THE INTERNATIONAL EMF PROJECT

WHO's AGENDA FOR EMF RESEARCH

INTRODUCTION

General

Potential effects of exposure to static and time varying electric and magnetic fields are causing significant public and occupational health concerns and need scientific clarification. Electromagnetic fields (EMF) represent one of the most common and the fastest growing environmental influences in our lives, about which anxiety and speculation are spreading. Health effects such as cancer, changes in behaviour, memory loss, Parkinson's and Alzheimer's diseases, and many others, have been suggested as resulting from exposure to EMF.

To address these concerns WHO established the International EMF Project and is collaborating with the International Commission on Non-Ionizing Radiation Protection, International Agency for Research on Cancer, International Electrotechnical Commission, International Labour Office, International Telecommunications Union, United Nations Environment Programme, North Atlantic Treaty Organization, European Commission, over 40 governmental agencies, and the following WHO collaborating institutions: National Radiological Protection Board, UK; Bundesamt für Strahlenschutz, Germany; Karolinska Institute, Institute of Environmental Medicine, Sweden; Food and Drug Administration, USA; National Institute of Environmental Health Sciences, USA; National Institute of Occupational Health, USA; and the National Institute for Environment Studies, Japan.

The International EMF Project is assessing health effects of exposure to static and time varying electric and magnetic fields in the frequency range 0 - 300 GHz. This range is divided into: static (0 Hz), extremely low frequency (ELF, > 0 - 300 Hz) and radiofrequency fields (RF, 300 Hz - 300 GHz). The Project was established by WHO in 1996 to:

(1) provide a coordinated international response to the concerns about possible health effects of exposure to EMF,
(2) assess the scientific literature and make status reports on health effects,
(3) identify gaps in knowledge needing further research to make better health risk assessments,
(4) encourage a focused research programme to fill important gaps in knowledge,
(5) incorporate research results into WHO Environmental Health Criteria monographs, in which formal health risk assessments of exposure to EMF will be made,
(6) provide information on risk perception, risk communication and risk management as they apply to EMF,
(7) provide advice and publications to national authorities on EMF issues
(8) facilitate the development of internationally acceptable standards for EMF exposure.

The International EMF Project, in collaboration with the International Commission on Non-Ionizing Radiation Protection (ICNIRP), has completed initial international scientific reviews of possible health effects of exposure to electromagnetic fields (EMF). These reviews provide interim conclusions on health hazards from exposure to EMF and gaps in knowledge requiring further research before better health risk assessments could be made by WHO. They are summarized in the Munich and Bologna meeting reports (Repacholi, 1998; Repacholi and Greenebaum, 1998), covering radiofrequency (RF: > 300 Hz to 300 GHz) and static and extremely low frequency (ELF: >0 to 300 Hz) fields, respectively.

The reviews identified research that had raised unresolved questions about whether exposure to low-level EMF, particularly over long periods, has any deleterious effects on human health. WHO's Research Agenda has been formulated to try to resolve these questions. The Agenda below resulted from an ad hoc Research Coordination meeting held in Geneva 4-5 December 1997. At this meeting, ongoing research was noted that would meet WHO's requirements for health risk assessment, and this was compared with research needs identified during the scientific reviews. The additional research still needed by WHO then formed the Agenda below.

For new studies to be useful to future health risk assessments, the research must be of high scientific quality with clearly-defined hypotheses, estimates of the ability of the study to detect small effects, and use protocols that are consistent with good scientific practice. Quality assurance procedures should be included in the protocol and monitored during the study. Criteria for assessment of EMF health risks used by WHO and the International Agency for Research on Cancer, are given in Repacholi and Cardis (1997).

This Research Agenda, publications of the Project, updates on activities and further information about the Project, can be found on the home page at: http://www.who.ch/emf/.

Definitions

The WHO constitution defines ***health*** as ***a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity***. This definition includes an important subjective component that must be taken into account in health risk assessments. Within the International EMF Project, a working definition of health hazard has been developed: ***A health hazard is a biological effect outside the normal range of physiological compensation that is detrimental to health or well-being***. In this definition, a ***biological effect is a physiological response to exposure***. For the biological effect to lead to some adverse health consequence, it should be ***outside the normal range of compensation***, in order to place it beyond normal variation in body responses.

