

An Overview of WHO's EMF Project and the Health Effects of EMF Exposure

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ABSTRACT

The World Health Organization (WHO), through its International EMF Project, has conducted a number of reviews of possible health effects from exposure to fields from various parts of the electromagnetic spectrum. These fields can be grouped into radiofrequencies (RF), intermediate frequencies (IF) and the static and extremely low frequencies (ELF). In addition, there have been substantial reviews published by other organizations, many of which WHO representatives have participated. This paper describes WHO's International EMF Project activities and their results so far, briefly reviews the biological effects from EMF exposure, identifies gaps in knowledge needing further research and overviews WHO's current published position on these issues.

The main conclusion from the WHO reviews is that EMF exposures below the limits recommended in the guidelines by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) do not appear to have any known consequence on health. However, there are still some key gaps in knowledge needing further research before better health risk assessments can be made. These research needs are being promoted to funding agencies by WHO. Because of remaining uncertainties in the science database, there has been some pressure to introduce precautionary measures until gaps in knowledge are filled. If precautionary measures are introduced to reduce EMF levels, it is recommended that they are made voluntary, and that health-based exposure limits be mandated to protect public health.

INTRODUCTION

The World Health Organization (WHO) takes seriously the concerns raised by reports about possible health effects from exposure to electromagnetic fields (EMF). Cancer, changes in behaviour, memory loss and many other diseases have been suggested as resulting from exposure to EMF. Everyone in the world is now exposed to a complex mix of EMF frequencies in the range 0-300 GHz. EMF has become one of the most pervasive environmental influences and exposure levels at many frequencies are increasing significantly as the technological revolution continues unabated and new applications using different parts of the spectrum are found.

Electromagnetic field sources to which people may be exposed are predominantly in three frequency ranges:

- § The static (0 Hz) and extremely low frequency range (ELF, > 0 to < 300 Hz) incorporates the 50 and 60 Hz frequencies of the electric power supply and of electric and magnetic fields generated by electricity power lines and electric/electronic appliances. Sources of static magnetic fields include magnetic resonance imaging (MRI) and industrial use of direct currents for electrolysis;

- § The intermediate frequency range (IF, 300 Hz to <10 MHz) are used in computer monitors, industrial processes and security systems
- § The radiofrequency range (RF, microwaves, 10 MHz-300 GHz) includes radars, radio and television broadcast and telecommunications.

Most research has been devoted to possible biological effects from exposure to ELF or RF fields. The IF range has received little attention despite the rapid development of appliances such as induction heating devices, anti-theft and remote detection systems.

This review gives a brief description of WHO's International EMF Project, with an update on activities and results, summarizes research on biological and health effects in the 3 frequency ranges and identify gaps in knowledge that need further research before better health risk assessments can be made. In addition, WHO has published the results of reviews and conclusions as WHO Fact Sheets in multiple languages, and they are available on the EMF Project web site at: <http://www.who.int/emf/>.

INTERNATIONAL EMF PROJECT

WHO established the International EMF Project to provide a forum for a coordinated international response to EMF issues and to assess health and environmental effects of exposure to static and time varying electric and magnetic fields in the frequency range 0 - 300 GHz. The Project commenced at WHO in 1996 and is scheduled for completion in about 2007. It has been designed to follow a logical progression of activities to produce a series of outputs that allow improved health risk assessments to be made and to identify any environmental impacts of EMF exposure. The ultimate objectives of the Project are to provide sound advice to national authorities on how best to manage EMF issues, and to complete health risk assessments that will lead to the development of an international consensus on exposure guidelines. An EMF Project overview is given in figure 1.

Definitions: To conduct reviews and assess health consequences from EMF exposure, it is necessary to have working definitions of biological effects and health hazards. Explicit distinctions are made between the concepts of interaction, biological effect, and health hazard, consistent with the criteria used by international bodies when making health assessments (Repacholi and Cardis, 1997). Biological effects occur when fields interact to produce physiological responses that may or may not be perceived by people. Deciding whether biological or physiological changes have health consequences depends, in part, upon whether they are reversible, are within the range for which the body has effective compensation mechanisms, or are likely, taking into account the variability of response among individuals, to lead to unfavourable changes in health.

WHO defines health as the state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity. Biological effects are defined as any measurable change in a biological system, though not all of them will be hazardous. Some may be innocuously within the normal range of biological variation and physiological compensation and others may be beneficial under certain conditions. The health implications of others may be simply indeterminate. In this case uncertainty adds to the lack of acceptability of scientific

