Scholten and Silny 2001a; Scholten and Silny 2001b; Frank et al., 2003; Trigano et al., 2005). Summarizing the specific findings of these studies is challenging because the pacemakers' responses varied significantly based on a number of factors, including the manufacturer and model of the pacemaker. In general, the magnetic field levels that caused pacing abnormalities in these experimental tests were much higher than the levels people encounter on an everyday basis, including the magnetic field levels from transmission lines. Interference from electric fields, on the other hand, occurred at levels that can be produced by certain electrical sources. Overall, the lowest electric field level that affected a pacemaker was approximately 1 kV/m. Most pacemakers, however, withstood much higher levels (i.e., up to 20 kV/m) without any pacing abnormalities. Single lead (unipolar) pacemakers were much more sensitive to interference, compared with two lead (bipolar) pacemakers. The most common response was a reversion to the asynchronous pacing mode. In the most recent study of electric fields and interference, the authors defined the conditions that influence the likelihood of interference, including the implantation position of the pacemaker, the pacemaker's configuration, and the geometry and anatomy of the patient's body (Scholten and Silny 2001a). The authors reported that the conditions when interference is conceivable are rare, such as bare feet, a raised arm, and a height of 2 meters.

No cases of interference to patients' pacemakers by EMF associated with transmission lines have been reported in the literature. As noted above, most devices are now constructed with features that prevent interference. The only limits that have been recommended to prevent pacemaker interference are for workers who might encounter high field sources in the course of their occupations. The American Conference of Governmental Industrial Hygienists (ACGIH) recommends that workers with pacemakers limit their exposure to 1 kV/m and 1,000 mG to protect against interference (ACGIH, 2001).

In summary, interference from strong electric fields is theoretically possible under certain circumstances. The likelihood of interference occurring is low, particularly with respect to sources that produce low levels of EMF. It is recommended that concerned patients contact their physician to discuss the make and model of their implanted device, their clinical condition, and any lifestyle factors that put them in close contact with strong electric or magnetic fields.

6 EMF and the environment

6.1 Fauna

Research has also been conducted on the possible effects of EMF on the health, behavior and productivity of wild and domestic animals. Since the 1970s, this research has been carried out in response to concerns about the effects of high-voltage and ultra-high-voltage transmission lines in the vicinity of farms and the natural habitat of wild animals. National agencies and agricultural universities overseas and across Canada and the US, (including McGill University, the University of Minnesota, Montana State University, Iowa State University, and Oregon State University), have conducted research on an assortment of animals using a variety of study designs, from observational studies of animals in their natural habitats to highly controlled experimental studies.

In summary, the research to date does not suggest that magnetic or electric fields result in any adverse effects on the health, behavior or productivity of fauna, including livestock such as cows, sheep, and pigs, and a variety of small mammals, deer, elk, birds and bees (Busby et al., 1974; Ware, 1974; Goodwin, 1975; Schreiber et al., 1976; Williams and Beiler 1979; Amustutz and Miller, 1980; Rogers et al., 1980; Rogers et al., 1981; Algers et al., 1982; Hennichs, 1982; Rogers et al., 1982; Mahmoud and Zimmerman, 1983; Mahmoud and Zimmerman, 1984; Algers and Hennichs, 1985; Picoton et al., 1985; Algers and Hultgren, 1987; Stormshak et al., 1992; Beaver et al., 1993; Hill et al., 1993ab; Lee et al., 1993; McCoy et al., 1993; Lee et al., 1995; Thompson et al., 1995; Burchard et al., 1996; Zapotosky et al., 1996; Miller and Lamont, 1996; Zapotosky et al., 1996; Burchard et al., 1998a,b,c; Burchard et al., 1999; Hefeneider et al., 2001; Rodriquez et al., 2002; Burchard et al., 2003; Rodriquez et al., 2003; Burchard et al., 2004; Rodriguez et al., 2004). The research indicates that some species of animals, unlike humans, are able to detect magnetic fields at levels that may be associated with transmission lines, and this detection may be important for navigational purposes in particular species such as birds. However, detection does not imply that the fields result in any effects, or that these effects are adverse. The best insight is offered by studies with continuous or semi-continuous exposure to high magnetic field levels under controlled conditions with a non-exposed group for comparison. Several of these studies were conducted on livestock, including cows, sheep and pigs (Stormshak et al., 1992; Lee et al., 1993; Thompson et al., 1995; Burchard et al., 1996; Burchard et al., 1998a,b,c; Burchard et al., 1999; Rodriquez et al., 2002; Burchard et al., 2003; Rodriquez et al., 2003; Burchard et al., 2004; Rodriguez et al., 2004). Overall, there were no significant differences between the animals living with constant, high levels of EMF and the animals with normal EMF exposure. Some differences were reported; however, they were not reported consistently between studies, the changes were still within the range of what is normal, and it did not appear that the changes were adverse in nature or had any ecological significance. Furthermore, studies of small mammals and birds associated with the research programs by the U.S. Navy and the Bonneville Power Administration reported that there were not any changes in the movement patterns of these animals to suggest that they were avoiding areas near high-voltage ROWs, nor were there any physiological changes or alterations in

