

# Health and Safety Implications of Exposure to Electromagnetic Fields in the Frequency Range 300 Hz to 10 MHz

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An international seminar on health effects of exposure to electromagnetic fields (EMF) in the frequency range from 300 Hz to 10 MHz (referred to as the Intermediate Frequency (IF) range) was held in Maastricht, Netherlands, on 7–8 June 1999. The seminar, organized under the International EMF Project, was sponsored jointly by the World Health Organization (WHO), the International Commission on Non-Ionizing Radiation Protection (ICNIRP), and the Government of the Netherlands. This report does not attempt to summarize all of the material presented at the conference, but focuses on sources of exposure, biophysical and dosimetric considerations pertinent to extrapolating biological data from other frequency ranges to IF and identifies potential health concerns and needs for developing exposure guidelines. This paper is based on presentations at the conference and reports of working groups consisting of the speakers and other experts. It concludes with recommendations for further research aimed at improving health risk assessments in this frequency range. *Bioelectromagnetics* 23:68–82, 2002. © 2002 Wiley-Liss Inc.

**Key words:** intermediate frequency fields; IF effects; health risks; research agenda; exposure guidelines

## INTRODUCTION

An international seminar entitled “Health Effects of Exposure to Electromagnetic Fields (EMF) in the Frequency Range 300 Hz to 10 MHz” was held in Maastricht, Netherlands, on 7–8 June 1999. The seminar, held under the World Health Organization (WHO) International EMF Project, was sponsored jointly by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) and the Government of the Netherlands. The conference is part of a series of WHO conferences on possible health risks of EMFs [Repacholi, 1998; Repacholi and Greenebaum, 1999].

The meeting considered the frequency range of 300 Hz–10 MHz, which in the discussion below is referred to as the Intermediate Frequency (IF) range. In more conventional terminology this frequency range corresponds to parts of the very low frequency (VLF; 0.3–30 kHz); low frequency (LF; 30–300 kHz); medium frequency (MF; 300–3,000 kHz); and high frequency (HF; 3–30 MHz) ranges. This report focuses on exposure assessment and on dosimetric and biophysical considerations that are pertinent to establishing exposure guidelines. While relevant epide-

miological and biological studies are mentioned, no attempt is made to review all bioeffects data for IF fields, much of which has uncertain relevance to establishing exposure guidelines.

Compared to the extremely low frequency (ELF) and radiofrequency (RF) range, the IF range has been the subject of few biological studies, and there have been only a few reviews focusing on possible health risks [World Health Organisation, United Nations Environment, International Radiation Protection Agency, 1993; International Commission on Non-Ionizing Radiation Protection, 1998]. In the absence of much direct data international EMF exposure guide-

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lines [International Commission on Non-Ionizing Radiation Protection, 1998] for IF have been established by extrapolating limits from the ELF and RF frequency ranges, based on dosimetric considerations and assumptions about the frequency dependence of effects. Because applications of IF fields are increasing rapidly, it is important to evaluate their possible health effects. The proceedings of this conference encompassed exposure assessment, dosimetry, interaction mechanisms, laboratory and human studies, health risk assessment, research needs and standards (Appendix A). This report is based on reviews prepared by three working groups at the conference (Appendix B). A complete summary of the conference proceedings is available elsewhere [Matthes et al., 1999].

## SOURCES OF EXPOSURE

Many different industrial and consumer devices produce IF fields, varying widely in frequency and strength; they have been reviewed elsewhere [Matthes et al., 1999]. Sources of comparatively high exposure include the following:

### Induction Heaters

These devices are used in industry for heating metal and other conductive materials. The devices vary widely in operating frequency—from 50 Hz to over 2 MHz and output power in the kW to MW range. They can produce some of the highest magnetic field exposures encountered in any industrial environment (Allen et al., 1994; Mantiply et al., 1997; Gaspard, 1998).

In these devices, alternating magnetic fields are generated by passing large currents through coils several tens of centimetres in diameter. Fields close to the coils can be very high, but they fall off rapidly with distance from the coil. In addition, high voltages may be present on the coil itself, giving rise to strong electric fields nearby. For example, Mantiply et al. [1997] reported electric fields ranging from 2 V/m to 8.2 kV/m and magnetic fields from 0.1 to 21 A/m at the operator's position near induction heaters operating at 250–790 kHz.

### Plasma Heaters

These devices employ RF plasmas for etching, sputtering, and epitaxy. In some units, high magnetic and electric fields can exist outside the heaters. Chadwick [1999] reported magnetic fields as high as 1 A/m and electric fields up to 275 V/m at 5 cm from such devices, with contact currents up to 120 mA.

## Broadcast and Communication Transmitters

Numerous transmitters operate at IFs. The field levels to which these might expose a person depend on the operating power of a transmitter and the distance to the source. Fields very close to transmitters can be very high. For example, fields up to 340 V/m and 0.5 A/m have been measured near civilian HF broadcast antennas. Contact currents up to 100 mA can occur when a subject touches large metal objects close to the transmitters or the towers themselves [Allen et al., 1994].

A number of military systems transmit high power levels at IFs, often in close proximity to personnel, and field strengths and, in particular, contact currents can approach acutely hazardous levels. For example, Olsen [1999] reported contact currents up to 130 mA in a person when touching conductive surfaces near a 400 W vehicle mounted HF system. Contact currents of 350–950 mA were produced in the hands of subjects who touched shipboard structures, such as hoists and cranes, or aircraft parked close to HF whip antennas. These levels are well above ICNIRP (1998) reference levels for contact current, which are 40 mA at HF frequencies. VLF submarine communications systems employ fixed transmitters operating at power levels above 1 MW, and field strengths near the antennas can exceed 600 V/m and 8 A/m.

## APPLIANCES

Various appliances and other electrical equipment used in commercial or residential settings result in human exposure to IF fields, although at levels far below those described above from industrial and military sources. Moreover, field levels very close to such equipment may exceed ICNIRP reference levels, although perhaps while not exceeding the basic restrictions because of the rapid falloff of field with distance from the devices. The numbers of exposed individuals can be very large.

Major sources of IF fields in commercial and residential environments include the following:

### Induction Cookers

These operate at 20 to 50 kHz. Magnetic fields near their coils have been reported to range from 0.7 to 1.6 A/m at a distance of 0.3 m from their coils to 25 A/m at the surface of the coils themselves [Stuchly and Lecuyer, 1987].

