National Toxicology Program
Toxicity Report Series
Number 58

NTP Technical Report
on Toxicity, Reproductive, and Developmental Studies of

60-Hz Magnetic Fields

Administered by Whole Body Exposure
to F344/N Rats, Sprague-Dawley Rats, and B6C3F$_1$ Mice

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United States Department of Health and Human Services
Public Health Service
National Institutes of Health

Note to the Reader

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- the National Cancer Institute (NCI) of the National Institutes of Health;
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- the National Center for Toxicological Research (NCTR) of the Food and Drug Administration; and
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The studies described in this toxicity study report were performed under the direction of NIEHS and were conducted in compliance with NTP laboratory health and safety requirements. These studies met or exceeded all applicable federal, state, and local health and safety regulations. Animal care and use were in accord and compliance with the Public Health Service Policy on Humane Care and Use of Animals.

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This NTP report on the toxicity studies of 60-Hz magnetic fields is based primarily on 8-week toxicity studies that took place from September through October 1993 and the teratology and continuous breeding studies that took place from September 1993 through August 1994.

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PEER REVIEW

The draft report on the toxicity studies of 60-Hz magnetic fields was evaluated by the reviewers listed below. These reviewers serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, reviewers determine if the design and conditions of these NTP studies are appropriate and ensure that the toxicity study report presents the experimental results and conclusions fully and clearly.

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CONTENTS

ABSTRACT

Electric and magnetic fields are associated with the production, transmission, and use of electricity; thus the potential for human exposure is high. These electric and magnetic fields are predominantly of low frequency (60 Hz) and generally of low intensity. The prevailing view among physicists is that exposure to these low-frequency, low-intensity fields does not pose a health hazard. However, this view has been challenged by reports linking magnetic field exposure to the development of leukemia and other cancers. Because multiple epidemiologic studies suggested a potential for increased cancer rates with increasing exposure, and because of public concern, the effects of 60-Hz magnetic field exposure were examined in F344/N rats and B6C3F_1 mice in 8-week full-body-exposure studies. Animals were evaluated for hematology and clinical chemistry (rats only) parameters, pineal gland hormone concentrations, and histopathology. Additional studies were performed in Sprague-Dawley rats to examine teratologic and reproductive effects of magnetic field exposure.

In the 8-week toxicity studies, groups of male and female F344/N rats and B6C3F_1 mice were exposed for 18.5 hours per day to 60-Hz magnetic fields at intensities of 0 (control), 0.02, 2, and 10 gauss (G). Additional groups of rats and mice were exposed to intermittent 10 G fields (1 hour on/1 hour off) for 18.5 hours per day. No evidence of toxicity associated with exposure to magnetic fields was observed in rats or mice. Clinical observations provided no evidence of adverse effects associated with magnetic field exposure. Compared to control rats and mice, there were no biologically significant differences in hematology or clinical chemistry parameters of rats exposed to magnetic fields. No gross lesions or histopathologic findings in rats or mice were attributed to exposure to 60-Hz magnetic fields. In addition, magnetic field exposure was not associated with a significant reduction in serum melatonin or pineal gland melatonin concentration, or pineal gland activity of *N*-acetyltransferase in either species.

One female rat in the 2 G exposure group died during the 8-week toxicity study from causes unrelated to magnetic field exposure; all other male and female rats and mice in the study survived until the end of the study. Final mean body weights and mean organ weights of a few groups of exposed animals differed from those of the control groups; however, no clear pattern of magnetic field effects was observed, and these differences are not considered to be biologically significant.

For the teratology study, groups of 55 pregnant female Sprague-Dawley rats were exposed to the same magnetic fields as in the toxicity study on gestation days 6 through 19. Fifteen pregnant females exposed to 85 mg ethylenethiourea/kg body weight served as positive controls. Except for the positive controls, there were no changes in maternal or fetal weights, nor were fetal abnormalities found. The number of pregnant females was

significantly lower in groups exposed to magnetic fields than in the control group; however, all breeding in the teratology study was completed prior to the first day of magnetic field or sham exposure. On this basis, this finding is unrelated to magnetic field exposure. In addition, there were no differences between control and exposed groups in the number of pregnant females in the continuous breeding study, in which breeding took place within the magnetic fields.

