

## 5. Summary of Data Reported and Evaluation

### 5.1 Exposure data

Static electric and magnetic fields arise from both natural and man-made sources, whereas electric and magnetic fields in the extremely low-frequency (ELF) range (3–3000 Hz) are mostly associated with man-made sources. These are numerous and include electric power systems, electric and electronic appliances and industrial devices. Environmental levels of ELF fields are very low. Exposure levels for the general population are typically 5–50 V/m for electric fields and 0.01–0.2  $\mu\text{T}$  for magnetic fields. Considerably higher exposure occurs for shorter durations and in some occupational settings.

It should be noted that the earth's magnetic field (25–65  $\mu\text{T}$ , from equator to poles) is a static field to which everyone is exposed.

Measurements of electric and magnetic fields are used to characterize sources and levels of exposure to humans. The capabilities of instruments to measure such fields have advanced in recent years, particularly for magnetic fields. In addition to simple, easy-to-use hand-held survey instruments, there are now portable personal exposure meters capable of recording and describing the statistical, threshold, frequency and waveform characteristics of magnetic field exposure. The limiting factor in exposure assessment is not instrumentation but the lack of a consensus as to what exposure characteristics should be measured that are biologically relevant.

Computational methods are available to calculate fields and their parameters for instrument calibration, laboratory exposure systems and certain categories of indoor and outdoor sources. The difficulties in the use of computation methods to characterize exposure to magnetic fields include the lack of complete knowledge as to the magnitude, direction and location of all relevant current flows on conductors. Such difficulties pose special challenges to the use of calculations of ELF magnetic fields to estimate historical exposure from power lines. Where computational methods are used to calculate human exposure in epidemiological studies, it is desirable to understand the overall uncertainty in the calculated values.

In order to understand the effects of electric and magnetic fields on animals and humans, their electrical properties have to be considered. Static magnetic fields, which are not attenuated by the organism, can exert forces on moving charges, orient magnetic structures and affect the energy levels of some molecules. Static and ELF electric fields are greatly attenuated inside the body.

Exposure to ELF electric and magnetic fields results in induction of electric fields and associated currents in tissues. The magnitudes and spatial patterns of these fields depend on whether the external field is electric or magnetic, its characteristics (e.g. frequency, magnitude, orientation and waveform) and the size, shape and electrical properties of the exposed body. This is a basic physical mechanism for interaction of ELF magnetic fields with tissues. The induced electric field increases with the frequency of the external field and the size of the object. A well-established effect of induced fields above a threshold level is the stimulation of excitable cells. Typical residential exposure results in very small induced electric fields, while some occupational exposure and exposure directly under very high-voltage power lines may result in electric fields of the order of 1 mV/m in some tissues. Non-perceptible contact currents under some conditions are calculated to produce electric fields exceeding 1 mV/m in the bone marrow of a child. Residential levels of ELF electric and magnetic fields produce much lower fields in tissues.

Beyond this well-established interaction mechanism, a number of hypotheses have been advanced: radical pair mechanisms, ion charge-to-mass resonance mechanisms, stochastic resonance, action on biogenic magnetite, etc. Theoretical and experimental evidence for the relevance of these mechanisms is being sought actively.

There are well established in-vivo and in-vitro exposure systems that can provide electric fields of up to the order of 150 kV/m and ELF magnetic fields up to 2 mT. Magnetostatic fields up to 5.0 T can be produced in the laboratory.

## **5.2 Human carcinogenicity data**

### *Effects in children*

Since the first report suggesting an association between residential ELF electric and magnetic fields and childhood leukaemia was published in 1979, dozens of increasingly sophisticated studies have examined this association. In addition, there have been numerous comprehensive reviews, meta-analyses, and two recent pooled analyses. In one pooled analysis based on nine well conducted studies, no excess risk was seen for exposure to ELF magnetic fields below 0.4  $\mu$ T and a twofold excess risk was seen for exposure above 0.4  $\mu$ T. The other pooled analysis included 15 studies based on less restrictive inclusion criteria and used 0.3  $\mu$ T as the highest cut-point. A relative risk of 1.7 for exposure above 0.3  $\mu$ T was reported. The two studies are closely consistent. In contrast to these results for ELF magnetic fields, evidence that electric fields are associated with childhood leukaemia is inadequate for evaluation.

No consistent relationship has been seen in studies of childhood brain tumours or cancers at other sites and residential ELF electric and magnetic fields. However, these studies have generally been smaller and of lower quality.