### Proximity Readers

They operate at 120 kHz or 13.6 MHz for remote reading of magnetic badges of personnel passing

through control gates. Magnetic fields at the center of the passage of proximity readers have been reported to be in the range of 0.7 to 6 A/m at an operating frequency near 120 kHz [Polichetti, and Vecchia, 1998]. For comparison, the ICNIRP reference levels for the general population at this frequency is 5 A/m.

### Electronic Article Surveillance (EAS)

Electronic article surveillance systems or anti-theft devices, which are commonly installed in shops and libraries, operate over a range of frequencies from tens of Hz to MHz. Field levels very close (approaching contact) to the coils of such devices may approach ICNIRP reference levels, although the basic restrictions might not be exceeded [Polichetti and Vecchia, 1998].

### Visual Display Units (VDUs) and Television Sets

These produce electric and magnetic fields in the frequency range 15–25 kHz, as well as at other frequencies. Exposure levels at IFs are quite low, with peak magnetic fields of a few A/m and peak electric fields at IF frequencies of a few V/m. However, there has been controversy about possible health effects from fields associated with VDUs, which has prompted considerable study of possible health risks associated with use of the devices (cf. Human Studies section, below).

## MEDICAL EQUIPMENT

Some medical equipment produces high fields at IFs. While exposure guidelines such as ICNIRP do not apply to exposures to patients for medical purposes, they do apply to occupational exposures to medical staff; and compliance with the guidelines, as well as possible health risks, needs to be examined.

### MRI Systems

MRI systems expose patients and, in recent “open” systems, medical staff as well to strong static magnetic fields, including flux densities up to about 4 T and high level RF fields, often at thermally significant levels. In addition, MRI imaging systems employ gradient field pulses whose waveforms generally sawtooth in form, are complex. A typical 1.5 T system uses field gradients of about 10 mT/m, which corresponds to a time rate of change of tens of T/sec. The gradient pulses have a rise time of about 0.3 msec and a period about ten times longer, and their peak magnetic field strengths are in the range of  $10^3$  to  $10^4$  A/m (flux densities of  $10^{-3}$ – $10^{-2}$  T). The gradients

induce IF electric currents within the patient’s body that can approach thresholds for producing peripheral nerve stimulation [Budinger et al., 1991]. Fields outside the scanner are much smaller: measurements on one 1.5 T system showed gradient pulses ranging from 2.0  $\mu$ T (1.6 A/m) RMS at the magnet to 0.07  $\mu$ T (0.06 A/m) RMS at the console [Bracken, 1994].

### Electromagnetic Nerve Stimulators

These apply time dependent magnetic fields to the body, usually the head, to excite nerves via induced electric fields in tissue. To induce sufficient currents in the body, such devices require very strong time dependent magnetic fields with very high time rates of change. These fields are typically produced by discharging high energy capacitors through magnetic coils. For example, one commercial device for magnetic transcranial stimulation discharges currents of approximately 5000 A peak current in pulses lasting approximately 300–500  $\mu$ s [Benecke et al., 1988]. The peak value of dB/dt is of the order of  $10^4$  T/s, resulting in peak induced currents in the brain of approximately 25 A. These currents take the form of damped sine-waves, whose spectral components are mainly in the IF range.

### Magnetic Bone Stimulators

Magnetic bone stimulators for treating bone nonunions employ pulsed magnetic fields of a complex and very specific waveform. Peak flux densities are of the order of 1.5 mT and the pulses contain spectral components into the kHz range [Polk, 1995].

### Electrosurgical Units

These use amplitude modulated currents at several frequencies, from tens of kHz into the MHz range, for tissue cutting and coagulation. Such units can produce magnetic fields as high as 0.2 A/m close to the cables and other parts of the equipment [Mantiply et al., 1997]. Moreover, electrosurgical units frequently use unshielded cables and thus produce strong electric fields near the cables and cutting electrodes, some parts of which may be close to the surgeon’s body. For example, Paz et al. [1987] reported electric field strengths as high as 3 kV/m at a distance of 20 cm from the active lead of a bipolar electrosurgical unit, with magnetic field of about 2 A/m.

Electrosurgical equipment is a well documented source of injury, both to patients and physicians. There is at least one report of serious burns, resulting from fields coupled into the eyeglass frame, to a physician performing a procedure that required his head to be close to the electrosurgical cutting tool [Geddes,

1998]. “Alternate site burns” are occasionally produced in patients in the skin beneath dispersive electrodes [Geddes, 1998].

In summary, a wide range of equipment produces electric or magnetic fields in the IF range. In nearly all cases the resulting human exposures are below recommended (e.g., ICNIRP) guidelines, although fields very close to coils or other parts of the equipment can exceed guideline values. The guidelines, however, apply to whole body exposure. Workers in a few occupational groups, e.g., operators of heat sealers and induction heaters, some military personnel, technicians working near high powered broadcast equipment, have the potential for exposure to IF fields at levels well above those experienced by members of the general population.

### COUPLING CONSIDERATIONS

The above considerations indicate the maximum fields that a person is likely to encounter in the environment. Because the internal fields induced within the body, rather than external fields, are more important in determining possible biological effects, the coupling between the body and externally imposed fields is an important consideration.

A few investigators have reported detailed dosimetric studies at IFs [e.g., Jokela, et al., 1994; Wainwright, 1999]. However, the much larger literature on ELF dosimetry is also relevant. In both the low and IF frequency ranges, the wavelength far exceeds body dimensions, and near field exposure situations predominate. In these circumstances, the induced fields in the body simply scale with frequency, other exposure parameters being constant. Moreover, exposure from electric and magnetic fields must be separately considered. Because body tissues are essentially nonmagnetic, the magnetic field within the body is essentially identical to the external field. However, the internal electric field is the sum of the fields induced by the external electric and magnetic fields.

### Electrically Induced Electric Field in the Body

Rather little work has been done to quantify the electric fields induced within the body by exposure to IF electric fields. However, in view of the quasistatic nature of the interaction, the extensive work on quantifying induced electric fields in the body from exposure to ELF fields can be extrapolated to IF fields by scaling the internal electric fields by the frequency. A quite different problem is the determination of contact currents, i.e., currents introduced into the body by contact with a charged conductor.

A well-studied example is that of a person standing erect on a grounded surface in a vertically oriented electric field [e.g., Kaune et al., 1997]. For this exposure situation, the induced electric field in the body is five to six orders of magnitude below the external field strength at 300 Hz and about one order of magnitude below the external field at 10 MHz.