homing behavior (Schreiber et al., 1976; Rogers et al., 1980; Rogers et al., 1981; Rogers et al., 1982; Zapotosky et al., 1996). Reports by two investigators found that commercial honeybees can be impacted by EMF from transmission lines because of a current induced by metal parts on the hive; however, this effect is easily remedied and does not apply to wild bees (Rogers et al., 1980; Greenberg et al., 1981; Rogers et al., 1981; Rogers et al.,1982; Lee et al., 1983; Zapotosky et al., 1996). In summary, the research does not suggest that EMF exposure, or audible noise, would cause any harm to fauna living in the vicinity of high-voltage transmission lines.

6.2 Flora

Numerous studies have been carried out to assess the possible effects of exposure to transmission-line EMF on plants (Hodges et al., 1975; Bankoske et al., 1976; McKee et al., 1978; Miller et al., 1979; Rogers et al., 1980; Lee and Clark, 1981; Warren et al., 1981; Rogers et al., 1982; Greene 1983; Hilson et al., 1983; Hodges and Mitchell, 1984; Brulfert et al., 1985; Reed and McKee, 1985; Parsch and Norman, 1986; Conti et al., 1989; Krizaj and Valencic 1989; Ruzic et al., 1992; Reed et al., 1993; Smith et al., 1993; Mihai et al., 1994; Davies 1996; Zapotosky et al., 1996). These studies have involved both forest species and agriculture crops and have taken place both inside and outside of the laboratory. At the levels of EMF produced by high-voltage transmission lines, researchers have found no adverse effects on plant responses, including seed germination, seedling emergence, seedling growth, leaf area per plant, flowering, seed production, longevity, and biomass production. The only confirmed adverse effect of transmission-line EMF on plants was damage to the tops of plants growing in close proximity to transmission lines with voltages above 1,200-kV. These effects were attributed to corona-induced damage to the branch tip. Furthermore, the trees on or near the ROW would be cleared or trimmed to prevent flash over and other interference.

Glossary

Association – An association is a measure of how things vary together. They are measured by odds ratios and relative risks. Associations are described as positive or negative. For example, a study may show that persons with coronary artery disease eat fewer vegetables than persons without the disease (i.e., a negative association). Or, persons with coronary artery disease may eat more vegetables than persons without the disease (i.e., a positive association).

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.

Case-series – A study design that analyzes the characteristics of a small group of persons with a disease, with no inclusion of persons without the disease.

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.

Cluster – A group of relatively uncommon diseases in space and/or time in amounts that are believed to be greater than what would be expected as a result of chance.

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 fields – 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.

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.

Etiological – Etiological means pertaining to the cause of an event or disease.

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.

Hazard ratio – Comparison of risk or occurrence of an event in two groups that were compared over a time to a specific endpoint or "failure." Hazard ratio is mathematically similar to the relative risk.

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.

Multivariate analysis – In statistics, any analytic method that allows for simultaneous study of two or more dependent variables on an outcome.

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.

Participation rate – A study's participation rate is the number of study subjects who participate in a study divided by the number of eligible subjects. Eligible subjects that do not participate in the study include study subjects who refuse to participate, study participants who are excluded, and study subjects who fail to complete the study's requirements.

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 are 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.

Source population – The population from which the study participants are 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.

Systematic review – The identification and review of a body of literature using explicit, thorough, and standardized methods that are designed to reduce bias or errors.

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.