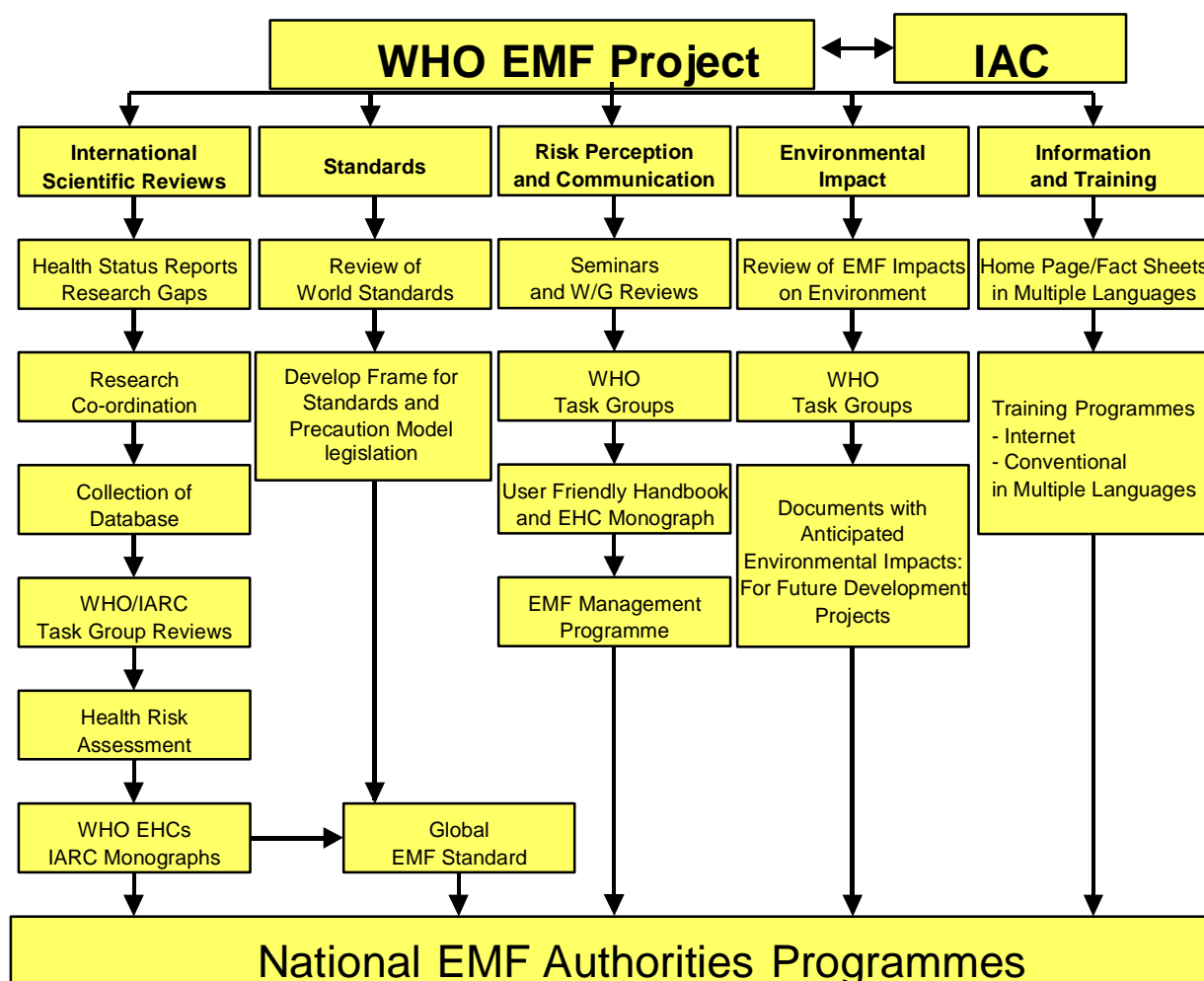
results. A health hazard is generally defined to result from a biological effect outside the normal range of physiological compensation or adverse to a person's well-being.

Scientific reviews: WHO, through its International EMF Project, has recently conducted a series of in-depth international reviews of the scientific literature on the biological and health effects of exposure to radiofrequency (RF), intermediate frequencies as well as static and extremely low frequency (ELF) fields. These reviews were conducted mainly with the purpose of identifying;

- health effects that can be substantiated from the literature, and
- biological effects that are suggestive of possible health effects, but require further research to determine if exposure to EMF at the low levels of exposure normally encountered in the living and working environment has any impact on health.

The results of these reviews have been published (Repacholi, 1998; Repacholi & Greenebaum, 1999; Litvak et al. 2002). The proceedings of all papers presented at the scientific review conferences have been published jointly by WHO and ICNIRP, and are available from ICNIRP (www.icnirp.de). Having completed the initial international scientific reviews, WHO is now urging EMF funding agencies worldwide to give priority to research related to possible health effects of EMF that will allow WHO to make better health risk assessments.

Fig. 1: A schematic outline of the activities and outputs of the International EMF Project.



Health risk assessments: Both WHO and the International Agency for Research on Cancer (IARC) have already established a timetable for assessing health effects of EMF fields. In June 2001 IARC formally evaluated the evidence for carcinogenesis from exposure to static and extremely low frequency (ELF) fields. The review concluded that there was sufficient evidence from the childhood leukaemia studies to classify ELF magnetic fields as a "possible human carcinogen". IARC will publish the results of this meeting in the IARC Monograph Series in 2002. A WHO fact sheet describing this result and implications was published in October 2001 (WHO Fact Sheet, 2001).

The International EMF Project will use the IARC conclusions on carcinogenesis and incorporate them into a full health risk assessment of exposure to static and ELF fields in 2002-3. The results and conclusions will be published in WHO's Environmental Health Criteria series. Sufficient results should be available for IARC to conduct a similar evaluation of evidence for carcinogenicity of RF fields in 2004-5. WHO would then complete an overall health risk assessment of exposure to RF fields in 2005-6.

STANDARDS, PRECAUTION AND MODEL LEGISLATION

A set of activities has been undertaken by WHO to enable national authorities to protect their citizens from EMF exposure that could have health consequences. These activities are complementary in that they enable countries to establish a comprehensive program for EMF protection. Essential to this is a framework for drafting standards that should be based on scientific assessments of health effects research. Where there is uncertainty in the science additional precautionary measures can be taken using the precaution framework. The above two frameworks can then be incorporated into legislation using the model being developed.

Standards framework: In November 1998, WHO commenced a process of harmonization of electromagnetic fields (EMF) standards worldwide. Over 45 countries and 8 international organizations are involved in the International EMF Project. Thus the Project provides a unique opportunity to bring countries together in a logical process to better define any health risks associated with EMF exposure and to encourage the development of harmonized exposure limits and other control measures that provide the same level of health protection to all people. Globalization of trade and the rapid introduction of mobile telecommunications worldwide, have focused attention on the large differences existing in standards limiting exposure to EMF. Differences in the EMF exposure limit values in standards in some Eastern European and Western countries are, in some cases, over 100 times. This has raised concerns about their safety and has led to public anxiety about increasing EMF exposures from the introduction of new technologies.

The purpose of this activity is work towards international agreement on a framework for developing guidelines on protection of the public and workers from exposure to EMF. EMF is defined as electromagnetic fields in the frequency range 0 to 300 GHz. It will take some years before this activity is complete, but it is hoped that the process will be finalised before the formal assessment of EMF health risk assessments by WHO and IARC. Thus the next generation of standards would be able to incorporate this health risk assessment information within the same harmonized standards framework.

Precaution framework: WHO is drafting a framework for generating options for public health protection in areas where there is scientific uncertainty. An international meeting convened by WHO and hosted by the European Commission and cosponsored with the US National Institute for Environmental Health Sciences was held in Luxembourg in February 2003. A wide range of stakeholders provided input into this framework which will be completed within the next 6 months.