### Magnetically Induced Electric Fields in the Body

Time dependent magnetic fields will induce electrical fields within the body, according to Faraday’s law of induction. The internal electric field strength depends on the area of the body that is exposed to the field and is proportional to the time derivative (or, for AC (sinusoidal) fields, the frequency) of the field. Thus, a given magnetic field will induce larger electric fields when applied to the whole body than to the extremities alone, and the strongest electric fields will be near the periphery of the exposed part of the body. The current density is proportional to the induced electric field multiplied by the conductivity of the tissue.

### Mechanisms of Interaction

In the absence of extensive data for hazard thresholds at IFs, exposure guidelines have to be established by extrapolating from lower and higher frequency ranges. Such extrapolation requires at least a preliminary understanding of the mechanisms for hazards. More generally, hypotheses about mechanisms of interaction can help to clarify biological interactions from exposure to fields and guide further experimentation.

Several mechanisms, both thermal and nonthermal, are well established by which electromagnetic (primarily, electric) fields can interact with biological systems. Thermal mechanisms are related to heating of tissue, either to temperature increase or to the rate of increase in tissue temperature. Nonthermal mechanisms are related to direct interactions with the fields themselves.

Existence of a mechanism, however, does not imply that it can lead to observable biological effects under realistic exposure conditions. Both thermal and nonthermal mechanisms are characterized by an interaction strength and response time. The first determines the threshold for producing observable effects in the presence of normal biological variation and random thermal agitation (noise). The second determines the variation in threshold for an effect with frequency.

### Thermal Mechanisms

When an electric field is created in tissue, heat is generated as the electrical energy is dissipated. The

specific absorption rate (SAR) is the local rate of energy absorption, and hence predictive of thermal effects:

$$S = \frac{\sigma E_i^2}{\rho} \quad (1)$$

where  $E_i$  is the local field in the tissue and  $\sigma$  and  $\rho$  are the electrical conductivity and density of tissue, respectively. Considerations of in situ field strengths resulting in thermally significant exposures are useful for a comparative analysis of biophysical mechanisms.

The conductivity of most soft tissues increases slowly with frequency; it rises by a factor of 2–8 over the whole IF range considered here [Foster and Schwan, 1995]. Thus the threshold in situ field strength for producing a given thermal effect, expressed in terms of the internal field strength  $E_i$ , will decrease by a factor of 3 or less over this range. The external field strength needed to produce such effects will vary by a far larger factor because of the frequency dependence of the coupling between external fields and the inside of the body.

A useful benchmark for the threshold for thermally significant effects is the basal metabolic rate, about 1 W/kg in man. Whole-body heating at or above this level, if sustained for sufficient time, will produce significant thermophysiological responses, depending on environmental conditions. This corresponds to tissue field strengths of approximately 50 V/m.

At higher exposure levels, burns and other gross heating effects can result. In the absence of any heat transport, a SAR of 1 W/kg will increase the tissue temperature by about  $2.5 \times 10^{-4}$  K/s. At sufficiently

high field strengths (tens of kV/m or higher), temperatures will reach damaging levels very quickly, perhaps faster than the subject can withdraw from the exposure. (For time-varying fields, these field strengths would be root mean square values.)

These considerations (summarized in Table 1) suggest that tissue field strengths above 30–100 V/m at IFs will lead to significant whole body heating, if sustained for sufficient lengths of time. Much higher field strengths (kV/m) will create acute thermal hazards, if sustained for sufficient times. When multiple hazard mechanisms are possible, the limiting hazard is that which produces adverse effects at the lowest in situ field strength.

### Membrane Excitation

Electric shock and other effects of electric current at low frequencies are associated with membrane excitation (for an extensive review see Reilly [1999]), whereas at higher frequencies thermal hazards generally have lower thresholds. Setting exposure guidelines at IFs requires some knowledge of the frequency dependence of the thresholds for membrane excitation, for which little direct data exist.

The frequency dependence of the thresholds for membrane stimulation is a function of two factors, the potential that is induced across cell membranes by an external field and the intrinsic kinetics of the membrane response to the induced potential. Both of these factors strongly depend on frequency. Two cases illustrate the nature of the frequency dependence and magnitude of induced potentials [Foster and Schwan, 1995; Reilly, 1999].

**Spherical cells.** For a spherical cell of radius  $R$  in an external field  $E$ , the induced membrane potential is

**TABLE 1. In Situ Electric Field Strength and Current Density for Different Benchmarks for Thermally Significant Exposures**

Benchmark	In situ electric field, <sup>a</sup> V/m	In situ current density, <sup>a</sup> A/m <sup>2</sup>
SAR of 0.4 W/kg (ICNIRP basic restriction for whole body occupational exposure)	35	11
SAR of 10 W/kg (ICNIRP basic restriction for localized occupational exposure to the head and trunk)	180	56
Threshold temperature increase in the skin for perception of warmth (0.07 °C after 3 s of heating) <sup>b</sup>	560	180
Thermal damage to skin (25 °C increase after 10 s) <sup>c</sup>	3500	1130

<sup>a</sup>These values are intended to give the order of magnitude of the in situ electric field corresponding to different thermal benchmarks; observed thresholds will vary considerably depending on environmental conditions and biological variations. The calculations assume a tissue conductivity of 0.32 S/m, which is appropriate for muscle at 1 kHz [Gabriel et al., 1996] and thermal properties similar to those of water. The SARs correspond to ICNIRP basic restrictions (occupational) for whole-body exposure (0.4 W/kg) or for localized exposure to the head and trunk (10/kg).

<sup>b</sup>Temperature increase based on model by Rin et al. [1997].

<sup>c</sup>Temperature increase based on model by Welch [1985].

simply  $1.5 E R$  at low frequencies. In response to a step change in the field, the membrane charges with a time constant  $\tau$  of approximately

$$\tau = RC_m(\rho_a/2 + \rho_i). \quad (2)$$

where  $C_m$  is the membrane capacitance, and  $\rho_a$  and  $\rho$  are the resistivities of the surrounding medium and cytoplasm, respectively. For AC fields, this corresponds to a cut-off frequency  $f_c$  of  $1/(2\pi\tau)$ . For a typical cell in biological media ( $R = 10 \mu\text{m}$ ,  $\rho_a = 1 \text{ ohm m}$ ), this corresponds to a charging time constant of about  $0.1 \mu\text{s}$  or to a cut off frequency of about 1 MHz. For AC fields above the cut off frequency, the induced membrane potential varies as the inverse of the frequency. By contrast the response times of ion channels in cell membranes are typically in the millisecond range.