The association between childhood leukaemia and high levels of magnetic fields is unlikely to be due to chance, but it may be affected by bias. In particular, selection bias

may account for part of the association. Case-control studies which relied on in-home measurements are especially vulnerable to this bias, because of the low response rates in many studies. Studies conducted in the Nordic countries which relied on historical calculated magnetic fields are not subject to selection bias, but suffer from very low numbers of exposed subjects. There have been dramatic improvements in the assessment of exposure to electric and magnetic fields over time, yet all of the studies are subject to misclassification. Non-differential misclassification of exposure (similar degrees of misclassification in cases and controls) is likely to result in bias towards the null. Bias due to unknown confounding factors is very unlikely to explain the entire observed effect. However, some bias due to confounding is quite possible, which could operate in either direction. It cannot be excluded that a combination of selection bias, some degree of confounding and chance could explain the results. If the observed relationship were causal, the exposure-associated risk could also be greater than what is reported.

Numerous studies of the relationship between electrical appliance use and various childhood cancers have been published. In general, these studies provide no discernable pattern of increased risks associated with increased duration and frequency of use of appliances. Since many of the studies collected information from interviews that took place many years after the time period of etiological interest, recall bias is likely to be a major problem.

Studies on parental occupational exposure to ELF electric and magnetic fields in the preconceptional period or during gestation are methodologically weak and the results are not consistent.

### *Effects in adults*

#### **Residential exposure**

While a number of studies are available, reliable data on adult cancer and residential exposure to ELF electric and magnetic fields, including the use of appliances, are sparse and methodologically limited. None of the studies reported so far has included long-term or personal measurements. Although there have been a considerable number of reports, a consistent association between residential exposure and adult leukaemia and brain cancer has not been established.

For breast cancer and other cancers, the existing data are not adequate to test for an association with exposure to electric or magnetic fields.

#### **Occupational exposure**

Studies conducted in the 1980s and early 1990s pointed to a possible increased risk of leukaemia, brain tumours and male breast cancer in jobs with presumed exposure to ELF electric and magnetic fields above average levels. The interpretation of these studies was difficult mainly due to methodological limitations and lack of

appropriate exposure measurements. Also, a bias towards publication of positive findings could not be excluded.

Several large studies conducted in the 1990s of both leukaemia and brain cancer made use of improved methods for individual assessment of occupational exposure to magnetic fields, and to potential occupational confounders, mainly through the combined use of systematic workplace measurements, individual job history descriptions, and the development of associated job–exposure matrices. However, because the exposure within occupational groups is highly variable, job–exposure matrices do not eliminate all uncertainties regarding the workers' exposure levels. Some of these studies reported increased cancer risk for intermediate or high magnetic field exposure categories. There was no consistent finding across studies of an exposure–response relationship and no consistency in the association with specific sub-types of leukaemia or brain tumour. Evidence for cancers at other sites was not adequate for evaluation.

Although the assessment of exposure to electric fields is difficult, these fields have been measured occasionally in populations of workers using individual exposure meters. Across the studies, no consistent association of electric field strengths with any particular malignancy was noted.

### **5.3 Animal carcinogenicity data**

Four long-term bioassays have been published in which the potential oncogenicity in experimental animals of exposure to ELF magnetic fields was evaluated in over 40 different tissues using standard chronic toxicity testing designs. Three of the studies were conducted in rats (two in both sexes including one with restricted histopathological evaluation, and one in females only) and one in mice (males and females). Three of the four studies (two rat studies and one mouse study) provide no evidence that exposure to ELF magnetic fields causes cancer in any target organ. The fourth found an increased incidence of thyroid C-cell tumours (adenomas plus carcinomas) in male rats exposed to ELF magnetic fields at two intermediate flux densities, which did not demonstrate a dose–response relationship, and a marginal increase at the highest flux density. In the lowest-exposure group, thyroid C-cell carcinomas significantly exceeded control response and were above the historical control range. Thyroid C-cell carcinomas were not seen in male mice, female mice or female rats exposed chronically to ELF magnetic fields in these oncogenicity bioassays.

A long-term oncogenicity bioassay of more limited design that was conducted to identify possible effects of exposure to ELF magnetic fields on the induction of leukaemia and lymphoma or of brain cancer in mice generated negative results.