Model legislation: Many countries do not have the basic legislation that would enable them to establish protective for the general public and workers from EMF. WHO is in the process of drafting legislation that can be used by countries to develop comprehensive enforceable protective measures, including regulations. It is anticipated that this activity will be completed by the end of 2003.

EMF risk perception, communication and management: One of the most concerning EMF issues is why people perceive risks differently to scientists involved in risk assessments, and why there seems to be a breakdown in communication between the public and scientists and government. In addition, EMF exposure seems to raise peoples concerns to a level that is incompatible with the known magnitude of other environmental hazards.

To address these concerns, international seminars were held in Vienna in 1997 and Ottawa in 1998 to discuss risk perception and management of EMF fields. The seminars were followed by working group meetings to compile a draft report on this topic. The proceedings of the Vienna seminar were published by ICNIRP (see www.icnirp.de), and of the Ottawa meeting by WHO in 1999 (see www.who.int/emf). From these reviews there will be publications by WHO in the form of a scientific monograph and a user-friendly Handbook. These publications are intended to:

- Supply governmental and non-governmental authorities, as well as individuals with a reliable source of information about this topic.
- Foster a better understanding of EMF issues, how they can be better communicated, and how fruitful resolution of disagreements can be achieved.
- Provide an easily readable overview of the characteristics and underlying assumptions of peoples perceptions of EMF risk, differences between scientific, governmental and popular views, and why these occur.
- Provide practical information for agencies and organizations to examine their current approaches to EMF and to design better and more effective information and risk management programmes.

Environmental impacts: As technology has progressed, levels of EMF in our environment have increased steadily over the past 50-100 years. At specific frequencies, EMF emissions from man-made sources now exceed those from natural fields by many orders of magnitude and are detectable everywhere in the world. Significant increases in environmental EMF levels have resulted from major development projects such as high voltage transmission lines, undersea power cables, radars, telecommunication and broadcast transmitters, and transportation systems. Research has been focused to determine if EMF exposure of humans has any deleterious health consequence. By comparison, influences of these fields on plants, animals, birds and other living

organisms have been less rigorously examined. Assessments of environmental impacts of EMF fields is important to:

- Ensure the preservation of balances in natural terrestrial and marine ecosystems, since these directly impact on human life.
- Preserve food supplies by ensuring there are no adverse impacts to fisheries, agricultural animals and plants.

An international seminar, organized by WHO and ICNIRP, and supported by the German Federal Office of Radiation Protection, was held in Ismaning, Germany in October 1999. It provided a summary of scientific knowledge about any consequences to the environment from man-made sources of EMF in the frequency range 0-300 GHz. Overviews of current knowledge in key areas were presented by a panel of recognized specialists. Working groups met to prepare conclusions and recommendations. The proceedings of all presentations have been published and are available from ICNIRP (see www.icnirp.de). The results of the working group meetings have been used to prepare a scientific paper for publication in a scientific journal (Foster et al., submitted).

It is not anticipated that further meetings will be organized on this topic. The main purpose of this activity was to provide information that specifically addresses environmental impacts of EMF fields. It is anticipated that the reports of the meeting will be useful for both governmental and non-governmental institutions when conducting environmental impact assessments, and will help address public concern that EMF could be adversely affecting our environment.

ELF FIELDS

Most public exposure to ELF fields comes from electrical appliances, household wiring, and AC transmission and distribution lines. In addition to the WHO review (Repacholi and Greenebaum, 1999), other recent reviews on the health effects of static and ELF electric and magnetic fields have been conducted by IARC (2001), the Health Council of the Netherlands (2001), and by an expert Advisory Group of the National Radiological Protection Board in the United Kingdom (AGNIR, 2001). All these reviews are in basic agreement with each other and are summarized below.

Interaction mechanisms: A well-known mechanism of interaction of ELF fields with biological tissues is the induction of time-varying electric currents and fields. At sufficiently high levels, these can produce direct stimulation of excitable tissues such as nerve and muscle cells. At the cellular level, the interaction induces voltages across the membranes of cells sufficient to stimulate nerves to conduct or muscles to contract. This mechanism accounts for the ability of humans and animals to perceive electric currents in their bodies and to experience electric shocks. Other mechanisms have been proposed, but there is little evidence to support them.

Electric fields: External ELF electric fields induce time-varying electric charges on the surface of the body. The magnitude and distribution of the charges depend on the body shape and its location and orientation relative to the field and ground plane. In addition, electric fields, electrical polarization changes, and currents are induced inside the body as a result of time-

variation of this surface charge density. Charges fixed on internal molecules polarize and depolarize as the field changes. Since time-variation in the ELF range is slow compared to the ability of charges to move, the fields and currents generated inside the body from this source are very small. The induced current density distribution depends on the electrical properties of the tissue and varies inversely with the body cross-section. Typically, the strength of the internal electric fields is less than about 10^{-6} of the external field.

Magnetic fields: The induced current density in the body is proportional to the rate of change of the magnetic flux density. For sinusoidal applied fields, the induced fields and currents are linearly dependent on frequency. The magnitude of the currents induced by pulsed magnetic fields will depend on the rise and fall time of the pulse. The highest current densities are induced in peripheral tissues, since these have the largest inductive loop radius in the body. However, tissue inhomogeneity and orientation of the body to the field will affect the current path. In general, the electric field induced in peripheral tissues by a horizontal magnetic field is approximately 1.5 times that induced by a vertical magnetic field of similar magnitude. Currents circulating from head to foot due to a horizontal magnetic field will be high in the neck because its small cross-section concentrates the flow.

For a human with torso radius of 0.15 m and tissue conductivity of 0.2 S/m, a 50 Hz magnetic field parallel to the long axis of the body will induce a current in the tissue periphery of about 5 A/m² per tesla. Since current density is proportional to body radius, current density values can be used to scale between animal and human exposure. Typical induced currents and fields for 1 μ T, 60 Hz uniform magnetic field-exposure of mice, rats and humans are in the range of 0.1-0.4, 0.3-1.3 and 1-20 μ A/m², respectively (Repacholi and Greenebaum, 1999).