**Cylindrical cell oriented parallel to the external field.** For a cylinder with radius  $R$ , oriented parallel to an external field, the maximum induced membrane potential is  $E\Lambda$  at low frequencies, where  $\Lambda$  is the space constant of the cell [Reilly, 1998]. The space constant is given by

$$\Lambda = \sqrt{\frac{r_{\text{mem}}R}{2\rho_i}} \quad (3)$$

where  $r_{\text{mem}}$  is the membrane resistance (typically of the order of  $1 \text{ ohm-m}^2$ ). For a cell of radius  $10 \mu\text{m}$  with  $r_{\text{mem}} = 1 \text{ ohm-m}^2$ , the space constant is 0.2 cm.

As the frequency increases, the induced membrane potential declines because of the capacitance of the cell membrane. The frequency dependence of the induced membrane potential can be estimated by replacing the membrane resistance  $r_{\text{mem}}$  in Eq. 3 by the

parallel combination of  $r_{\text{mem}}$  and the membrane reactance  $1/(2\pi f C_m)$ , where  $C_m$  is the membrane capacitance (about  $1 \mu\text{F/cm}^2$ ). At frequencies above  $1/(2\pi f C_m r_{\text{mem}})$  (15 Hz for the parameter values given above) the capacitive term dominates, and  $\Lambda$  (and hence the maximum induced membrane potential) falls off as  $f^{-\frac{1}{2}}$ .

These considerations highlight the effect of cell geometry on thresholds and frequency dependence of responses. Compared to a spherical cell of the same radius, a cylindrical cell oriented parallel to the field will have a far lower excitation threshold but a much lower cutoff frequency, assuming the same membrane kinetics. For example, for the cylindrical cell discussed above, the cut-off frequency, at which the induced potential is reduced by a factor of two below its low-frequency limit, is approximately 70 Hz; it is 1 MHz for the spherical cell. The field required to induce a membrane potential of 0.1 V, which is of the order needed to induce an action potential in an excitable cell, is about 50 V/m, compared with about 6000 V/m for the spherical cell.

The above considerations pertain to the excitation of single cells and do not consider other factors that can lead to much lower thresholds for some effects. For example, visual sensations (phosphenes) can be elicited in human subjects by passing alternating currents through the retina, either directly introduced via electrodes or indirectly induced via alternating magnetic fields. The thresholds correspond to an electric field strength within the retina of the order of 0.05 V/m at low frequencies [Reilly, 1998] or 1 V/m at 60 Hz [Carstensen et al., 1985]. The phenomenon is associated with changes in presynaptic potentials in the retina and perhaps higher order signal processing in the brain as well. The low thresholds for producing phosphenes, compared to those for producing electrical shock, are accompanied by very low cut off frequencies for the effect, about 20 Hz for phosphenes.

Reilly [1999] suggested that the time or frequency dependence of the stimulation threshold can be

**TABLE 2. Thresholds for Some Biological Effects of Sinusoidal Electric Currents, Indicating Approximate Thresholds and Optimum Frequencies [from Reilly, 1999]**

Biological effect	Internal electric field, V/m <sup>a</sup>	Optimum frequency
Synapse activity alteration via membrane polarization (phosphenes)	0.05	20 Hz
Peripheral nerve excitation via membrane depolarization	6	200 Hz
Muscle cell excitation via membrane depolarization, skeletal	6	50 Hz
Muscle cell excitation via membrane depolarization, cardiac	12	50 Hz
Electroporation, reversible	50	< 1 kHz
Electroporation, irreversible	300	< 1 kHz

<sup>a</sup>Measurable response threshold values for median individual with optimized waveform.

**TABLE 3. Reaction Thresholds for Pulsed Stimulation**

Responding tissue	Rheobase E-field (V/m-pk)*	Strength-duration time constant $\tau_s$ (ms)
Retinal synapse	0.075	25.0
20- $\mu$ m	6.2	0.12
10- $\mu$ m nerve fiber	12.3	0.12
Cardiac muscle	12.0	3.0

\*Median response; peak E-field. [From Reilly, 1999].

described by a single parameter, the strength-duration (S-D) time constant  $\tau_s$  or the optimal frequency  $f_o = 1/(2\pi\tau_s)$ . The rheobase is the lowest current needed to produce stimulation at the optimal frequency (Tables 2 and 3). Reilly [1999] also extended these results to square-wave currents for (Fig. 1) which the thresholds show a broader minima than for sine waves.

This same analysis can be extended to estimate thresholds for nerve stimulation from exposure to external magnetic fields (Fig. 2) based on [Reilly, 1999]. These thresholds were calculated for whole-body exposure to a large adult human; higher thresholds would be found for smaller bodies or for partial body exposure. The frequency dependence in Figure 2 arises from two factors: the frequency dependence of

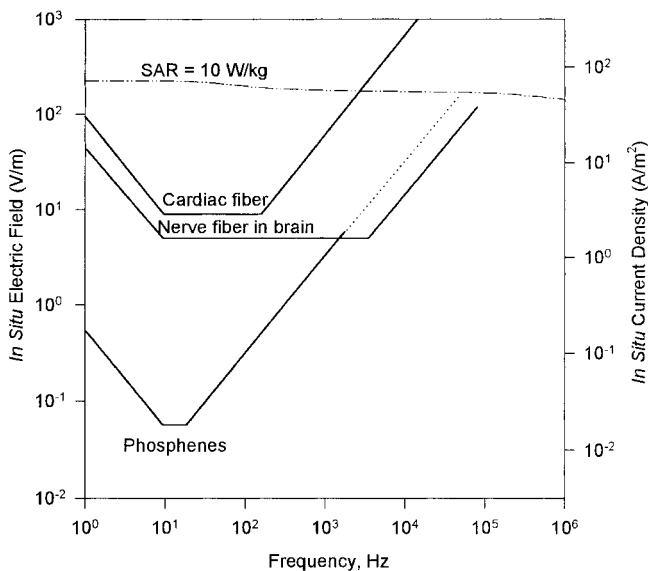


Fig. 1. Median human response thresholds: (a) phosphenes, (b) 20- $\mu$ m diameter myelinated nerve, and (c) cardiac excitation. The thresholds were calculated for sinusoidal (phosphene) or square wave excitation (heart and nerve), using a first order model based on measured responses for single current pulses. The responses indicate a much broader minimum threshold for square wave vs. sinusoidal stimulation. The dotted section of line for phosphenes indicates a lack of experimental data available to test the theory. Also shown is the in situ field strength in muscle that produces a SAR of 10 W/kg based on dielectric data for muscle [Gabriel et al., 1996]. [Adapted from Reilly, 1999].