Two multistage carcinogenesis studies combining exposure to *N*-methyl-*N*-nitrosourea with exposure to static or 50-Hz magnetic fields were performed in the same laboratory using an uncharacterized outbred rat strain. The first study demonstrated an increase in mammary tumour incidence with exposure to the fields regardless of

exposure to *N*-methyl-*N*-nitrosourea. The second study showed no effect at similar exposure levels.

Eleven multistage carcinogenesis studies combining exposure to 7,12-dimethylbenz[*a*]anthracene with exposure to 50- or 60-Hz magnetic fields were performed in three different laboratories. One laboratory performed six 13-week studies and one 27-week study aimed at addressing exposure–response relationships for different magnitudes of exposure to magnetic fields. These studies reported significant increases in mammary tumour incidence at higher exposure levels. A pooled analysis of exposure–response from these studies yielded an average slope significantly different from zero. A second laboratory conducted three studies (two of which were considered inadequate to assess tumour incidence) to replicate these findings at the highest field strengths, but saw no enhancement of mammary tumorigenesis by exposure to ELF magnetic fields in one study, in which the sham control incidence was low enough to detect an increase. In the two other studies, high incidences of mammary tumours in sham controls limited comparisons to possible increases in tumour multiplicity; none were found. The third laboratory studied the impact of intermittent exposure to magnetic fields and saw no changes in tumour incidence or tumour multiplicity in either of two experiments.

Eight studies were performed in five different laboratories on promotion and/or co-promotion of skin tumorigenesis by 50- or 60-Hz magnetic fields using conventional mouse strains. The results of these studies were generally negative. However, a suggestion of accelerated progression to malignancy was observed in one study and a change in tumour multiplicity was observed in another. There was no consistent pattern of response in these studies, which were of effectively equivalent design. One study using a transgenic mouse model demonstrated an acceleration of skin tumorigenesis by ELF magnetic fields.

Three studies have been performed using the enzyme-altered liver foci model in rats or mice to determine tumour promoting and co-promoting effects of 50-Hz magnetic fields (0.5–500  $\mu$ T). No enhancement of liver foci by magnetic field exposure was reported in two studies in rats. In the third study which used ionizing radiation with and without exposure to magnetic fields, the incidence of basophilic liver foci was significantly increased in exposed mice. This finding was not associated with a significant increase in liver cancer incidence.

Multistage studies have been carried out in both mice (conventional and transgenic strains) and rats to evaluate the effects of ELF magnetic fields on the development of leukaemia and lymphoma. In no study did exposure to ELF magnetic fields cause an increased incidence of leukaemia or lymphoma.

One study was performed to identify possible promoting effects of ELF magnetic field exposure on the induction of neurogenic tumours. The results of this study showed no enhancement of neurogenic tumour induction.

## 5.4 Other relevant data

### *Reproductive effects in humans and animals*

Taken as a whole, the results of human studies do not establish an association of adverse reproductive outcomes with exposure to ELF electric and magnetic fields. Such adverse outcomes have been reported in a few studies, particularly at higher field intensities and in people exposed for longer durations. With exposures from video display terminals, a greater number of studies have been performed and these generally found no adverse reproductive effects.

Experiments with many different mammalian and non-mammalian experimental models consistently indicate lack of adverse effects on reproduction and development from exposure to strong static magnetic (0.25–1.0 T) and ELF electric (up to 150 kV/m) fields. Static magnetic fields with high spatial gradients and those mixed with alternating fields have been reported to affect embryonic development in frogs and mice, although the number of studies is small.

Prenatal exposure to ELF magnetic fields generally does not result in adverse effects on reproduction and development in mammals. When effects are observed, they usually consist of minor developmental anomalies. Non-mammalian classes of animals (fish, frogs, birds) show inconsistent effects of ELF electric and magnetic fields on development (including increased malformations).

### *Other effects in humans*

Due to the small number of immunological and haematological studies in humans and very small sample sizes within the reported studies, no health-related conclusions can be drawn from the data on immunological and haematological effects after exposure to ELF electric and magnetic fields.

In humans, the principal element of neuroendocrine response to exposure to ELF electric and magnetic fields that has been investigated is the circadian production and release of melatonin. No effect on melatonin was seen following night-time exposure of human volunteers to 50 or 60-Hz magnetic fields under controlled laboratory conditions. In contrast, a small reduction in melatonin concentration has been observed in occupational and residential environments, but it is difficult to distinguish between effects of the magnetic field and those of other environmental factors.