Validity – An expression meaning the degree to which a measurement reflects what it purports to measure.

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

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

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

References

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

Al-Akhras MA, Darmani H, and Elbetieha A. Influence of 50 Hz magnetic field on sex hormones and other fertility parameters of adult male rats. Bioelectromagnetics 27:127-31, 2006.

Algers B, Ekesbo I, Hennichs K. The effects of ultra high-voltage transmission lines on the fertility of dairy cows: A preliminary study. Swedish Agricultural University. 1982.

Algers B, Hennichs K. The effect of exposure to 400-kV transmission lines on the fertility of cows: A retrospective cohort study. Prev Vet Med 3:351-361, 1985.

Algers B, Hultgren J. Effects of long-term exposure to a 400-kV, 50-Hz transmission line on estrous and fertility in cows. Prev Vet Med 5:21-36, 1987.

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

Amstutz HE, Miller DB. A study of farm animals near 765 kV transmission lines. The Bovine Practitioner 15:51-62, 1980.

Anselmo CW, Santos AA, Freire CM, Ferreira LM, Cabral Filho JE, Catanho MT, and Medeiros Mdo C. Influence of a 60 Hz, 3 microT, electromagnetic field on the reflex maturation of Wistar rats offspring from mothers fed a regional basic diet during pregnancy. Nutr Neurosci 9:201-6, 2006.

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

Astridge PS, Kaye GC, Whitworth S, Kelly P, Camm AJ, Perrins EJ. The response of implanted dual chamber pacemakers to 50 Hz extraneous electrical interference. Pacing Clin Electrophysiol 16:1966-1974, 1993.

Babbitt, JT, Kharazi AI, Taylor JM, Bonds CB, Mirell SG, Frumkin E, Zhuang D, and Hahn TJ. Hematopoietic neoplasia in C57BL/6 mice exposed to split-dose ionizing radiation and circularly polarized 60 Hz magnetic fields. Carcinogenesis 21:1379-89, 2000.

Bankoske JW, Graves HB, McKee GW. The Effects of High Voltage Electric Fields on the Growth and Development of Plants and Animals. In: Proceedings of the first national symposium on environmental concerns in rights-of-way management. Tillman R (Ed.). Mississippi State University. Mississippi State, Mississippi. 112-123, 1976.

Beaver DL, Hill RW, Lederle PE. Assessment of the effects of extremely low frequency electromagnetic radiation on growth and maturation in nestling tree swallows and deermice. In: Electricity and Magnetism in Biology and Medicine. Blank M (Ed.). San Francisco Press, Inc. 925-926, 1993.

Boorman GA., McCormick DL, Findlay JC, Hailey JR, Gauger JR, Johnson TR, Kovatch RM, Sills RC, and Haseman JK. Chronic toxicity/oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in F344/N rats. Toxicol Pathol 27 (3):267-78, 1999.

Brown RC, Lockwood AH, Sonawane BR. Neurodegenerative diseases: an overview of environmental risk factors. Environ Health Perspect 113:1250-1256, 2005.

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

Burchard JF, Nguyen DH, Richard L, Block E. Biological effects of electric and magnetic fields on productivity of dairy cows. J Dairy Sci 79:1549-1554, 1996.

Burchard JF, Nguyen DH, Block E. Effects of electric and magnetic fields on nocturnal melatonin concentrations in dairy cows. J Diary Sci 81:722-727, 1998a.

Burchard JF, Nguyen DH, Block E. Progesterone concentrations during estrous cycle of dairy cows exposed to electric and magnetic fields. Bioelectromagnetics 19:438-443, 1998b.

Burchard JF, Nguyen DH, Richard L, Young SN, Heyes MP, Block E. Effects of electromagnetic fields on the levels of biogenic amine metabolites, quinolinic acid, and B-Endorphin in the cerebrospinal fluid of dairy cows. Neurochem Res 23:1527-1531, 1998c.

Burchard JF, Nguyen DH, Block E. Macro- and trace element concentrations in blood plasma and cerebrospinal fluid of dairy cows exposed to electric and magnetic fields. Bioelectromagnetics 20:358-364, 1999.

Burchard JF, Monardes H, Nguyen DH. Effect of 10 kV, 30 mT, 60 Hz electric and magnetic fields on milk production and feed intake in nonpregnant dairy cattle. Bioelectromagnetics 24:557-563, 2003.