Groups of 40 breeding pairs of Sprague-Dawley rats were exposed to the same magnetic fields as in the toxicity study during the breeding and lactation of five litters in a continuous breeding study. The fifth litter was exposed during gestation and lactation; one male and one female from each litter were raised to sexual maturity receiving the same exposures as the parents; rats were mated to nonsibling rats and allowed to deliver the third-generation offspring. The results of the continuous breeding study demonstrated no effects of magnetic field exposure on reproductive performance in either male or female rats.

INTRODUCTION

PHYSICAL PROPERTIES, USE, AND EXPOSURE

Electric and magnetic fields associated with the production, transmission, and use of electricity are ubiquitous in industrialized societies. These electric and magnetic fields are predominantly of low frequency (60 Hz) and are generally of low intensity. Electric fields exist when there is electric potential in a line, while magnetic fields exist only when there is current flow (Miller and Schroeer, 1987). Because electric and magnetic fields often occur together and are interactive, these fields have often been referred to as *electromagnetic fields*, or EMFs. Electric fields are easily shielded by trees, walls, and other objects, while magnetic fields usually penetrate nonferrous material. Thus, most exposure in the home is to magnetic fields, and recent research has focused on potential adverse biological effects of exposure to magnetic fields.

Most residential exposure is to magnetic fields that are less than 0.2 μT (microtesla; 1 μT = 10 milligauss) although many commonly used household appliances generate fields that exceed this intensity (Gauger, 1985). High-frequency fields, such as ionizing radiation, have sufficient energy to damage DNA; however, low-frequency (i.e., 60-Hz) fields are of very low energy and are not sufficient to alter DNA structure or directly cause genetic injury (Juutilainen and Saali, 1986; Rosenthal and Obe, 1989). Further, the magnetic fields produced by 60-Hz alternating current are of much lower intensity than the earth's static magnetic fields, which are 300 to 500 mG, depending on the geographic location, presence of ferrous materials, and other factors. Thus, physicists have assumed that exposure to low-frequency, low-intensity magnetic fields does not pose a health hazard. This view was challenged by Wertheimer and Leeper (1979), who reported that children living in homes with potentially high magnetic fields had a greater incidence of childhood leukemia than children living in homes that would be expected to have lower 60-Hz magnetic field exposures.

TOXICITY

The literature on the potential toxicity of 60-Hz magnetic fields includes human (epidemiology) studies, animal studies, and *in vitro* studies. Most of the literature is complicated due to the complex nature of the fields and does not usually provide adequate descriptions of the exposures or the potential confounders such as transients, harmonics, heat, vibration, and other environmental cues. Epidemiology studies can provide only an estimate of the exposures, because the exposure in the home varies by location within the house; the number and type of appliances in use; the current load on the outside lines, which varies with electrical demand; and development

and changes within a community that cause variations in the fields over time. Further, residential exposures account for only a portion of the total magnetic field exposures for children, because exposures also occur during outdoor activities.

Experimental animal studies are also difficult to conduct and the exposure variables are difficult to control. Most animal studies do not give sufficient details on the exposure parameters or the earth's static magnetic fields, which can interact with the experimental fields. Animal studies in the literature have given conflicting results on the potential hazards of exposure to electric and magnetic fields (Kavet and Banks, 1986; Anderson, 1993). There is a need for additional research on interaction mechanisms and animal studies that emphasize confounding factors (Lin, 1991).

Finally, *in vitro* and mechanistic studies are complicated by potential induced currents in the culture media, exposure of cells to stray electric and magnetic fields (i.e., motors in incubators and centrifuges), exposure of cells to fields created during centrifuging (by passing the cells rapidly through the earth's static fields), the density and location of the cells within the cultures, the presence of ferrous material in culture media, and the presence of magnetite in the cells (Kirschvink *et al.*, 1992). These confounding factors make validation of any *in vitro* study very difficult.

Reproductive Toxicity

The epidemiologic studies of the reproductive effects of EMF exposures in humans include studies of exposures to video display terminals (VDTs), power lines, and household appliances. The VDT studies are generally negative for reproductive effects, while the reproductive risks of power lines and home appliances are less consistent (Brent *et al.*, 1993).