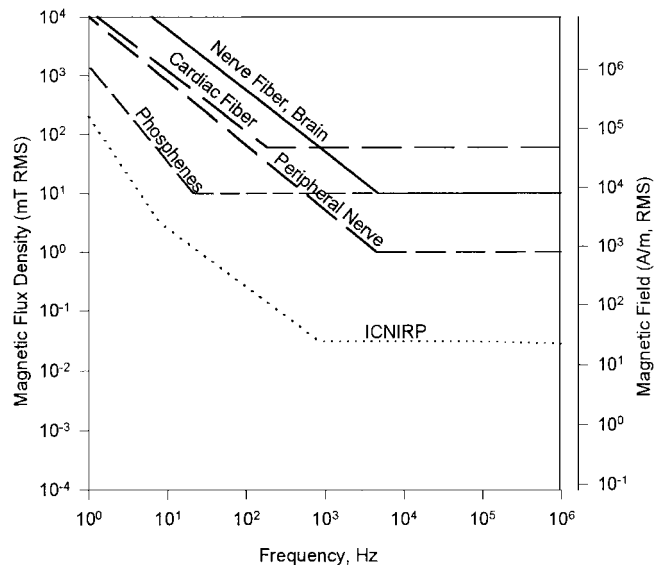


Fig. 2. Calculated thresholds for short term effects from whole-body exposure to sinusoidal magnetic fields for a large adult person. Curves indicate estimated thresholds for different stimulatory effects (excitation of 10  $\mu$ m nerve fibers in the brain, excitation of cardiac fibers, production of phosphenes). Also shown are ICNIRP reference levels for occupational exposure to magnetic fields. Adapted from Reilly [1999].

the induced electric field and the frequency dependence of the excitation threshold itself.

## Electroporation

When the induced potential across a cell membrane exceeds 0.5 to 1.0 V, the membrane will break down (electroporate), either reversibly or at higher membrane potentials, irreversibly [Weaver and Chizmadzhev, 1996]. Because electrical breakdown is a very fast process, the frequency dependence of the threshold in terms of tissue field strength is chiefly determined by the charging time constant of the cells.

Electroporation generally requires very high in situ field strengths (60,000 and 500 V/m for the spherical and cylindrical cells modeled above). Such field strengths could not be maintained for any substantial period in normal biological media without excessive heating. However, electroporation is a very fast process (time constants of nanoseconds or less) compared with membrane excitation (milliseconds), and there may be circumstances where electroporation can occur in the absence of nerve stimulation. These would require unusual exposure conditions involving brief but very intense pulses, particularly pulses with a DC component.

## Field-Induced Forces

Several classes of nonthermal interaction mechanisms are well established which involve mechanical

forces exerted on structures by an electric field; for a recent review see [Foster, 2000]. These mechanisms can be classified by order of interaction:

**Field-charge interaction.** Electric fields exert forces on charges and in principle will displace them. However, anticipated thresholds for producing effects that are noticeable on top of random thermal agitation are very high. For example, the mobility of simple ions in an aqueous electrolyte solution is of the order of  $10^{-7}$  (m/s)/(V/m). Thus, a field of 1 kV/m will induce a velocity of  $\sim 10^{-4}$  m/s in a small ion in an electrolyte. This is 8 to 9 orders of magnitude below the root mean square velocity of the same ion due to Brownian motion.

**Field-permanent dipole interactions.** A distribution of charges within a molecule or colloidal particle will result in a permanent dipole moment  $\mu$ . An electric field  $E$  will induce a torque  $\tau = E \mu \cos(\theta)$  on the dipole, where  $\theta$  is the angle between the field and the dipole moment, which will tend to align the dipole parallel to the field.

The motion of the dipole in response to this torque will be determined by the viscosity of the surrounding medium and can be characterized by a time constant ranging from seconds for large macromolecules, such as DNA or colloidal particles, to picoseconds for, e.g., water molecules. There is a vast literature on the use of pulsed static fields or gated RF fields to align molecules and colloidal particles, mostly in connection with electro-optic studies on biological molecules [Stoylov, 1991]. However, to produce significant alignment requires very strong fields, and these mechanisms are not plausible candidates for biological effects from exposure to EMF at normal or foreseeable environmental field strengths.

**Electric field-induced dipole interactions.** Electric fields exert forces and torques on uncharged objects through their interaction with induced dipole moments. The force is nonlinear (proportional to the square of the field strength) and will result in forces from modulated high frequency fields that are at the modulation frequency. Such forces, known as dielectrophoretic forces, find practical application in the manipulation of cells, for example by causing them to line up as a “pearl chain” effect [Schwan, 1982]. The response time for such effects depends on complex hydrodynamic effects and the field strength. The response times are generally quite long; they are of the order of 1 s for the pearl chain effect with typical cells. Moreover, the thresholds for such effects are also high, on the order of kV/m or higher for the pearl chain

effect. Therefore, such forces are unlikely candidates as hazard mechanisms under real world exposure conditions.

### Speculated Mechanisms

Many other mechanisms of EMF interaction with biological systems have been proposed, most with reference to ELF or RF effects that cannot be readily explained in terms of the classical mechanisms discussed above. These include nonlinear effects and solitons [Lawrence and Adey, 1982], ion resonance [Lednev, 1991] and stochastic resonance [Krugilikov and Dertinger, 1994]. So far, these theories lack experimental verification and in many cases they have been criticised on theoretical grounds [e.g., Adair, 1995]. At present they are not useful to predict the occurrence of biological effects from exposure to IFs.