Determining Research Needs

The criteria used to evaluate health risks by the International EMF Project were adapted from those used by WHO's International Agency for Research on Cancer (IARC) (Repacholi and Cardis, 1997). Research needs were identified when the evidence for a health risk was judged suggestive, but insufficient to meet the criteria for assessing health risk. Research needs were established on the basis of unconfirmed effects having implications for health, and replication of key studies to confirm effects. Thus, the overall goal is to promote studies which demonstrate a reproducible effect of EMF exposure that has the likelihood to occur in humans and has a potential health consequence.

While *in vitro* studies can provide important insights into fundamental mechanisms for biological effects from exposure to low-level EMF, *in vivo* studies, whether on animals or human beings, provide more convincing evidence of adverse health consequences.

Epidemiological studies provide the most direct information on risks of adverse effects in human beings. However, these studies have limitations, especially when low relative risks are found. Epidemiological studies are important for monitoring public health impact of exposure, particularly from new technologies.

In these times of scarce budgetary resources it is of importance that the correct mix of priority studies is performed. Obviously, only studies likely to provide useful results should be conducted. In addition to scrutinizing the goals of a proposal, it is important to assess its feasibility and probability that it can detect an effect. Proposed studies should be also evaluated for:

(i) characterization and/or control of potential confounders,
(ii) reproducibility of exposure conditions or measurements and their relevance to human exposures, and
(iii) ongoing quality assurance.

Priority should be given to studies designed to investigate health hazards of concern to the general public, hazards of potential public health importance (based on the size of the populations potentially exposed, the extent of their exposure, and the seriousness of the hypothesized adverse effect), and studies of scientific importance (e.g., testing the relevance of effects observed or mechanisms postulated on the basis of *in vitro* or *in vivo* results).

EMF RESEARCH PRIORITIES

Radiofrequency Fields

Relatively high-intensity RF fields have been shown to cause adverse health consequences by heating tissues. No adverse health effects have been scientifically confirmed from exposure to low-level RF fields for extended periods, but certain questions have not been thoroughly studied. There is very little information available in the scientific literature to assess any health risks from exposure to pulsed RF fields. Studies are needed that seek to identify any biological effects produced by pulsed RF fields, of both high and low peak pulse intensities. Examples of current and future technologies using pulsed RF fields are telecommunications, civilian and military radar

systems, including emerging radar technology such as ultra-wide band radars. Current and future research applicable to mobile telephone systems should focus on the 900-2000 MHz frequency range and appropriate pulsing and modulation patterns. For radars, the frequency and pulsing regimes should be applicable to current and emerging systems.

It is essential for high quality research that accurate assessment of RF field exposure be an integral part of all future studies and that each research team include scientists skilled in RF dosimetry. It is recommended that studies have a dosimetric precision of 30% or better. Development of instruments or assessment methods that can conveniently and accurately measure an individual's exposure to RF over an extended period is a high priority for future epidemiological studies.

(i) Several animal experiments, using various RF exposure regimens, are currently under way, and their results should add to the required database for health risk assessment. However, at least two more, large-scale standard 2-year animal bioassays, such as those typically conducted by the US National Toxicology Program, are needed to test for cancer initiation, promotion, co-promotion and progression. These experiments should expose normal animals and animals initiated with chemical carcinogens to RF fields in the mobile telephone frequency range, using one of the common mobile telephone system pulsing patterns, for 2-6 hours daily. Each study should use a range of intensities (normally 4 different SARs), with the highest being just below the level that may induce temperature changes.

(ii) A large study has suggested that exposure to RF fields increases the incidence of lymphomas in genetically manipulated (transgenic) mice. There is need for at least a further two large studies, using designs similar to (i) above, to clarify the issues raised by this study. Follow-up research is also needed that provides information on the health implications of effects found in transgenic animals.

(iii) Additional studies are needed to test the reproducibility of reported changes in hormone levels, effects on the eye, inner ear and cochlea, memory loss, neurodegenerative diseases and neurophysiological effects. These studies can be performed on animals, but where possible, they should be conducted on human volunteers.

(iv) Analysis of current epidemiological studies of people exposed to low levels of RF has not shown any adverse health effects. However, mobile telephone use is relatively new, and further work is needed. As a general principle, studies on populations exposed to RF at higher levels, though still below the threshold of heating, are more likely to provide information regarding the existence of any health effects, even though such exposure levels may not be representative of general-population exposure. Because of exposure to low levels, causing limitations on exposure assessment, studies of populations exposed to point sources, such as broadcast towers or mobile telephone base stations, are unlikely to be informative about the existence of health effects. Suggestions of an increased incidence of cancer in populations around mobile telephone base stations have not been substantiated.