There are over 70 animal and *in vitro* studies on low-frequency (30-300kHz) and very low-frequency (30 kHz or less) EMF exposure that evaluate some aspect of reproduction or teratology (Delgado *et al.*, 1982; Juutilainen and Saali, 1986; Beers, 1989; Eckert, 1992). Many embryology studies use the chick embryo to evaluate teratogenesis after 48 to 52 hours of development (Martin, 1992; Brent *et al.*, 1993; Koch *et al.*, 1993). In chicken eggs exposed to magnetic fields, some embryos showed slowed development (Juutilainen and Saali, 1986; Martin, 1988), while in other studies, there were no differences in embryos from exposed, sham-exposed, and control eggs (Maffeo *et al.*, 1984). Medaka fish embryos exposed to a 60-Hz magnetic field showed no gross abnormalities, but the embryos' development was slowed (Cameron *et al.*, 1985). Magnetic field exposures inhibited proliferation of sea urchins (Cameron *et al.*, 1993). A review of the literature concluded that laboratory and epidemiology studies have not yielded conclusive data to suggest that magnetic field exposures induce adverse reproductive effects under the conditions studied (Chernoff *et al.*, 1992). Others

have also suggested that the evidence for any reproductive effects is very weak (Maffeo *et al.*, 1988; Jauchem, 1993).

Neuroendocrine Toxicity

Several studies suggest that electric or magnetic field exposures may depress nocturnal melatonin levels in rodents (Wilson *et al.*, 1986, 1989; Lerchl *et al.*, 1991; Reiter, 1992; Stevens *et al.*, 1992; Anderson, 1993; Stevens, 1994). In one study, pineal melatonin synthesis in rats was not reduced, but serum melatonin levels were reduced, suggesting that degradation or tissue uptake of melatonin may be stimulated by exposure to electric fields (Grota *et al.*, 1994). Other studies report that serotonin-*N*-acetyltransferase, the rate-limiting enzyme for melatonin production, may be depressed by magnetic field exposure (Olcese and Reuss, 1986). Melatonin suppression may be associated with breast cancer, one of the cancers hypothesized to be increased by magnetic field exposure (Stevens *et al.*, 1992). This hypothesis has been supported by reports that melatonin is oncostatic to breast cancer cells *in vitro* (Reiter, 1992, 1993a; Liburdy *et al.*, 1993).

Carcinogenicity

The carcinogenic potential of magnetic field exposure has been suggested by several epidemiology studies, but the data are far from conclusive. Wertheimer and Leeper (1979) and Savitz *et al.* (1988) classified the residences of children by using wiring codes as surrogates for predicted magnetic fields within the home (Barnes *et al.*, 1989). Some epidemiology studies of residential exposure showed little or no correlation between estimated home exposure to magnetic fields and the incidence of childhood leukemia (Fulton *et al.*, 1980; Ahlbom, 1988; Coleman *et al.*, 1989; Myers *et al.*, 1990). Epidemiology studies of workplace exposure suggested a potential occupational risk of EMF exposure for increased leukemia rates (Gilman *et al.*, 1985), while other studies were negative (Fulton *et al.*, 1980; Myers *et al.*, 1990); however, these studies have questions concerning matching controls and tumor groupings (ORAU, 1992). A high variability in electric and magnetic field exposures was associated with these occupational studies (Deadman *et al.*, 1988).

Several short-term rodent carcinogenesis studies have also been conducted (Anderson, 1993). Static magnetic fields did not enhance the development of spontaneous lymphoblastic leukemia in female AKR mice (Bellossi, 1986). Alternating-current fields have been reported to enhance the development of chemical-induced mammary gland tumors in rats, but the effects on tumor incidence have been marginal (Beniashvili *et al.*, 1991; Mevissen *et al.*, 1993; Löscher *et al.*, 1993, 1994; Löscher and Mevissen, 1994). In skin tumor promotion models, there has been either a marginal increase in the incidence of skin papillomas with magnetic field exposure (McLean *et al.*, 1991) or no increase in neoplasm incidence (Rannug *et al.*, 1993a). In SENCAR mice, intermittent magnetic field exposure caused a marginal increase in the accumulated number of skin tumors per tumor-bearing animal (Rannug *et al.*, 1994). In Sprague-Dawley rats, there was no increase in the incidence of liver foci following magnetic field exposure (Rannug *et al.*, 1993b), and following partial

hepatectomy and chemical treatment, magnetic field exposure resulted in a slight reduction in size and number of liver foci compared to unexposed controls (Rannug *et al.*, 1993c). Thus neither epidemiology studies nor animal studies have provided conclusive evidence that magnetic fields can increase the incidence of cancer or alter the carcinogenic process.