### DISCUSSION

Both thermal and nonthermal mechanisms exist by which IF fields can interact with biological systems. Of these, three phenomena heating, membrane stimulation, and electroporation are established mechanisms for hazards from short term exposure to IFs. The threshold for each varies in a different way with exposure parameters:

- At low frequencies, the threshold for membrane effects is lower than for thermal injury, and electric shock and other excitation effects is usually the limiting hazard
- The threshold for membrane excitation increases rapidly with frequency, while that for heating, if expressed in terms of in situ field strength, decreases slowly with frequency. Above some frequency, thermal effects will become limiting hazards.
- Electroporation of cell membranes requires very high tissue field strengths, but the process is very fast. For some exposure conditions involving high field pulses of short duration, electroporation may be the limiting effect.

The above discussion implies that a crossover frequency will exist, above which thermal effects dominate over membrane excitation phenomena. As indicated from Figure 1, this crossover is expected to be somewhere in the kHz frequency range. However, the crossover frequency will vary widely depending on the particular effects being considered and the exposure characteristics. Chatterjee et al. [1986] measured thresholds between 10 kHz and 3 MHz for perception and pain in 367 human subjects from contact currents due to touching metallic surfaces. Below appro-



ximately 150 kHz, the subjects reported a tingling sensation, presumably due to nerve stimulation; at higher frequencies they reported sensations of warmth.

Because of the weak coupling between external fields and the body at IFs, the effects discussed above require very high external field strengths, above those found in nearly all occupational or nonoccupational environments. Indeed, reported injuries from IF fields are typically the result of excessive contact currents, rather than excessive exposure to fields per se.

## REPORTED BIOLOGICAL EFFECTS OF IF FIELDS

The hazard mechanisms discussed above are associated with a limited range of phenomena and apply to acute exposures. The question arises whether biological evidence might exist for other hazards, perhaps associated with chronic exposures at lower exposure levels.

Numerous biological studies have been reported involving a broad range of endpoints, many of which are summarized in Matthes et al. [1999]. Most of these studies have employed field levels in the biological preparation that considerably exceed ICNIRP basic restrictions, i.e., exceed fields levels permitted within humans, which limits their relevance to human health questions. Virtually none of the effects described below have any apparent explanation in terms of the biophysical mechanisms discussed above. For some of the studies, questions of validity in study design or lack of reproducibility of the results can be raised.

## IN VITRO STUDIES

Numerous in vitro studies have been reported using electric or magnetic fields whose frequency content was partially or entirely in the IF range. A frequent motivation for these studies was to clarify mechanisms of bone healing using pulsed magnetic fields, but many of these studies have explored basic cellular phenomena whose significance extends beyond this particular clinical application [Glaser, 1999].

Few if any of these studies were designed to identify potential human health risks, and their role in risk assessment is unclear at best. Also, in many cases, the field strengths exceeded realistic levels of human exposure. For these reasons, no attempt will be made to comprehensively review this large body of work. Such a review is currently being undertaken by ICNIRP for the European Commission and will be published soon.

An extensive series of in vitro studies by Blank and Soo [1998] is noteworthy because of the very low field levels used, i.e., 0.5 mV/m in the exposed pre-

paration and 5–50  $\mu$ T, corresponding to magnetic field strengths of 4–40 A/m, at frequencies between 0.1 and 1 kHz. The studies reported a variety of effects, for example, an increase in the activity of cytochrome oxidase with exposure to 10  $\mu$ T flux density (8 A/m field strength) magnetic fields over a very wide frequency range of 10 to 2,500 Hz. The health significance of these findings is difficult to establish, but the exposures corresponded to in situ field strengths that are within levels permitted by ICNIRP exposure guidelines. For this reason, these findings warrant follow up study.

As with bioeffects studies at other frequency ranges, many reported effects of fields at IFs are difficult to interpret because of inconsistencies in the data and the possibility of artifact. For example, evidence for an effect of IF electric fields on intracellular calcium has been inconsistent among different laboratories. Moreover, Glaser and colleagues [Ihrig et al., 1999] have shown that ultraviolet radiation, used to excite fluorescent dyes in intracellular calcium assays, has an effect on  $\text{Ca}^{++}$  regulation in cells; this result may have been a confounding factor in such studies.

## IN VIVO STUDIES

A scattering of in vivo studies has been reported, using fields having a spectral content partially or entirely in the IF range. Many of these were intended to have some bearing on possible health risks from such fields.

### General Toxicity

In a short-term toxicology study using B6C3F1 mice exposed to a 10 kHz sinusoidal magnetic field at flux densities of 0.1, 0.3, and 1.0 mT for 22.6 h daily for 14 or 90 consecutive days, Robertson et al. [1996] found no indications of animal morbidity, changes in behaviour or any exposure related differences in body weight. Biochemical and haematological parameters were unaffected and all organs were macroscopically and microscopically normal.

### Carcinogenesis

Only a few in vivo studies relating to carcinogenesis have been reported at IFs. Svedenstål and Holmberg [1993] investigated the combined effects of 20 kHz magnetic fields and X-rays on the development of lymphoma in 227 mice. One group was exposed to X-rays and magnetic fields, a second to X-rays only, a third to magnetic fields only, and a fourth group was an unexposed control. A total dose of 5.24 Gy was divided in four subdoses. The magnetic field had a sawtooth waveform with a peak-to-peak flux density of

15  $\mu\text{T}$ . No differences were reported in lymphoma development between the X-ray plus magnetic field and X-ray only groups, or between the magnetic field only and unexposed groups. Working group members at the Maastricht meeting considered this study to be relevant to risk assessment, but judged the X-ray dose to be quite high for a co-carcinogenesis study.

### Reproduction and Development

Many *in vivo* studies have searched for effects of low frequency magnetic fields on embryogenesis and pregnancy, most of them motivated by concerns about possible reproductive effects of VDUs. Most studies that employed IF magnetic fields used 18–20 kHz sawtooth fields, representative of fields from VDUs, with peak flux densities of approximately 10  $\mu\text{T}$  (8 A/m). The endpoints related to embryogenesis and development, typically in rats but in other animals as well, e.g., chicks. The studies are reviewed by Huuskonen et al. [1998].

The results of these studies have been mixed. Some studies reported effects of EMF on embryogenesis and fetal development, others found no such effects. The data as a whole are conflicting and inconsistent, and the positive results have been difficult to confirm. In the opinion of the working group at the Maastricht meeting, there is no convincing evidence for an increase in malformations from exposure to electric or magnetic fields at IFs, but some reports of minor skeletal abnormalities warrant attempts at independent confirmation. Interpretation of the chick teratology findings is particularly difficult because of the large biological variability of the birds; and their extrapolation to humans is even more difficult. However, these studies involved magnetic field exposures considerably below present guidelines and for that reason demand careful consideration.