There needs to be conducted at least two large-scale epidemiological studies with well characterized, higher-level RF exposures to investigate cancers, particularly in the head and neck, and any disorders associated with the eye or inner ear. These studies should preferably be on mobile telephone users or on workers in industries giving high RF exposures provided valid exposure assessments can be developed.

(v) Both epidemiological and laboratory studies are needed to provide basic information that allows better assessments of any health risks from exposure to radar technology, particularly emerging systems such as ultra-wide band radars.

(vi) Well controlled studies are needed to test people reporting specific symptoms, such as headache, sleep disorders or auditory effects, and who attribute these symptoms to RF exposure. Past human volunteer studies of this type have not successfully linked the symptoms and exposure. Several more controlled investigations should be performed to investigate neurological, neuroendocrine, and immunological effects.

(vii) *In vitro* studies normally have a lower priority than *in vivo* or human studies in health risk assessment. However, such studies can be of great assistance if they are directly relevant to possible *in vivo* effects, and address the issues of RF exposure thresholds and reproducibility for reported positive effects on cell cycle kinetics, proliferation, gene expression, signal transduction pathways and membrane changes. Theoretical modelling investigations can be useful if they support *in vivo* studies by proposing testable basic mechanisms of RF field exposure.

ELF Electric and Magnetic Fields

Some epidemiological studies have suggested an increased risk of leukaemia in children living near power lines. Whether this is due to exposure to ELF magnetic fields or some other factor in the environment, has yet to be determined. Other unresolved issues for health relate to studies suggesting that ELF exposure may be associated with increases in breast and other cancers in adults, neurodegenerative diseases, such as Alzheimer's, and subjective or non-specific effects, e.g. "hypersensitivity" to electricity.

There have been no published studies specifically investigating possible biological effects from exposure to transients (from switching electric currents) or high frequency harmonic fields that are normally superimposed on 50/60 Hz fields in living and working environments. On theoretical grounds, transient or high frequency harmonic fields are more likely to cause biological effects than sinusoidal 50/60 Hz fields. Additional studies identified as necessary to complete WHO's EMF Research Agenda include:

(i) Thorough surveys of transients and other perturbations of 50/60 Hz fields are needed to better characterize actual fields and to determine their prevalence in the environment. These fields are more likely to produce biological effects that pure sinusoidal 50/60 Hz since they may induce signals in cells above their normal electrical noise levels.

(ii) At least two 2-year standard bioassay animal studies, like those conducted by the US National Toxicology Program, with exposures to ELF fields that include transients (described in (i) above), that test for common types of cancer.

(iii) At least one 2-year standard bioassay animal study, similar to that described in (ii) above, using sinusoidal 50/60 Hz fields and two such studies using transient-perturbed fields, to test specifically for breast cancer.

(iv) Epidemiologists and physical scientists should discuss how to refine their methodologies and assessment of past and present exposure to 50/60 Hz fields and transients. This should be followed by pilot studies that test and validate these refinements. At least two further large, multi-centred epidemiological studies of childhood leukemia are needed that use the best available methods of exposure assessment, including assessment of transient and higher frequency harmonic fields.

(v) Large epidemiological studies are also needed to investigate possible associations between exposure to 50/60 Hz fields and breast cancer or neurodegenerative diseases. These studies should be conducted on highly exposed occupational groups using the best available methods of exposure assessment.

(vi) Human volunteer studies are needed to determine whether ELF fields affect certain hormone levels (e.g. melatonin). These studies should extend the exposures beyond the one night used in past experiments and also test both sexes. It is important that future studies test for effects caused by transients and other perturbed fields.

If results of current studies of people claiming hypersensitivity ELF fields are confirmed, particularly studies of their responses to fields applied in controlled laboratory situations, these reports should be investigated to determine what further research is needed.

(vii) *In vitro* studies are needed that are directly relevant to possible *in vivo* effects, and that address the issues of ELF exposure thresholds and reproducibility for reported positive effects on cell cycle kinetics, proliferation, gene expression, signal transduction pathways and membrane changes.