ELF BIOLOGICAL EFFECTS

Laboratory studies: The AGNIR (2001) review concluded that there is no consistent evidence that exposure to ELF fields experienced in our living environment causes direct damage to biological molecules, including DNA. Since it seems unlikely that ELF fields could initiate cancer, a large number of investigations have been conducted to determine if ELF exposure can influence cancer promotion or co-promotion. Results from animal studies conducted so far suggest that ELF fields do not promote cancer.

Above about 0.1 mT, a variety of studies have demonstrated effects *in vitro* on ornithine decarboxylase (ODC) activity. Not all replication attempts have succeeded, however. Many other biological effects have been reported above about 1 mT (NIEHS, 1998). How magnetic field exposure produces such effects is unknown. For most effects, such as those reported on genotoxicity, intracellular calcium concentrations, or general patterns of gene expression, convincing and reproducible results have not been observed. None of the *in vitro* effects are necessarily indicative of an adverse health effect. Without knowledge of the mechanisms involved, effects observed at high field strengths cannot be extrapolated to lower fields, since the mechanisms may be different.

While there is no convincing evidence that ELF fields cause cancer in animals, only a limited number of studies have been conducted to test this hypothesis. Some recent studies suggest a

positive relationship between breast cancer in animals treated with carcinogens and ELF magnetic field exposure at approximately 0.02-0.1 mT. The importance of these findings needs to be investigated further (Repacholi and Greenebaum, 1999). Currently available data do not provide convincing evidence of adverse effects from exposure to power frequency fields on reproduction or development in mammals. There is evidence of behavioural and neurobehavioural responses in animals, but only following exposure to strong ELF electric fields.

Neuroendocrine changes are associated with exposure to ELF magnetic fields, but these alterations have not been shown to cause adverse effects in animals. Some studies suggest magnetic fields of strength between 0.01 and 5.2 mT might inhibit night-time pineal and blood melatonin concentrations in experimental animals. However, such effects have not been demonstrated in humans.

HUMAN LABORATORY STUDIES

Perception: Exposure to ELF electric fields can result in field perception as a result of alternating electric charge induced on the surface causing body hair to vibrate. Most people can perceive electric fields greater than 20 kV/m, and few people perceive field strengths below 5 kV/m. In two well-controlled studies, humans were unable to perceive magnetic fields at levels up to 1.5 mT (Repacholi and Greenebaum, 1999).

During exposure to ELF magnetic fields above 3-5 mT, volunteers experience faint visual flickering sensations or magnetophosphenes. The threshold current density in the retina for induction of magnetophosphenes is about 10 mA/m² at 20 Hz, well above typical endogenous current densities in electrically excitable tissues. Higher thresholds have been observed for both lower and higher frequencies (Repacholi and Greenebaum, 1999).

Cardiovascular system: Several reports indicate that ELF fields influence the cardiovascular system. Exposure of human volunteers to combined 60 Hz electric and magnetic fields (9 kV/m, 0.02 mT) resulted in small changes in cardiac function. Resting heart rates were found to be slightly but significantly reduced (about 3-5 beats/minute) during or immediately after exposure. This response did not occur with exposure to stronger (12 kV/m, 0.03 mT) or weaker (6 kV/m, 0.01 mT) fields and was reduced if the subject was mentally alert (NIEHS, 1998). In these double-blind studies, subjects were unable to detect the presence of the fields. While continuous exposure to combined electric and magnetic fields at 9 kV/m, 0.02 mT slows the heart, intermittent exposure can result in both slowing and increasing heart rate. None of the effects on heartbeat exceeded the normal range. No obvious acute or long-term cardiovascular-related hazards have been demonstrated at levels below current exposure standards for ELF or radio frequency fields.

Hormone and immune system effects: No changes in blood chemistry, blood cell count, blood gases, lactate concentration, skin temperature or circulating hormones have been observed. Field-related suppression of the hormone melatonin has been proposed as a mechanism for the relationship between exposure to magnetic fields and increased cancer risk (Repacholi and Greenebaum, 1999). However, well-controlled laboratory studies report mostly negative results, although some laboratory studies have reported positive results. No published reports have

examined possible differential effects in women, possible influence of longer exposure or of altering field polarization.

Epidemiological studies: ELF fields are known to interact with tissues by inducing electric fields and currents in them. This is the only established mechanism of action of these fields. However, the electric currents induced by ELF fields commonly found in our environment are normally much lower than the strongest electric currents naturally occurring in the body such as those that control the beating of the heart. Since 1979 when epidemiological studies first raised a concern about exposures to power line frequency magnetic fields and childhood leukaemia, a large number of studies have been conducted to determine if measured ELF exposure can influence cancer development, especially in children.

A Working Group formed by the National Institute of Environmental Health Sciences (NIEHS, 1998) to evaluate the health effects from exposure to ELF concluded that ELF magnetic fields are a *possible human carcinogen*. The evidence in support of this decision resulted from studies on childhood leukemia in residential environments and on chronic lymphocytic leukaemia (CLL) in adults in occupational settings. This conclusion is essentially in agreement with recent reviews in the UK (AGNIR, 2001), the Netherlands (Health Council of the Netherlands, 2001) and the IARC (2001) classification discussed below.

Pooled analyses (Ahlbom et al, 2000; Greenland et al 2000) of the epidemiological studies on exposure to ELF magnetic fields suggest that residence in homes near external power lines is associated with an approximate 1.5-2.0 fold relative risk of childhood leukaemia. These studies suggest that, in a population exposed to **average** magnetic fields in excess of 0.3 to 0.4 μT , twice as many children might develop leukaemia compared to a population with lower exposures. In spite of the large numbers in the database, some uncertainty remains as to whether magnetic field exposure or some other factor(s) might have accounted for the increased leukaemia incidence. These uncertainties occur for a number of reasons. Childhood leukaemia is a rare disease with 4 out of 100,000 children between the age of 0 to 14 diagnosed every year. Also average magnetic field exposures above 0.3 or 0.4 μT in residences are rare. Less than 1% of populations using 240 volt power supplies are exposed to these levels, although this may be higher in countries using 120 volt supplies.