Genetic Toxicity

The genotoxic effects of low-frequency EMFs have been investigated in a variety of studies covering a broad range of test types and endpoints; a review of the data was presented by McCann *et al.* (1993). With few exceptions, the data from laboratory experiments support the conclusion that low-frequency electromagnetic fields, as well as electric and magnetic fields separately, present little or no risk of induced genetic damage under the laboratory conditions used. Electric fields characterized by sparking, high-intensity pulsing, or corona effects may represent a greater genotoxic risk, although the information from studies that involved such exposures is not definitive (McCann *et al.*, 1993). Significantly increased chromosomal aberration frequencies in peripheral blood lymphocytes of switchyard workers exposed to 50-Hz sinusoidal EMFs, electric shocks, and other hazards of this work environment have been reported (Nordenson *et al.*, 1984, 1988). Additionally, El Nahas and Oraby (1989) demonstrated dose-related increases in the incidence of micronuclei in bone marrow cells of mice exposed to 50 Hz sinusoidal electric fields of varying intensities (170-290 kV/m). These results raise concerns about the genetic effects of these exposure conditions, but neither of these studies has been independently replicated, and numerous *in vitro* investigations conducted under carefully controlled laboratory conditions with human cells (Nordenson *et al.*, 1984; Cohen *et al.*, 1986a,b; Livingston *et al.*, 1991; Scarfi *et al.*, 1991) and rodent cells (Wolff *et al.*, 1980; Livingston *et al.*, 1991) have not confirmed the potential for EMF-induced genetic damage. All results from DNA repair studies with mammalian cells were negative (Pino *et al.*, 1985; Whitson *et al.*, 1986; Reese *et al.*, 1988; Frazier *et al.*, 1990), and an investigation of EMF exposure showed no exposure-related changes on clonogenicity or cell cycle time of cultured Chinese hamster ovary cells (Livingston *et al.*, 1991). Investigations of EMF-induced mutagenicity in bacterial assays have also yielded negative results (Moore *et al.*, 1981; Thomas and Morris, 1981; Juutilainen and Liimatainen, 1986; Shimizu *et al.*, 1989). Not all exposure categories or all types of assays are represented in the list of well-designed and well-conducted EMF genotoxicity experiments (McCann *et al.*, 1993). However, the accumulated evidence implies little risk of adverse genetic effects from low-frequency EMF exposure.

STUDY RATIONALE AND DESIGN

In 1988, in response to an epidemiology report (Savitz *et al.*, 1988) that appeared to confirm an earlier study by Wertheimer and Leeper (1979), the Department of Energy and the Electric Power Research Institute nominated 60-Hz EMFs for consideration for evaluation by the NTP. At that time, many scientists considered

the relationship between residential or occupational exposure to magnetic fields and increased cancer rates unresolved because of conflicting results and the many confounding factors (Greenberg and Shuster, 1985; Michaelson, 1987). The few existing animal studies were generally short-term promotion studies and not long-term studies that would address the potential carcinogenic hazard of magnetic fields, such as the studies that have traditionally been conducted by the NTP. In 1990, the National Association of Regulatory Utility Commissioners (representing all 50 states; Washington, D.C.; Puerto Rico; and the Virgin Islands) and the Large Public Power Council (representing 17 of the largest publicly owned utilities in the United States) also requested that the National Institute of Environmental Health Sciences (NIEHS) undertake studies to evaluate the effects of exposure to electric and magnetic fields. Therefore, given the intense public concern, the lack of definitive answers from the epidemiology studies, and the widespread exposure to low-intensity, 60-Hz magnetic fields in industrialized societies, standard toxicity studies were conducted using traditional rodent models. Long-term carcinogenesis studies will be reported separately.

Because there were multiple reported effects in the literature, a draft protocol was circulated to experts in EMF exposure to solicit comments on appropriate studies for magnetic field evaluation. The selection of toxicity, developmental, reproductive, and carcinogenicity studies was based on concerns raised by published reports and epidemiology studies. Standard comprehensive protocols for the assessment of developmental toxicology in female Sprague-Dawley rats and for a continuous breeding study in Sprague-Dawley rats (the usual strain and species for NTP assessment of developmental and reproductive effects) were included. The toxicity studies in F344/N rats and B6C3F$_1$ mice included evaluation of pineal gland function in addition to the standard histopathology, hematology, and clinical chemistry evaluations.