Burchard JF, Nguyen DH, Monardes HG, Petitclerc D. Lack of effect of 10 kV/m 60 Hz electric field exposure on pregnant dairy heifer hormones. Bioelectromagnetics 25:308-312, 2004.

Busby K, Driscoll D, Washbon WE. A Field Survey of Farmer Experience with 765 kV Transmission Lines. Agricultural Resources Commission. State Campus, Albany, NY. 1974.

Butrous GS, Meldrum SJ, Barton DG, Male JC, Bonnel JA, Camm AJ. Effects of high-intensity power-frequency electric fields on implanted modern multiprogrammable cardiac pacemakers. J R Soc Med 75:327-331, 1982.

Butrous GS, Male JC, Webber RS, Barton DG, Meldrum SJ, Bonnell JA, Camm AJ. The effect of power frequency high intensity electric fields on implanted cardiac pacemakers. PACE. 6:1282-1292, 1983.

Brulfert A, Miller MW, Robertson D, Dooley DA, Economou P. A cytohistological analysis of roots whose growth is affected by a 60-Hz electric field. Bioelectromagnetics 6:283-291, 1985.

Chung MK, Kim JC, and Myung SH. Lack of adverse effects in pregnant/lactating female rats and their offspring following pre- and postnatal exposure to ELF magnetic fields. Bioelectromagnetics 25:236-44, 2004.

Conti R, Nicolini P, Cerretelli P, Maronato V, Veicsteinas A, Floris C. Enel's research activity on possible biological effects of 50 Hz electromagnetic fields – results and plans of a large research programme. Alta Frequenza. 58:395-378, 1989.

Davanipour Z, Tseng CC, Lee PJ, and Sobel E. A case-control study of occupational magnetic field exposure and Alzheimer's disease: results from the California Alzheimer's Disease Diagnosis and Treatment Centers. BMC Neurol 7:13, 2007.

Davies, MS. Effects of 60 Hz electromagnetic fields on early growth in three plant species and a replication of previous results. Bioelectromagnetics 17:154-161, 1996.

Davis S, and Mirick DK, and Stevens RG. Night shift work, light at night, and risk of breast cancer. J Natl Cancer Inst 93:1557-62, 2001a.

Davis S, Kaune WT, Mirick DK, Chen C, and Stevens RG. Residential magnetic fields, light-at-night, and nocturnal urinary 6-sulfatoxymelatonin concentration in women. Am J Epidemiol 154:591-600, 2001b.

Davis S, and Mirick DK. Circadian disruption, shift work and the risk of cancer: a summary of the evidence and studies in Seattle. Cancer Causes Control 17:539-45, 2006.

Davis S, Mirick DK, Chen C, and Stanczyk FZ. Effects of 60-Hz magnetic field exposure on nocturnal 6-sulfatoxymelatonin, estrogens, luteinizing hormone, and follicle-stimulating hormone in healthy reproductive-age women: results of a crossover trial. Ann Epidemiol 16:622-31, 2006.

Davis S, and Mirick DK. Residential magnetic fields, medication use, and the risk of breast cancer. Epidemiology 18:266-9, 2007.

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

Fadel RA, Salem AH, Ali MA, and Abu-Saif AN. Growth assessment of children exposed to low frequency electromagnetic fields at the Abu Sultan area in Ismailia (Egypt). Anthropol Anz 64:211-26, 2006.

Feizi AA, and Arabi MA. Acute childhood leukemias and exposure to magnetic fields generated by high voltage overhead power lines - a risk factor in Iran. Asian Pac J Cancer Prev 8:69-72, 2007.

Feychting M, Pedersen NL, Svedberg P, Floderus B, and Gatz M. Dementia and occupational exposure to magnetic fields. Scand J Work, Environ Health 24:46-53, 1998.

Feychting M, Jonsson F, Pedersen NL, Ahlbom A. Occupational magnetic field exposure and neurodegenerative disease. Epidemiology 14:413-419, 2003.

Feychting M, and Forssén U. Electromagnetic fields and female breast cancer. Cancer Causes Control 17:553-8, 2006.

Foliart, DE, Pollock BH, Mezei G, Iriye R, Silva JM, Ebi KL, Kheifets L, Link MP, and Kavet R. Magnetic field exposure and long-term survival among children with leukaemia. Br J Cancer 94:161-4, 2006.