These pooled analyses were influential for a working group of the International Agency for Research on Cancer (IARC) concluding that ELF magnetic fields were a "possible human carcinogen" for childhood leukaemia. "Possibly carcinogenic to humans" is a classification used to denote an agent for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence for carcinogenicity in experimental animals.

This classification is the weakest of three categories ("is carcinogenic to humans", "probably carcinogenic to humans" and "possibly carcinogenic to humans") used by IARC to classify potential carcinogens based on published scientific evidence. Some examples of well-known agents that have been classified by IARC are given in table 1. A full listing of the evaluations of carcinogenicity to humans of all physical, chemical and biological agents classified by IARC is available from their web page on: <http://www.iarc.fr>. WHO has published a fact sheet (WHO Fact Sheet, 2001) that explains this classification and advises on options that can be taken to address the concerns raised by such a classification.

Table 1: Examples of physical and chemical agents classified for carcinogenicity by IARC

Classification	Examples of Agents
Carcinogenic to humans (usually based on strong evidence of carcinogenicity in humans)	Asbestos Mustard gas Tobacco (smoked and smokeless) Gamma radiation
Probably carcinogenic to humans (usually based on strong evidence of carcinogenicity in animals)	Diesel engine exhaust Sun lamps UV radiation Formaldehyde
Possibly carcinogenic to humans (usually based on evidence in humans which is considered credible, but for which other explanations could not be ruled out)	Coffee Styrene Gasoline engine exhaust Welding fumes ELF magnetic fields

Occupational studies have generally used job titles, sometimes in combination with workplace ELF field measurements, to determine if any association exists between exposure to these fields and cancer. Elevated risks of various cancers have been reported, especially leukaemia, nervous system tumours and breast cancer; but the lack of uniformity of the results has been a major concern. Any excess cancer risk among electrical workers, compared to other occupations, is small and difficult to detect using epidemiological methods. Studies so far have been complicated by the lack of adequate exposure assessment in the workplace and possible confounding factors.

The basic problem with all epidemiological studies so far has been the lack of any concept of dose or an exposure metric established from laboratory studies. Metrics used have generally been cumulative exposure or time-weighted average field strength. Very little information has been obtained about exposure from appliances, ground currents or devices that may be associated with transient fields. Brief exposures to high-amplitude magnetic field transients or to high-frequency harmonics have not been assessed in published studies. Personal dosimeters do not exist that can capture this information.

ELF RESEARCH NEEDS

Independent replication of some key studies is a high priority. When effects are robust, replication should be straightforward and can be used as a basis for extending observations. It is important to characterize the dose-response relationship (field strength, threshold and exposure duration) of any effect, particularly at environmentally relevant field strengths. Where possible, *in vivo* studies should consider exposures that include intermittence, transients, and duration as important variables. In addition, it would be valuable to consider the interactions of ELF fields with other agents, such as ionizing radiation and chemicals. These interactions should test the hypothesis that ELF fields may act as a co-promoter for cancer, but other end points suggested by the *in vitro* literature should also be examined. Wherever possible, exposures should be relevant to those experienced by humans in occupational and residential settings. Some cancer-related

studies using various animal models are currently under way. Research gaps identified by WHO are as follows:

- Confirmation and extension of animal studies reporting increased tumour incidence when magnetic fields are applied in combination with chemical carcinogens. These experiments should focus on dose-response relationships and the relationship between different exposure conditions.
- Confirmation and extension of studies suggesting that magnetic field exposure influences mammary cancer development. Possible changes in relevant hormonal factors in magnetic field-exposed animals and controls should be investigated to examine potential mechanisms.
- Neurophysiology/neurobehavioural studies using models of neurodegenerative diseases are indicated because of recent reports of possible ELF-field influence on human neurodegenerative diseases, such as Alzheimer disease.
- While most studies of ELF field effects on various end points in reproduction and development have been negative, new studies should provide information on long-term neurobehavioural consequences following *in utero* exposure to magnetic fields. These studies should address whether ELF fields can produce effects on early brain development as measured in functional behaviour in adult animals.

Epidemiology research needs: The most important prerequisite for future epidemiological studies is a clearer understanding of what metric should be used to characterize ELF field exposure. This may come from laboratory work or from additional hypothesis-generating epidemiological studies, each of which has advantages and disadvantages in cost, time, and precision. Project designs for new epidemiological research should, within the limits of what is possible, increase the role of measured past and present exposures. Dependence on surrogates, such as wire codes and job classifications, should decrease, particularly if data do not exist that establish how well the surrogates select for historical exposure. The *a priori* estimates of the power of future studies must be strong enough to predict useful information, given the outcomes of past research.

Because many, but not all studies show a small but significant excess in childhood leukaemia associated with residence in high wire code homes in the US (the only country where this surrogate has been used) a concerted effort is needed to explain this association. While efforts have been made to define the relationship between wire codes and average magnetic field exposure or socio-economic confounding factors, little evidence is available about the relationship between wire codes and high-amplitude transient fields or high-frequency harmonics. Future studies should include these and ground currents in the exposure assessments. Another aspect to be seriously pursued in future studies is the inclusion of non-occupational exposure.

With the above caveats, needed future epidemiological studies should:

- Address the relationship between exposure and cancer incidence that properly assess both residential and occupational exposure over long periods, including transient magnetic-field exposure and high-frequency harmonics.

- Determine if correlates of wire codes, such as traffic density, age of home and socio-demographic characteristics of home occupants, can explain the statistical relationship between wire codes and childhood leukaemia.
- Study the relationship between breast cancer and field exposure, including evaluation of both average field levels and of transients and high-frequency components and taking into account both occupational and non-occupational exposures.
- Investigate the relationship between neurodegenerative disorders and field exposure, including an evaluation of the role of average fields levels, transients and high-frequency components. Both occupational and non-occupational exposures should be considered.
- Study the relationship between heart disease end points and exposure to ELF fields, including evaluation of the role of transient and high frequency components and taking into account both occupational and non-occupational exposures.