Because electric and magnetic field exposures are very complex and there was an infinite combination of field parameters that could be evaluated, the circulated draft protocol solicited comments on appropriate field parameters for evaluation. A workshop was held at the NIEHS to assist in finalizing the field parameters for study. While there are different frequencies of exposure in homes with different appliances, and 50 Hz is the predominant field frequency in western Europe and Japan, in American homes the predominant frequency is 60 Hz; therefore, it was decided that all exposures would use a 60-Hz frequency.

The field intensities were limited by design considerations. The creation of magnetic fields for animal exposure requires large coils. As field intensities increase, noise, heat, vibration, and stray fields become a problem for technicians and control animals. A manageable maximum field intensity of 10 G was selected; this is approximately 5,000-fold greater than what was considered high intensity for homes in the epidemiology studies. Because it was possible that on-and-off changes in the magnetic field, and not necessarily the field intensity itself, were important, a second high-intensity group was included, with 1-hour-on and 1-hour-off exposures. Rodents have 10- to 15-fold fewer induced currents than humans from equivalent electric field

exposures (Kaune and Anderson, 1990); thus, the lowest field intensity (0.02 G) gives rodents an exposure that may be slightly higher than residential exposures for humans. The third field intensity, 2 G, was an intermediate intensity between the other two fields.

While power line magnetic field exposures are predominantly sine-wave fields, residential and occupational exposures may include square waves, sawtooth waves, and other wave forms. Harmonics (120 Hz, 180 Hz, etc.) may also be found. Further, as appliances are switched on and off, spikes or transients in fields may occur. It is not feasible to evaluate all possible variables in large animal studies. Therefore, these studies used linearly polarized, pure sine-wave exposures at 60 Hz, with the fields turned on when the sine wave was at zero amplitude and gradually increased over seven to nine cycles (between 0.11 and 0.15 seconds) to full intensity, and similarly gradually decreased to avoid transients. These studies evaluate the predominant component (60-Hz sine-wave magnetic fields) without all the complexities of the exposures that occur in residential and occupational settings.

MATERIALS AND METHODS

MAGNETIC FIELD PRODUCTION AND MONITORING

The magnetic field exposure system consisted of five identical field-generating coil sets, each located in one of five animal exposure rooms. Each coil set consisted of seven pairs of rectangular, vertically oriented coils connected in series and spaced uniformly through the room. Pairs of coils were stacked one above the other, the bottom coils produced a linear 60-Hz magnetic field in one direction while the top coils produced a similar field in the opposite direction (Figure 1).

The coil arrangement in each room protected against field overlap between rooms. The opposing fields produced by coil pairs functioned to cancel one another outside the area of the exposure room. Additional field cancellation was provided by horizontally positioned steering coils located at the ends of each coil set. Compensating capacitors were located between each coil to cancel the inductive reactance at 60 Hz and to control the voltage differential between adjacent coils (Figure 1).

During a preliminary study, an animal rack instrumented with eight thermocouples was placed in the animal rooms to record temperatures when fields were on and off. No differences in temperature were found with magnetic field exposures. In addition, the exposure system was validated by a representative of the National Institute of Standards and Technology (NIST), who found that the intensities and spatial uniformity of the earth's static magnetic fields within the animal exposure area were within 10% of the expected intensities. Using a NIST fluxgate magnetometer, measurements were made of the direct-current (DC) magnetic field component that was parallel to the direction of the alternating-current (AC) magnetic field in each exposure room in a north-south direction. The measurements were performed in the top and bottom coil systems at the level of the rat and mouse enclosures in each exposure bay. The results are presented in Table 1. The calibration uncertainty of the fluxgate magnetometer is estimated to be less than 2%; however, the measurements are sensitive to probe alignment because of the nonuniformity of the field and the presence of a significant vertical magnetic field component. Therefore the measurements should be considered approximate. The full NIST validation report is available from the National Institute of Environmental Health Sciences upon request.