Foliart DE, Mezei G, Iriye R, Silva JM, Ebi KL, Kheifets L, Link MP, R. Kavet, and B. H. Pollock. Magnetic field exposure and prognostic factors in childhood leukemia. Bioelectromagnetics 28:69-71, 2007.

Forssén UM, Rutqvist LE, Ahlbom A, and Feychting M. Occupational magnetic fields and female breast cancer: a case-control study using Swedish population registers and new exposure data. Am J Epi 161:250-259, 2005.

Forssén UM, Lonn S, Ahlbom, Savitz DA, and Feychting M. Occupational magnetic field exposure and the risk of acoustic neuroma. Am J Ind Med 49:112-8, 2006.

Frank R, Souques M, Himbert C, Hidden-Lucet F, Petitot JC, Fontaine G, Lambrozo J, Magne I, Bailly JM. Effects of 50 to 60 Hz and of 20 to 50 kHz magnetic fields on the operation of implanted cardiac pacemakers. Arch Mal Coeur Vaiss, (French). 96:35-41, 2003.

Federal-Provincial-Territorial Radiation Protection Committee (FPTRPC) – Canada. Position statement for the general public on the health effects of power-frequency (60 Hz) electric and magnetic fields.
http://www.bccdc.org/downloads/pdf/rps/reports/ELF%20position%20statement%20E-050120.pdf

Goodwin JG. Big Game Movement Near a 500-kV Transmission Line in Northern Idaho. Prepared for the Bonneville Power Administration, Engineering and Construction Division, Portland, OR. Intern with the Western Interstate Commission for Higher Education (WICHE), Resources Development Internship Program (RDIP). Boulder, CO. June 27, 1975.

Government of Canada. A Framework for the Application of Precaution in Science-based Decision Making about Risk. C2003-98208.
http://www.who.int/ifcs/documents/forums/forum5/precaution_e.pdf

Greenberg B, Bindokas VP, Gauger JR. Biological effects of a 765-kV transmission line: Exposures and thresholds in honeybee colonies. Bioelectromagnetics 2:315-328, 1981.

Greene RW. 60 Hz ultra-high voltage electric field effect on onion root mitotic index: a lack of impact. Environ Exp Bot 23:355-360, 1983.

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

Hakansson N, Floderus B, Gustavsson P, Johansen C, and Olsen JH. Cancer incidence and magnetic field exposure in industries using resistance welding in Sweden. Occup Environ Med 59:481-486, 2002.

Hakansson N, Gustavsson P, Johansen C, Floderus B. Neurodegenerative diseases in welders and other workers exposed to high levels of magnetic fields. Epidemiology 14:420-426; discussion 427-428, 2003.

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

Health Canada. It's your health: Electric and magnetic fields at extremely low frequencies. 2004. http://www.hc-sc.gc.ca/iyh-vsv/environ/magnet_e.html

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

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

Hefeneider SH, McCoy SL, Hausman FA, Christensen HL, Takahashi D, Perrin N, Bracken TD, Shin JY, Hall AS. Long-term effects of 60-Hz electric vs. magnetic fields on IL-1 and IL-2 activity in sheep. Bioelectromagnetics 22:170-177, 2001.

Hennichs K. Cows Exposed to 400-kV Lines: Inventory and Fertility Study. Swedish University of Agricultural Sciences. Report 7, 1982.

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

Hill RW, Beaver DL, Lederle P. Ecological Studies on Effects of ELF Electromagnetic Fields: Maximal Cold-Induced Rate of Oxygen Consumption in Mice and Birds. In: Electricity and Magnetism in Biology and Medicine, Blank M (Ed). 822-824, 1993a.

Hill SD, Beaver DL, Lederle PE, Herman DL. An Investigation of the Effect of ELF Electromagnetic Radiation on Embryological Development in Free-living Tree Swallows,

Tachycineta bicolor. In: Electricity and Magnetism in Biology and Medicine, Blank M (Ed). San Francisco, CA: San Francisco Press, Inc. 347-348, 1993b

Hilson DW, Noggle JC, Burns ER. Effects of Electric Field on Plants Growing Under High Voltage Transmission Lines. Office of Natural Resources, Air Quality Branch. Tennessee Valley Authority. Chattanooga, Tennessee. 1983.