Volunteer studies: Further studies are needed, especially using transient and high frequency components typical of environmental ELF fields, to determine:

- Whether any component of the human melatonin hormone system is susceptible to ELF field exposure and, if so, the likely health consequence of this susceptibility.
- Whether sleep disruption, changes in neurotransmitter metabolism, and learning and memory are associated with ELF field exposure.
- The relationship between field exposure and slowing and variability in heart rate.
- Whether electrophysiological indices of central nervous system activity and function are affected by ELF fields.

Subjective effects: Given the limited evidence, but widespread concern about subjective effects, more research is needed to determine whether these health effects can be substantiated and can be related to EMF exposure. The current laboratory results should be extended, and their relevance clarified.

INTERMEDIATE FREQUENCIES (IF)

Compared to the extremely low frequency (ELF) and radiofrequency (RF) range, few biological effects studies have been conducted and few reviews have been published that focus on health risks from IF sources. International EMF exposure guidelines (ICNIRP, 1998) at IFs have been established by extrapolating limits from the ELF and RF frequency ranges, based on principles of coupling of external fields with the body and assumptions about the frequency dependence of bioeffects. Because applications of EMF in this frequency range are increasing rapidly, it is important to properly evaluate the significance of any effects on human health.

A wide range of equipment produces electric or magnetic fields in the IF range. Common sources of IF fields include: monitors and video display units (3 - 30 kHz), AM radio (30 kHz - 3 MHz), industrial induction heating devices (0.3 - 3 MHz), and anti-theft and remote detection systems. In most cases the exposures to humans from these devices are within recommended limits, although the guidelines may be exceeded in some cases. Workers in a few occupational groups (operators of heat sealers and induction heaters, some military personnel, technicians working

near high powered broadcast equipment) are undoubtedly exposed to considerably higher levels of IF fields than the general population.

Mechanisms of Interaction: Understanding the mechanisms of interaction between EMF and biological systems is important for several reasons. First, determining the thresholds for hazard at IFs currently requires extrapolation of biological data from lower and higher frequency ranges. For this, an understanding of the mechanisms for effects is important. More generally, hypotheses about mechanisms of interaction can help clarify biological phenomena and guide further experimentation.

Several mechanisms, both thermal (above about 100 kHz) and non-thermal (below about 100 kHz), by which electromagnetic (primarily, electric) fields can interact with biological systems are well established. Each mechanism is characterised by a strength of interaction and a response time (Litvak et al., 2002). The first determines the threshold for producing observable effects in the presence of random thermal agitation (noise). The second determines the frequency response of the effect, which is typically characterised by a cut-off frequency (above which the threshold increases with frequency). In addition, EMF can heat tissue, resulting in a variety of thermal effects. The limiting hazard will arise from the adverse effect (thermal or non-thermal) that has the lowest threshold under given exposure conditions.

INTERMEDIATE FREQUENCY BIOLOGICAL AND HEALTH EFFECTS

Most biological effects studies in the IF range have employed field levels far above exposure guidelines, and above realistic exposure levels for humans. However, in some cases the exposure levels have been below recommended limits. Virtually none of the effects described below have any apparent explanation in terms of accepted biophysical mechanisms of interaction. The results and conclusions included here are from a recent WHO meeting (Litvak et al., 2002).

Most studies have used field levels above international guidelines for human exposure or otherwise have unclear relevance to normal exposure situations. As with other EMF ranges, few reported effects of IF fields have been subject to independent confirmation, and in some cases investigators have suggested the presence of confounding effects that may have led to previously reported effects of IF. Most epidemiological studies on human exposure to IFs concern possible reproductive effects and were motivated by health concerns from exposure to fields emitted by VDUs. Other studies have been reported on workers occupationally exposed to fields in the IF range. However, because of the weak associations in these studies, the use of multiple comparisons in the data analysis, and other uncertainties, they provide no strong evidence for health hazards.

The working group formed during the WHO meeting on the IF range, held in Maastricht in June 1999, felt that the health implications of these findings are difficult to assess. The general consensus was that current scientific evidence does not show the presence of health hazards from IFs at exposures below recommended guidelines. However, the biological data are sparse, particularly related to effects of low-level exposure. A few epidemiology studies have suggested links between IF exposure and health effects, but they are compromised by technical problems and cannot be reliably interpreted. Even for established hazards, there is a need to better

determine thresholds, particularly for fields with complex waveform or pulsed fields. Any epidemiological studies at IFs should be preceded by pilot studies demonstrating their feasibility.

RADIOFREQUENCY (RF) FIELDS

Common sources of RF fields include: RF heat sealers, medical diathermy (3 - 30 MHz), FM radio (30 - 300 MHz), mobile telephones, television broadcast, microwave ovens, medical diathermy (0.3 - 3 GHz), radar, satellite links, microwave communications (3 -30 GHz) and the sun (3 -300 GHz).

Hazards of exposure to high levels of RF fields, which result in tissue heating, are basically understood, although there are still a number of unresolved issues. Thermal hazards are associated with acute exposures and are thought to be characterized by thresholds, below which they are not present. However, many studies have suggested that RF exposure at lower than thermal levels may have biological effects, but they have either not been consistently replicated or else their significance for human health cannot be adequately assessed using information currently available. Scientific research into possible health effects has been unable to keep pace with the rapid advances in the applications of RF fields in our working and living environment. This delay has led to widespread concerns among the general public and workforce that there are unresolved health issues that need to be addressed as a matter of urgency.

Although many reports in the scientific literature claim effects in biological systems exposed to low levels of RF, the mechanisms for these reported effects are unknown, and their relevance for human health uncertain.. In this respect, one of the major challenges is to better understand and more clearly establish the effects reported at low RF levels.

Mechanisms of interaction: RF fields induce torques on molecules, which can result in displacement of ions from unperturbed positions, vibrations in bound charges (both electrons and ions), and rotation and reorientation of dipolar molecules such as water. These mechanisms, which can be described by classical electrodynamic theory, are not capable of producing observable effects from exposure to low-level RF fields, because they are overwhelmed by random thermal agitation. Moreover, the response time of the system must be fast enough to allow it to respond within the time period of the interaction. Both considerations imply that there should be a threshold (below which no observable response occurs) and a cut-off frequency (above which no response is observed). These thresholds would be expected to be present even in more refined models if they correctly take into account thermal noise and the kinetics of the system.