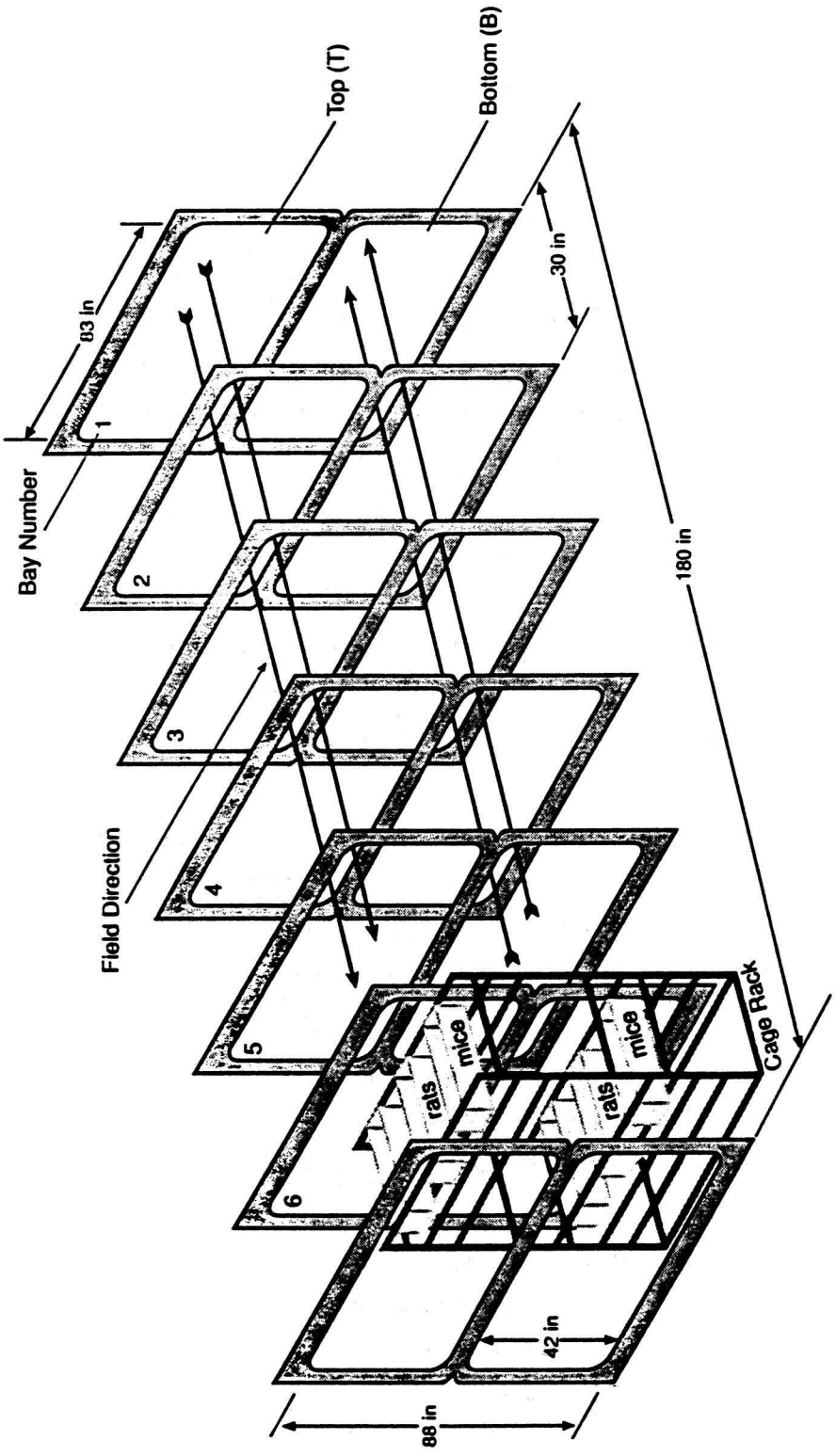

FIGURE 1 Magnetic Fields Unit

TABLE 1 Summary of Earth Static Magnetic Field Intensities Measured Within Exposure Rooms prior to the Studies of 60-Hz Magnetic Fields

		Field Intensity (T)	
	Rack Bay	Top	Bottom
Room 1	1	10.5	1.30
	2	14.5	7.77
	3	15.6	13.8
	4	15.4	4.8
	5	15.8	11.3
	6	16.9	13.7
Room 2	1	11.3	0.44
	2	11.6	3.18
	3	13.6	3.17
	4	18.4	26.4
	5	21.5	38.5
	6	21.5	29.4
Room 3	1	14.2	8.42
	2	14.2	9.67
	3	14.8	13.5
	4	15.8	19.4
	5	16.8	22.8
	6	17.0	23.3
Room 4	1	20.1	21.3
	2	19.2	15.9
	3	18.3	18.2
	4	16.2	18.8
	5	14.0	9.78
	6	12.0	2.2
Room 5	1	19.3	25.4
	2	20.7	23.2
	3	18.5	11.5
	4	15.5	–5.5
	5	12.4	–10.7
	6	10.8	–4.5