### Nervous System

Takashima et al. 1979 exposed a rabbit to 1–10 MHz fields modulated at 15 Hz in the air near the animal's head for six weeks, 2 h/day at 0.5–1.0 kV/m. The investigators reported changes in the power spectrum of the EEGs of the animal after exposure. However, the study is limited by its very small size, since only a single animal was used, and by the strong likelihood of technical artifacts due to the use of implanted metal screws in the animal's head for recording the EEG.

### Musculoskeletal System

Many *in vivo* studies have been conducted since the mid 1970s in relation to use of magnetic

fields for stimulation of bone and soft tissue repair [for a review, see Polk 1995]. Most employed fields with spectral components largely below the IF range; however some employed pulsed magnetic fields (PEMF) containing significant frequency components into the range of tens of kHz. Typical peak flux densities employed in these studies are of the order of 1 mT (800 A/m).

Such fields are above levels encountered in nearly all environments and generally below exposure guidelines. Moreover, the studies were designed to explore clinical applications of pulsed magnetic fields, not for purposes of health risk assessment. Consequently, their significance to human health risks is difficult to judge. However, the reports of biological effects from chronic exposures to such fields warrant further examination to determine any possible relevance to human health risks.

## HUMAN AND EPIDEMIOLOGICAL STUDIES

Numerous studies have been reported on cancer and other risks associated with ELF exposure, and a smaller number here related to RF exposure [for reviews, see Repacholi, 1998; Repacholi and Greenbaum, 1999]. Relatively few studies have addressed possible health risks from exposure to IF fields.

### Cancer

In the late 1980s, Milham and colleagues reported several epidemiological studies on radio amateur operators and suggested that an association exists between being a radio amateur and mortality from lymphatic or other tumours [e.g., Milham, 1988]. The value of these studies is of limited value because of their lack of exposure assessment and the many difficulties in interpreting data from death certificates [Feinstein, 1985].

More recently Tynes et al. [1996] studied breast cancer incidence in 2619 female (shipboard) radio and telegraph operators, using the national cancer databases for comparison. They considered exposure to light at night, hypothesized to have an effect on melatonin, exposure to RF fields (405 kHz–25 MHz) and to some extent exposure to ELF fields (50 Hz). The investigators reported an overall excess risk for breast cancer measured using the Standard Incidence Ratio (SIR = 1.5) and suggested the possible existence of an association between work as a radio and telegraph operator and breast cancer. However, because of the weak associations in the study, the use of multiple comparisons in the data analysis, and other uncertainties, the working group concluded that the study provided no strong evidence for health hazards from EMF.

## Reproduction and Development

Concerns about possible reproductive effects of working with VDUs arose in the late 1970s, with reports of “clusters” of women with adverse pregnancy outcomes in Australia, Europe, and North America who used VDUs on the job. To address these concerns, approximately 20 epidemiologic studies have been reported on possible links between VDUs and adverse reproductive outcomes.

Among these studies, only three directly assessed EMF exposure of their subjects, which includes a variety of static electric, ELF electric and magnetic, and IF magnetic fields with complex wave forms. One was a large cohort study performed on a population of telephone operators by Schnorr et al. 1991. The study found no statistically significant difference in reproductive outcomes of exposed vs. non exposed women, when exposure was assessed for the entire pregnancy or by month of gestation. Lindbohm et al. [1992] investigated associations between work with VDUs and spontaneous abortion. The study included direct measurements of magnetic field exposures to the subjects. The study reported an increase in the odds ratio for adverse reproductive outcome in women using the highest exposure terminals; but the authors noted potential difficulties with the study, including exposure misclassification and incomplete identification of confounding factors, which limit the interpretation of the findings. Grajewski et al. [1997] reported no association between reduced birth weight and pre-term birth and use of VDUs in a cohort of telephone operators.

Several recent reviews of epidemiological studies with VDUs [World Health Organisation/United Nations Environment International Radiation Protection Agency, 1993; Lindbohm and Hietanen, 1995; International Commission on Non-Ionizing Radiation Protection, 1998; Robert, 1999] have concluded that use of VDUs does not increase the risk of adverse reproductive outcomes or other health problems.

## Nervous System

Correlations between certain environmental electrical fields associated with weather (sferics) and several diseases or biological parameters have been reported by Hoffmann et al. [1991]. Ruhenstroth-Bauer et al. [1984 and 1995] reported that seizures in humans are positively correlated with 28 kHz pulsed signals and negatively correlated with 10 kHz signals from sferics. However, a subsequent study by Juutilainen et al. [1988], using audiogenic seizure-susceptible rats exposed to simulated sferics (with electric field strengths in air below 1 V/m and magnetic field

strengths in the range of mA/m) found no supporting evidence for these claims.

In another series of studies, Schienle et al. [1997] reported effects of sferics on the EEG of human subjects. Most recently, this group has claimed that exposure to sferics causes a change in “extrasensory perception performance” [Houtkooper et al., 1999].

These studies involve natural, not technologically produced fields, but their reports of physiological effects in humans associated with very low exposure levels would have significant health implications if correct. However, the reports are very difficult to interpret and some are open to question, for example in their choice of endpoints examined, e.g., extrasensory perception.

## Cardiovascular Effects

Szmigielski and co workers reported a series of studies on cardiac and circulatory function of workers exposed to IF fields in the broadcasting industry [Bortkiewicz et al., 1997; Szmigielski et al., 1998]. For example, Bortkiewicz et al. [1997] examined 71 workers at four AM broadcast stations (0.738–1.503 MHz). The controls consisted of 22 workers at “radio link stations” (microwave relay stations transmitting at 4 to 6 GHz). The investigators reported a number of health effects associated with IF EMF exposure, including a higher number of cardiac rhythm disturbances, mostly ventricular extrasystoles, in the AM broadcast station workers compared to controls.

The working group felt that the health implications of these findings are difficult to assess. The study included direct assessment of exposure. However, the effects were generally small and not of clear health significance. Moreover, the associations were reported after the investigators conducted extensive post hoc analysis of the data that included many different comparisons, and may have been false positive findings, i.e., multiple comparison artifacts.

## Conclusions and Recommendations

One of the main goals of the International EMF Project is to identify gaps in knowledge and establish an agenda to guide further research. This review and the reports of the working groups at the Maastricht meeting indicate several areas of scientific uncertainty and need for future research.