Theoretical modelling investigations are also needed that support *in vivo* studies by proposing testable basic mechanisms on how low-intensity fields and realistic environmental transients might interact with biological systems.

Static Fields

Research to date indicates that static electric fields do not produce deleterious health effects in humans at levels found in the environment or workplace. Therefore, further research into their possible effects is not recommended at this time.

Static magnetic fields are known to produce health effects only at very high field strengths. Technologies, such as magnetically levitated trains, medical diagnosis and treatment, and industrial applications are increasing in use or are being developed. They use intermediate or high-intensity static magnetic fields, which could increase public and worker exposure significantly. More information on possible long-term effects on health from exposure to static magnetic fields is needed. Studies needed to provide this information include:

(i) At least two standard 2-year animal bioassay studies concentrating on cancer-related effects. These studies should follow criteria used by the US National Toxicology Program.

(ii) At least two large-scale, multi-centre epidemiological studies on workers that characterize static magnetic field exposure well, minimize confounding factors, and include measurements of exposure from other sources of EMF.

(iii) Additional studies are needed that examine biological effects of exposure to combined static and time-varying fields, including transients, particularly those found in transportation systems.

GUIDELINES FOR QUALITY EMF RESEARCH

Introduction

The following set of guidelines has been summarized from the scientific reviews into the biological effects of EMF exposure held under the International EMF Project (Repacholi, 1998; Repacholi and Greenebaum, 1998). They are intended to assist researchers to complete studies that will be useful to WHO for health risk assessments. Studies with methodology deviating significantly from these guidelines may not provide information useful for health risk assessments. These guidelines have been developed for *in vitro*, *in vivo*, human volunteer and epidemiological studies.

General Experimental Design

1. The project should test a clearly defined hypothesis, using a detailed protocol that would lead to information directly or indirectly relevant to assessment of health risk from EMF exposure.

2. The biological system used should be appropriate to the end-point(s) studied. Threshold and dose-response data (using at least 3 levels of exposure, in addition to sham-exposed controls) are sought where possible.

3. Well-characterized biological systems or assays should be used, preferably ones that are well-established from the scientific literature available.

4. The *a priori* estimated power of the experiment, based on prior knowledge and the number of tests planned, should be sufficient to detect reliably the expected size of the effect (often as small as 10-20%).

5. Good Laboratory Practice (GLP) should be used throughout the design and conduct of the study (see, e.g. FDA, 1993). A specific protocol, consistent with the GLP guidelines, should be established and documented. Any changes instituted during the course of the study should also be documented. The protocol should include randomized, symmetric handling of specimens and their sources, except when precluded by the nature of the experiment or biological system. The protocol should include all appropriate controls (positive, negative, cage controls, sham-exposed etc.). Investigators should be blind to whether they are working with exposed or control materials; human subjects in laboratory experiments should be similarly unaware of their exposure status.

6. Quality assurance (QA) procedures should be included in the protocol, including dosimetry and monitoring of the programme by both a team from within the experimental staff and an independent group, as required by GLP.

Experimental System and Dosimetry

1. Environmental conditions, such as temperature, humidity, light, vibration and sound, and background EMF's, should be measured and recorded periodically. All experimental conditions should be the same for all groups, except for EMF exposure.

2. EMF's should be fully characterized and remeasured periodically. Waveform, pulse shape and timing, frequency spectrum, harmonics and transients from both continuous sources and from switching exposure systems on and off, should all be measured where appropriate. Background fields, such as ambient, equipment-derived, and cross-over fields from other exposure systems, are also important and need to be characterized. Time-varying and static components should be measured, as well as the polarization and directions of the fields. Field modulation introduced by experimental factors such as motion of sample shakers should be noted and measured whenever possible. Positioning of cultures or animals within exposure systems should be noted and randomized where appropriate.

Data collection and quality assurance

1. The full protocol, including QA, should be followed strictly, as should GLP provisions for monitoring this.

2. Data should be recorded contemporaneously and back-up copies kept.

3. No data should be discarded without valid reason (e.g. equipment failure, procedures not followed). Reasons for this should be recorded.

4. As part of the QA programme, at least one independent reassessment should be made of all or an appropriate sample of specimens, when assays require an independent judgement by the investigator (e.g. histological evaluations).

5. Where possible, samples should be stored for future reference.