Coils were held in place by fiberglass supports and were protected from moisture by Plexiglas™ enclosures. Durometer™ neoprene pads between the coils and supports isolated coil vibrations. Each coil set was controlled from an electronics control room. In three rooms the fields had intensities of 0.02, 2, and 10 G, and in a fourth room the field was manipulated to produce an intermittent 10 G field (1 hour on and 1 hour off). Harmonic distortion was less than 3%. A fifth room with an identical coil apparatus that was not operating served as the 0 G control room. Fiberglass cage racks were constructed to prevent disruption of the experimentally generated fields. The stainless steel automatic watering system was designed and configured to eliminate possible current loops. Fiberglass guides and floor plates were located in each room to provide precise alignment of racks and cages within the magnetic field. Racks held equal numbers of polycarbonate cages in either the top or the bottom field of the coil sets (Figure 1). Cages were alternated between the top and bottom fields on a weekly basis.

Fields were monitored by a MultiWave™ Monitoring System (Electric Research and Management, Inc., Pittsburgh, PA) which consisted of a microcomputer, an external tie-in, and data multiplexors that were located in the control room. In exposure rooms, monitoring system components included a series of three-axis AC magnetic field probes (two per room), AC voltage probes, and environmental sensor probes (to measure rack vibration, noise, light intensity, temperature, and humidity). The magnetic probes, which were located at the end of each exposure module in the center of the steering coils to detect faults in the coils, allowed monitoring of the ambient magnetic fields during the "off" periods of intermittent exposure and during daily field shutdowns. The computer program (WAVE-C) continuously monitored and collected sensor data. Data samples were electronically stored every 30 minutes, and data were off-loaded from the system on a daily basis. The system was equipped with alarms to alert project personnel in the event that measured parameters deviated from set ranges.

Average field intensities measured during the 8-week studies are given in Table 2. All exposures were within 10% of the target; the maximum magnetic field intensity in the control room did not exceed 1 mG.

TABLE 2 Summary of Average Field Intensities and Exposure Conditions in the 8-Week Study of 60-Hz Magnetic Fields

	0 G	0.02 G	2 G	10 G Intermittent	10 G
Magnetic Field Intensity (G)					
Fields on					
Average	0.0004	0.020	2.00	9.93	9.90
Minimum	0.0003	0.020	1.84	9.74	9.65
Maximum	0.0006	0.021	2.04	10.11	10.17
Fields off					
Average	0.0004	0.0005	0.0003	0.0006	0.0005
Minimum	0.0003	0.0004	0.0003	0.0003	0.0003
Maximum	0.0006	0.0007	0.0005	0.0009	0.0007
Sound Levels (dB)					
Fields on					
Average	69	71	71	69	70
Minimum	50	50	50	50	50
Maximum	77	77	77	77	77
Fields off					
Average	69	71	70	69	70
Minimum	50	50	50	50	50
Maximum	77	77	77	77	77

TABLE 2 Summary of Average Field Intensities and Exposure Conditions in the 8-Week Study of 60-Hz Magnetic Fields (continued)

	0 G	0.02 G	2 G	10 G Intermittent	10 G
Vibrations[a]					
Fields on					
Average	0.001	0.001	0.001	0.001	0.005
Minimum	0.000	0.000	0.001	0.001	0.002
Maximum	0.070	0.009	0.004	0.004	0.009
Fields off					
Average	0.001	0.001	0.001	0.001	0.006
Minimum	0.000	0.000	0.001	0.001	0.001
Maximum	0.070	0.070	0.184	0.055	0.032
Lights on					
Average	0.001	0.001	0.001	0.001	0.005
Minimum	0.001	0.000	0.001	0.001	0.001
Maximum	0.070	0.070	0.184	0.055	0.032
Lights off					
Average	0.001	0.001	0.001	0.001	0.005
Minimum	0.000	0.000	0.001	0.001	0.002
Maximum	0.008	0.005	0.004	0.004	0.009