Exposure to EMF at frequencies above about 100 kHz can lead to significant absorption of energy and temperature increases. In general, exposure to a uniform (plane-wave) electromagnetic field results in a highly non-uniform deposition and distribution of energy within the body, which must be assessed by dosimetric measurement and calculation. For absorption of energy by the human body, electromagnetic fields can be divided into four ranges:

- frequencies from about 100 kHz to less than about 20 MHz, where absorption in the trunk decreases rapidly with decreasing frequency, and significant absorption may occur in the neck and legs;
- frequencies in the range from about 20 MHz to 300 MHz, at which relatively high absorption can occur in the whole body, and to even higher values if partial body (e.g., head) resonances are considered;
- frequencies in the range from about 300 MHz to several GHz, at which significant local, non-uniform absorption occurs;
- frequencies above about 10 GHz, at which energy absorption occurs primarily at the body surface.

RADIOFREQUENCY BIOLOGICAL EFFECTS

The information below is taken from reviews by WHO (Repacholi, 1998), the International Commission on Non-Ionizing Radiation (ICNIRP, 1998) and an Independent Expert Group on Mobile Phones (IEGMP, 2000) in the UK.

In Vitro: Reports from *in vitro* research indicate that low-level RF fields may alter membrane structural and functional properties that trigger cellular responses. It has been hypothesized that the cell membrane may be susceptible to low-level RF fields, especially when these fields are amplitude-modulated at ELF frequencies. At high frequencies, however, low-level RF fields do not induce appreciable membrane potentials. They can penetrate the cell membrane and possibly influence cytoplasmic structure and function. These RF field-induced alterations, if they occur, could be anticipated to cause a wide variety of physiological changes in living cells that are only poorly understood at the present time.

A lack of effect of RF exposure on mutation frequency has been reported in a number of test samples including yeast and mouse lymphoid cells. No effect of RF-field exposure on chromosome aberration frequency in human cells has been confirmed (Repacholi, 1998).

Animal studies: In contrast to the evidence given above, several rodent studies indicate that RF fields may affect DNA directly. These papers report quantitative data subject to sources of inter-trial variation and experimental error such as incomplete DNA digestion or unusually high levels of background DNA fragmentation. These experiments need to be replicated before the results can be used in any health-risk assessment, especially given the weight of evidence that RF fields are not genotoxic. Further, in animal studies, most well conducted investigations report a lack of clastogenic effect in the somatic or germ cells of exposed animals (ICNIRP, 1998). Other investigations that require further attention relate to possible synergistic action of RF exposures with chemical or physical mutagens or carcinogens.

Most cancer studies of animals have sought evidence of changes in spontaneous or natural cancer rates, enhancement by known carcinogens, or alterations in growth of implanted tumours (ICNIRP, 1998). However, they have provided only equivocal evidence for changes in tumour incidence. Chronic RF field exposure of mice at 2-8 W/kg resulted in an SAR-dependent increase in the progression or development of spontaneous mammary or chemically induced skin tumours. In a further study, exposure at 4-5 W/kg, followed by application of a sub-carcinogenic

dose of a chemical carcinogen to the skin, a procedure repeated daily, eventually resulted in a three-fold increase in skin tumours. However, at these high exposures, temperature-mediated effects cannot be excluded.

Studies in which cancer cells were injected into animals have reported a lack of effect of exposure to CW and pulsed RF fields on tumour progression. Progression of melanoma in mice was unaffected by daily exposure to pulsed or CW RF fields following subcutaneous implantation, and progression of brain tumours in rats was not affected by CW or pulsed RF fields following the injection of tumour cells into the brain.

Moderately lymphoma-prone E μ -*Pim1* oncogene-transgenic mice were exposed or sham-exposed to radiofrequency fields for 1 h/day for up to 18 months using pulse modulations similar to that used for digital mobile telephones. Exposure was associated with a statistically significant, 2.4-fold increase in the risk of developing lymphoma (Repacholi *et al.* 1997). This long-term study needs replication and extension to other exposure levels and animal models before it can be used for health-risk assessments. Further research is also needed to determine the significance of effects in this transgenic model for human health risk.

Although weak evidence exists, it fails to support an effect of RF exposure on mutagenesis or cancer initiation. There is scant evidence for a co-carcinogenic effect or an effect on tumour promotion or progression. However, only a few studies have been published and these are sufficiently indicative of an effect on carcinogenesis to merit further investigation.

Effects on other systems: While many studies have been conducted at high-levels of RF exposure few relevant studies have used low-levels. Some of the more important studies are described below.

The blood-brain barrier (BBB) is a specialised neurovascular complex that functions as a differential filter permitting selective passage of material from the blood into the brain. It maintains the physiological environment of the brain within certain limits that are essential for life. Although extensive previous research has been unable to reliably identify permeability changes at low levels of RF exposure, in recent studies, increased BBB permeability was reported for RF exposures at SARs as low as 0.016 W/kg. These studies need replication and extension to allow a better determination of any possible health consequence.

Exposure to very low levels of amplitude modulated RF fields were reported to alter electrical activity in the brain of cats and rabbits. These experiments need replication and extension.

Early signs of neurotoxicity are often behavioural rather than anatomical. Current Western standards are based on behavioural changes occurring in response to temperature elevations in excess of one degree Celcius. However few studies have been conducted at low RF levels and there is a need to do these (IEGMP, 2000).

Pulsed radiation: Exposure to low-level pulsed and CW RF fields has been reported to affect brain neurochemistry in a manner consistent with responses to stress. Effects on behaviour and drug interaction have been obtained with the same exposure parameters. Replication studies are needed to establish and provide further information on these effects.

Exposure to very intense pulsed RF fields suppresses the startle response and evokes body movements in conscious mice (ICNIRP, 1998). The mechanism for these effects is not well established, and is clearly associated with heating at higher absorbed energies.