Hitzler JK, and Zipursky A. Origins of leukaemia in children with Down syndrome. Nat Rev Cancer 5:11-20, 2005.

Hodges TK, Mitchell CA, Heydt G. Effect of Electric Fields from 765-kV Transmission Lines on Plant Growth. A report by Purdue University for Indiana and Michigan Electric Company, a Subsidiary of American Electric Power. New York, New York. 1975.

Hodges TK, Mitchell CA. Influence on High Intensity Electric Fields on Yield of Sweet Corn and Dent Corn-1982. A report for the American Electric Power Service Corporation. North Liberty, Indiana. 1984.

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

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

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

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

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

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

International Commission on Non-Ionizing Radiation Protection (ICNIRP). Exposure to static and low frequency electromagnetic fields, biological effects and health consequences (0-100 kHz) – review of the scientific evidence on dosimetry, biological effects, epidemiological observations, and health consequences concerning exposure to static and low frequency electromagnetic fields (0-100 kHz). Matthes R, McKinlay AF, Bernhardt JH, Vecchia P, Beyret B (eds.). International Commission on Non-Ionizing Radiation Protection, 2003.

Ivancsits S et al. Induction of DNA strand breaks by intermittent exposure to extremely-low-frequency electromagnetic fields in human diploid fibroblasts. Mutat Res 519:1-13, 2002a.

Ivancsits S et al. Vanadate induces DNA strand breaks in cultured human fibroblasts at doses relevant to occupational exposure. Mutat Res 519:25-35, 2002b.

Ivancsits S et al. Age-related effects on induction of DNA strand breaks by intermittent exposure to electromagnetic fields. Mech Ageing Dev 124:847-850, 2003a.

Ivancsits S et al. Intermittent extremely low frequency electromagnetic fields cause DNA damage in a dose-dependent way. Int Arch Occup Environ Health 76:431-436, 2003b.

Jelenkovic A, Janac B, Pesic V, Jovanovic DM, Vasiljevic I, and Prolic Z. Effects of extremely low-frequency magnetic field in the brain of rats. Brain Res Bull 68:355-60, 2006.

Johansen C, and Olsen JH. Mortality from amyotrophic lateral sclerosis, other chronic disorders, and electric shocks among utility workers. Am J Epidemiol 148:362-8, 1998.

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

Juutilainen J, Kumlin T, Naarala J. Do extremely low frequency magnetic fields enhance the effects of environmental carcinogens? A meta-analysis of experimental studies. Int J Radiat Biol 82:1-12, 2006.

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

Karipidis K, Benke G, Sim M, Fritschi L, Yost M, Armstrong B, Hughes AM, Grulich A, Vajdic CM, Kaldor J, and Kricker A. Occupational exposure to power frequency magnetic fields and risk of non-Hodgkin lymphoma. Occup Environ Med 64:25-9, 2007a.

Karipidis KK, Benke G, Sim MR, Yost M, and Giles G. Occupational exposure to low frequency magnetic fields and the risk of low grade and high grade glioma. Cancer Causes Control 18:305-13, 2007b.

Kaye GC, Butrous GS, Allen A, Meldrum SJ, Male JC, Camm AJ. The effect of 50 Hz external electrical interference on implanted cardiac pacemakers. Pacing Clin Electrophysiol 11:999-1008, 1988.

Kheifets L, Swanson J, and Greenland S. Childhood leukemia, electric and magnetic fields, and temporal trends. Bioelectromagnetics 27:545-52, 2006.

Kliukiene J, Tynes T, Andersen A. Residential and occupational exposures to 50-Hz magnetic fields and breast cancer in women: a population-based study. Am J Epidemiol 159:852-861, 2004.

Krizaj D, Valencic V. The effects of ELF magnetic fields and temperature on differential plant growth. Journal of Bioelectricity 8:159-165, 1989.

Labreche F, Goldberg MS, Valois MF, Nadon L, Richardson L, Lakhani R, Latreille B. Occupational exposures to extremely low frequency magnetic fields and postmenopausal breast cancer. Am. J Ind Med 44:643-52, 2003.

Lee JM, Reiner GL. Transmission line electric fields and the possible effects on livestock and honey bees. Transactions of the American Society for Agricultural Engineers. 279-286, 1983.