- Even for known hazards, few data exist for the thresholds for hazards at IFs, particularly for fields with complex waveform. This is important because ICNIRP and other exposure guidelines at IFs were developed by extrapolating the thresholds for known

hazards measured at lower frequencies, e.g., for shock, and at higher frequencies, principally thermal effects. Reilly [1999] argued that this extrapolation relied on unsupported assumptions about the frequency dependence of the thresholds.

- Thresholds for hazards from partial body exposures, in particular for the limbs where exposure to the central nervous system is not involved, remain poorly established and in need of further study.
- Few toxicological and epidemiological studies have been conducted in this frequency range. While there is no clear evidence that IF field exposure at levels below present guidelines has any health consequences, the body of relevant bioeffects literature is very limited. By contrast, various biological effects from IF fields have been reported, some at levels below present exposure guidelines (ICNIRP). The significance of these, if any, to human health needs to be clarified.
- More data are needed on characteristics of exposure to IF fields from various applications and sources in occupational settings and for the general public. This is critical for exposure assessment in future epidemiological studies, for reproducing exposure conditions in laboratory studies and for determining compliance with exposure limits.

The working groups agreed that high quality epidemiological studies are important for health risk assessments. However, given the difficulty in exposure assessment with IF fields, the groups felt that such studies should be avoided until appropriate subject groups and relevant end points can be identified. Any proposed epidemiology study should be preceded by feasibility studies demonstrating that high quality exposure data can be obtained, and the studies should have adequate statistical power. The choice of health end-points to examine is also problematic, given the paucity of toxicological or epidemiological evidence for any hazard from IF fields under real world exposure conditions.

The working groups also agreed that future animal studies should attempt to use exposure conditions that are similar to real world exposures from industrial and other sources, but should also explore higher exposure levels. Furthermore, any identified biological effects should be examined for exposures of variable duration and intensity and at different frequencies, to verify the existence and type of dose–response relationships. Requirements of high quality animal studies have been described by Repacholi and Cardis [1997]. The Maastricht working group on animal studies felt that some previously reported effects of IF fields, e.g., on reproduction and development or the nervous system,

should be independently confirmed before searching for other effects or interaction mechanisms.

## CONCLUSIONS

This report presents views of the present authors, based in part on conclusions of expert working groups meeting at an international seminar organized as part of WHO's International EMF Project. The general consensus of the working groups was that present scientific evidence does not show health hazards from IFs at exposures below recommended guidelines. However, the biological data are sparse, particularly in relation 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 determine thresholds better, particularly for fields with complex waveform, pulsed fields, and for partial-body exposures. Any epidemiological studies at IFs should be preceded by pilot studies demonstrating their feasibility.

## ACKNOWLEDGMENTS

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#### APPENDIX A. SPEAKERS AT SYMPOSIUM

Prof Jürgen Bernhardt	Institut für Strahlenhygiene	Germany
Dr Philip J Chadwick	National Radiological Protection Board	United Kingdom
Dr Geraint Davies	Innovia Technology Ltd	United Kingdom
Prof Kenneth R. Foster	University of Pennsylvania	USA
Dr Roland Glaser	Humboldt Universität	Germany
Dr Martino Grandolfo	Istituto Superiore di Sanita	Italy
Dr Maila Hietanen	Finnish Institute of Occupational Health	Finland
Dr Kari Jokela	Radiation and Nuclear Safety Authority	Finland
Dr Jukka Juutilainen	University of Kuopio	Finland
Dr B. Jon Klauenberg	Air Force Research Laboratory	USA
Dr Thomas McManus	Department of Transport, Energy and Communications	Ireland
Prof Luis Miro	University of Montpellier	France
Dr Richard Olsen	NHRC Detachment, Brooks Air Force Base	USA
Dr Christopher J. Portier	National Institute of Environmental Health Sciences	USA
Dr Michael H Repacholi	World Health Organization	Switzerland
Dr J. Patrick Reilly	Metatec Associates	USA
Dr Paolo Vecchia	Istituto Superiore di Sanita	Italy

#### APPENDIX B. WORKING GROUPS

##### Group 1 (exposures, dosimetry, and measurement)

Chair	Dr Phil Chadwick	National Radiological Protection Board	United Kingdom
Rapporteur	Dr Tony Muc	World Health Organization	Switzerland
Members	Dr Paolo Vecchia	Istituto Superiore di Sanita	Italy

## Appendix B. (Continued)

	Dr Richard Tell	Richard Tell Associates	USA
	Dr Kari Jokela	Radiation and Nuclear Safety Authority	Finland
	Dr Geraint Davies	Innovia Technology Limited	United Kingdom
	Dr Michel Israel	National Centre of Hygiene, Medical Ecology and Nutrition	Bulgaria
	Dr Gert Anger	Swedish Radiation Protection Institute	Sweden
	Dr Art Thansandote	Health Canada	Canada
	Dr Peter Lee	Ministry of Health	Malaysia
	Dr A Polichetti	Istituto Superiore di Sanita	Italy
Group 2 (mechanisms, in vitro studies)			
Chair	Professor Kenneth R Foster	University of Pennsylvania	USA
Rapporteur	Dr Eric Litvak	World Health Organization	Switzerland
Members	Dr Patrick Reilly	Metatec Associates	USA
	Dr Jürgen Bemhardt	Institut für Strahlenhygiene	Germany
	Dr Roland Glaser	Humboldt Universität	Germany
Group 3 (in vivo, human, and epidemiological studies)			
Chair	Dr René de Seze	DRC-Toxicologie	France
Rapporteur	Dipl-Ing Rüdiger Matthes	Institut für Strahlenhygiene	Germany
Members	Professor Luis Miro	University of Montpellier	France
	Dr John d' Andrea	Brooks Airforce Base	USA
	Dr Martino Grandolfo	Istituto Superiore di Sanita	Italy
	Dr Jukka Juutilainen	University of Kuopio	Finland
	Dr Maila Hietanen	Finnish Institute of Occupational Health	Finland
	Dr Chiyoji Ohkubo	National Institute of Public Health	Japan
	Dr Paul Schreiber	Bundesanstalt für Arbeitsschutz	Germany
	Dr Eric van Rongen	Health Council of the Netherlands	The Netherlands
Mr Young-Pyo Kim	Ministry of Information and Communication	Republic of Korea	

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