Apart from established perceptual responses in humans to ELF electric fields at levels of tens of kilovolts per meter and the occurrence of magnetophosphenes (faint, flickering visual sensations) in response to exposure to relatively strong ELF magnetic fields (> 10 mT at 20 Hz), few behavioural effects of exposure to ELF electric and magnetic fields have been observed. Changes in electroencephalograms, cognition, mood, sleep electrophysiology and cardiac response tend to be few, subtle and transitory when they do occur during exposure. The evidence from epidemiological studies of residential and occupational exposure to ELF electric and magnetic fields in

relation to the incidence of neurodegenerative disease, depression and suicide and cardiovascular disease is generally weak and inconsistent.

#### *Other effects in animals*

Studies to evaluate immune function and host resistance in animals have given negative effects for exposure to ELF electric and magnetic fields. In-vitro exposure of immune system cells generally did not cause changes in proliferation capacity.

Apart from occasional changes in some haematological parameters in one rat study, no consistent effects on blood formation were seen in experimental animals or their offspring exposed to either static magnetic fields or to 50- or 60-Hz electric and/or magnetic fields.

Most animal studies of endocrine function concern the pineal gland and melatonin, because of concerns related to cancer. Fewer studies have been carried out on the effects of exposure to ELF electric and magnetic fields on the pituitary hormones or those of other endocrine glands.

Some, but not all, studies of the effects of 50- or 60-Hz electric and magnetic fields in rodents show a reduction in pineal and/or serum melatonin concentrations. Differences in response have been reported for linearly polarized compared with circularly polarized magnetic fields. No convincing effect on melatonin concentrations has been seen in non-human primates chronically exposed to 50- or 60-Hz electric or magnetic fields.

With the possible exception of short-term stress (duration of minutes) following the onset of exposure to ELF electric fields at levels significantly above perception thresholds, no consistent effects have been seen in the stress-related hormones of the pituitary–adrenal axis in a variety of mammalian species.

Animals can perceive ELF electric fields (threshold 3–35 kV/m) and respond with activity changes or aversion. Such responses are generally not observed with magnetic fields.

Although exposure to magnetic fields has been reported to influence spatial learning and memory in rodents, it appears that no long-term behavioural deficits occur due to exposure to static or ELF electric and magnetic fields.

#### *Genetic and related effects*

A few studies on genetic effects have examined chromosomal aberrations and micronuclei in lymphocytes from workers exposed to ELF electric and magnetic fields. In these studies, confounding by genotoxic agents (tobacco, solvents) and comparability between the exposed and control groups are of concern. Thus, the studies reporting an increased frequency of chromosomal aberrations and micronuclei are difficult to interpret.

Many studies have been conducted to investigate the effects of ELF magnetic fields on various genetic end-points. Although increased DNA strand breaks have been reported in brain cells of exposed rodents, the results are inconclusive; most of the studies show no effects in mammalian cells exposed to magnetic fields alone at levels below 50 mT. However, extremely strong ELF magnetic fields have caused adverse genetic effects in some studies. In addition, several groups have reported that ELF magnetic fields enhance the effects of known DNA- and chromosome-damaging agents such as ionizing radiation.

The few animal studies on cancer-related non-genetic effects are inconclusive. Results on the effects on in-vitro cell proliferation and malignant transformation are inconsistent, but some studies suggest that ELF magnetic fields affect cell proliferation and modify cellular responses to other factors such as melatonin. An increase in apoptosis following exposure of various cell lines to ELF electric and magnetic fields has been reported in several studies with different exposure conditions. Numerous studies have investigated effects of ELF magnetic fields on cellular end-points associated with signal transduction, but the results are not consistent.

## 5.5 Evaluation

There is *limited evidence* in humans for the carcinogenicity of extremely low-frequency magnetic fields in relation to childhood leukaemia.

There is *inadequate evidence* in humans for the carcinogenicity of extremely low-frequency magnetic fields in relation to all other cancers.

There is *inadequate evidence* in humans for the carcinogenicity of static electric or magnetic fields and extremely low-frequency electric fields.

There is *inadequate evidence* in experimental animals for the carcinogenicity of extremely low-frequency magnetic fields.

No data relevant to the carcinogenicity of static electric or magnetic fields and extremely low-frequency electric fields in experimental animals were available.

### Overall evaluation

Extremely low-frequency magnetic fields are *possibly carcinogenic to humans (Group 2B)*.

Static electric and magnetic fields and extremely low-frequency electric fields are *not classifiable as to their carcinogenicity to humans (Group 3)*.