Lee JM, Stormshak F, Thompson JM, Thinesen P, Painter LJ, Olenchek EG, Hess DL, Forbes R, Foster DL. Melatonin secretion and puberty in female lambs exposed to environmental electric and magnetic fields. Biol Reprod 49:857-864, 1993.

Lee JM, Stormshak F, Thompson JM, Hess DL, Foster DL. Melatonin and puberty in female lambs exposed to EMF: A replicate study. Bioelectromagnetics 16:119-123, 1995.

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

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

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

Lope V, Perez-Gomez B, Aragones N, Lopez-Abente G, Gustavsson P, Floderus B,

Dosemeci M, Silva A, Pollan M. Occupational exposure to ionizing radiation and electromagnetic fields in relation to the risk of thyroid cancer in Sweden. Scand J Work Environ Health 32:276-84, 2006.

Lowenthal RM, Tuck DM, and Bray IC. Residential exposure to electric power transmission lines and risk of lymphoproliferative and myeloproliferative disorders: a case-control study. Intern Med J, 2007.

Mahmoud AA, Zimmerman DR. High voltage transmission and environmental effects. Right-of-way December 15-19, 1983.

Mahmoud AA, Zimmerman DR. Reproductive performance of pigs exposed to high voltage electric field: Second generation (Draft). Presented at the Summer Meeting of the American Society of Agricultural Engineers, 1984.

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

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

McCoy SL, Hefeneider SH. Effect of 60 Hz electric and magnetic fields from a 500 kV transmission line on interleukin 1 production and antibody response by ewe lamb. In: Electricity and Magnetism in Biology and Medicine, Blank M (Ed). San Francisco, CA: San Francisco Press, Inc. 633-636, 1993.

McElroy JA, Egan KM, Titus-Ernstoff L, Anderson HA, Trentham-Dietz A, Hampton JM, and Newcomb PA. Occupational exposure to electromagnetic field and breast cancer risk in a large, population-based, case-control study in the United States. J Occup Environ Med 49:266-74, 2007.

McKee GW, Knievel DP, Poznaniak DT, Bankoske JW. Effects of 60 Hz high intensity electric fields on living plants. IEEE Transactions on Power Apparatus Systems. 97:1177-1181, 1978.

McNally RJQ, Eden TOB. An infectious aetiology for childhood acute leukaemia: a review of the evidence. Br J Haematol 127:243-263, 2004.

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

Mejia-Arangure JM, Fajardo-Gutierrez A, Flores-Aguilar H, Martinez-Garcia MC, Salamanca-Gomez F, Palma-Padilla V, Paredes-Aguilera R, Bernaldez-Rios R, Ortiz-Fernandez A, Martinez-Avalos A, and Gorodezky C. Environmental factors contributing to the development of childhood leukemia in children with Down's syndrome. Leukemia 17:1905-7, 2003.

Mejia-Arangure JM, Fajardo-Gutierrez A, Perez-Saldivar ML, Gorodezky C, Martinez-Avalos A, Romero-Guzman L, Campo-Martinez MA, Flores-Lujano J, Salamanca-Gomez F, and Velasquez-Perez L. Magnetic fields and acute leukemia in children with Down syndrome. Epidemiology 18:158-61, 2007.

Mester B, Nieters A, Deeg E, Elsner G, Becker N, and Seidler A. Occupation and malignant lymphoma: a population based case control study in Germany. Occup Environ Med 63:17-26, 2006.

Mezei G, Bracken TD, Senior R, and Kavet R. Analyses of magnetic-field peak-exposure summary measures. J Expo Sci Environ Epidemiol 16:477-85, 2006.

Michaelis J, Schüz J, Meinert R, Menger M, Grigat JP, Kaatsch P, Kaletsch U, Miesner A, Stamm A, Brinkmann K, and Karner H. Childhood leukemia and electromagnetic fields: results of a population-based case-control study in Germany. Cancer Causes Control 8:167-74, 1997.

Michaelis J, Schüz J, Meinert R, Zemann E, Grigat JP, Kaatsch P, Kaletsch U, Miesner A, Brinkmann K, Kalkner W, and Karner H. Combined risk estimates for two German population-based case-control studies on residential magnetic fields and childhood acute leukemia. Epidemiology 9:92-4, 1998.