People having normal hearing perceive pulse-modulated RF fields with carrier frequencies between about 200 MHz and 6.5 GHz; the so-called *microwave hearing* effect. The sound has been variously described as a buzzing, clicking, hissing or popping sound, depending on modulation characteristics. Prolonged or repeated exposure may be stressful (Repacholi, 1998).

The retina, iris and corneal endothelium of the primate eye were reported to be susceptible to low-level RF fields, particularly when pulsed. Various degenerative changes in light sensitive cells in the retina, were reported at specific energies per pulse (10-m pulses at 100 pps), as low as 2.6 mJ/kg after the application of a drug used in glaucoma treatment. However, these results could not be replicated for CW fields (Repacholi, 1998).

EPIDEMIOLOGICAL AND HUMAN VOLUNTEER STUDIES

Cancer: By far the greatest public concern has been that exposure to low-level RF fields may cause cancer. Of the epidemiological studies addressing possible links between RF exposure and excess risk of cancer, some positive findings were reported for leukaemia and brain tumours. Review groups that evaluated possible links between RF exposure and excess risk of cancer have concluded that there is no consistent evidence of a carcinogenic hazard. In some studies there are significant difficulties in assessing disease incidence with respect to RF exposure and with potential confounding factors such as ELF and chemical exposure. Overall the epidemiological studies suffer from inadequate assessment of exposure and confounding, and poor methodology (IEGMP, 2000).

Overall, the results are inconclusive and do not support the hypothesis that exposure to RF fields causes or influences cancer. However, epidemiological studies in some 14 countries, coordinated by IARC, are under way to determine if there is any relationship between mobile phone use and head or neck cancers. These studies should provide substantial new information on RF exposure and its relationship to cancer causation. Further studies are under way to evaluate potential carcinogenic effects of chronic exposure to low-level RF fields and more are needed.

Other outcomes: Other health outcomes investigated following RF exposure, include headaches, general malaise, short-term memory loss, nausea, changes in EEG and other central nervous system functions, and sleep disturbances. There have also been anecdotal reports from several countries of subjective disorders such as headaches associated with the use of mobile telephones. Whether exposure to RF fields at very low-levels can cause such subjective effects has not been substantiated from current evidence, but further research is indicated.

Individuals have claimed to be hypersensitive to electromagnetic fields. The most common symptoms are headaches, insomnia, tingling and rashes of the skin, difficulty in concentrating and dizziness. Given the limited evidence and widespread concerns that the above effects have provoked, more research is needed to determine if these health effects can be substantiated.

Adverse maternal health outcomes, particularly spontaneous abortions and haematological or chromosome changes, have been reported to occur in certain populations exposed to RF fields. Some of these changes have also been reported in users of video display units. Taken overall, the studies in this area have not substantiated these effects (Repacholi, 1998; ICNIRP, 1998; IEGMP, 2000).

RF FIELD RESEARCH NEEDS

Since the EMF Research Agenda was first published by WHO in 1996, many national and international agencies have funded research that contributes substantially towards the studies needed to make better health risk assessments. Most of the *in vivo* and *in vitro* studies have now been completed or are under way. An updated RF research agenda has been drafted following a meeting in Geneva in June 2003. This has been posted on the WHO EMF Project web site at: <http://www.who.int/peh-emf/research/rf03/en/>

Human laboratory studies: By far the most important deficiency in the RF research under way is in the area of effects on human volunteers. There is still a basic need to perform studies on human volunteers under laboratory conditions to determine basic physiological responses to pulsed, non-thermal levels of RF similar to those emitted by mobile telephones. It is anticipated that following the recommendations of the Stewart report (IEGMP, 2000), a further \$10 million will be devoted to this research, with emphasis on human laboratory studies. Using established batteries of tests or study designs, there is a need to investigate:

- Psychological effects related to the use of mobile phones as well as measurable changes in blood pressure, brain and cognitive function (including memory or learning), any other effects likely to effect the CNS, reaction times, auditory evoked potentials, EEG, ECG, EKG and others
- Biological effects on human brain function to determine if it is affected by different RF pulsing regimens (test to Hyland-Frölich hypothesis)
- RF effects on children to determine if they are more sensitive than are adults
- People who claim to show a greater sensitivity to RF fields; hypersensitivity reactions, sleep disturbance, other subjective effects.

Animal studies: While a number of studies are in progress under contracts from the 5th framework program of the European Commission, and a major study has been announced under the US National Toxicology Program, there is still a need for the following:

- Address long-term memory and behavioural studies in animals since this cannot be done effectively in humans.
- Follow-up study on cancer promotion using DMBA.

In vitro studies: As a lower priority, there is a need to conduct:

- *In vitro* investigations of ODC and cell signalling molecules. The ODC results need to be resolved, as well as the ongoing debate about calcium efflux.
- Hippocampal slice preparation studies showing transient changes in evoked and spontaneous activity
- More complete studies of the possibility that pulsed RF fields can initiate gene expression.

CONCLUSIONS AND RECOMMENDATIONS

All reviews conducted so far have indicated that exposures below the limits recommended in the ICNIRP (1998) EMF guidelines, covering the full frequency range from 0-300 GHz, do not produce any known adverse health effect. While there is more research needed in areas already identified before better health risk assessments can be made, it is likely that if any adverse effect on health is found from EMF exposure, it will likely be minor.

WHO is now in the process of making a complete assessment of health risks and risk estimation for the whole EMF range. The results of this will not be available for a few years, but it is expected that they will impact on the management of EMF. The degree of public concern and remaining uncertainties in the science base (mainly whether long-term, low-level exposures will impact on health), have meant that there has been a significant move towards determining whether precautionary measures should be invoked until science is able to address remaining issues. WHO has provided information on this (Foster et al., 2000; WHO Backgrounder 2000) for member states.

Recommendations have been issued by WHO through a series of fact sheets (WHO Fact Sheets numbers 193, 205 and 263). They deal with EMF exposure limitation and precautionary measures that might be adopted and can be summarized as follows:

- Adopt mandatory health-based EMF exposure limits (such as ICNIRP, 1998) to protect public health
- Adopt, as needed, voluntary precautionary measures that reduce unnecessary EMF exposure to address public concern

Examples of possible precautionary measures that could be adopted have been published in the WHO Backgrounder (2000).

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