[a] Expressed as percent of gravity; 1 g = 9.8 m/s^2

STUDY DESIGNS

Toxicity Studies

Core Studies

Male and female F344/N rats and B6C3F_1 mice were obtained from Taconic Farms (Germantown, NY). On receipt, rats were 4 weeks old and mice were 4 to 5 weeks old. Animals were quarantined for 13 days; rats were 6 weeks old and mice were 6 to 7 weeks old on the first day of the studies. Groups of 10 male and 10 female rats and mice were exposed to 60-Hz magnetic fields at intensities of 0, 0.02, 2, and 10 G for 18.5 hours per day, 7 days per week, for 8 weeks. The exposure was continuous for 4 hours (11 a.m. to 3 p.m.), discontinued for 1.5 hours (3 p.m. to 4:30 p.m.), continuous for 14.5 hours (4:30 p.m. to 7 a.m.), and then discontinued for an additional 4 hours (7 a.m. to 11 a.m.). Groups of 10 male and 10 female rats and mice were intermittently exposed (1 hour on and 1 hour off, starting at 11 a.m.) to a 10 G 60-Hz field 18.5 hours per day, 7 days per week, for 8 weeks, with similar 4-hour and 1.5-hour gaps in exposure included for husbandry operations and animal observations. Before the studies began, five male and five female rats and mice were randomly selected for parasite evaluation and gross observation for evidence of disease. At the end of the studies, blood samples were collected from five male and five female control rats and mice. The sera

were analyzed for antibody titers to rodent viruses (Boorman *et al.*, 1986; Rao *et al.*, 1989a,b); all results were negative.

Male and female rats and female mice were housed five per cage and male mice were housed individually. The bedding was certified Beta-Chips® (Northeastern Products, Inc., Warrensburg, NY). NIH-07 open formula diet (Zeigler Brothers, Inc., Gardners, PA) and water were available *ad libitum*. All food and bedding materials were changed twice weekly for group-housed animals and once weekly for the individually housed male mice. Clinical observations were recorded weekly. The animals were weighed at the time of randomization into groups, weekly during exposures, and at the end of the studies. Details of the study design and animal maintenance are summarized in Table 3.

Necropsies were performed on all core-study animals. The right adrenal gland, heart, right kidney, liver, lungs, right testis, and thymus were weighed. Organs and tissues were examined for gross lesions and fixed in 10% neutral buffered formalin. Tissues to be examined microscopically were trimmed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Complete histopathologic examinations were performed on all control and exposed rats and mice. Tissues examined microscopically are listed in Table 3.

Upon completion of the laboratory pathologist's histologic evaluation, the slides, paraffin blocks, and residual wet tissues were sent to the NTP Archives for inventory, slide/block match, and wet tissue audit. The slides, individual animal data records, and pathology tables were sent to an independent pathology laboratory where quality assessment was performed. Results were reviewed and evaluated by the NTP. Details of these review procedures have been described by Maronpot and Boorman (1982) and Boorman *et al.* (1985).

Clinical Laboratory Analyses

Clinical Pathology

The effects of magnetic field exposure on hematology and clinical chemistry parameters were tested on additional groups of male and female rats receiving the same exposure intensities as core-study animals. After 7 weeks of exposure, 9 or 10 rats per exposure group were anesthetized with CO_2 and blood samples were drawn from the retroorbital sinus. Samples for hematology analyses were placed in tubes containing EDTA. Samples for clinical chemistry were placed in tubes without anticoagulant and were allowed to clot at room temperature; the samples were then centrifuged and serum was removed. Automated hematology measurements were performed using a Serono Baker Diagnostic Systems 9000 Automated Cell Counter (Serono-Baker Diagnostics, Allentown, PA) with reagents provided by the instrument manufacturer. Differential leukocyte counts, reticulocyte counts, and evaluations of erythrocyte and platelet morphology were performed by light microscopy of blood smears stained with Wright-Giemsa. Packed cell volume measurements were made with a Damon/IEC Dividion IEC MB microhematocrit centrifuge (International Equipment Company, Needham

Heights, MA). Clinical chemistry parameters were measured using a Beckman Instruments Synchron CX5 Clinical System with reagents provided by the instrument manufacturer.

Pineal Gland Hormone Analyses

Supplemental groups of 12 male and 12 female rats and mice were exposed for 10 weeks to the same magnetic field intensities as in the core studies. Six animals from each group were killed within 4 hours of the beginning of the light cycle; blood was collected and pineal glands were removed from each animal. The remaining animals from each group were killed by decapitation at the time of peak blood melatonin levels (7 to 10 hours into the dark cycle); blood was collected under dim red light and pineal glands were removed from all animals. Parameters were measured as described by Deguchi and Axelrod, 1972; Troiani *et al.*, 1987, 1988; and Aldhous and Arendt, 1988, and are listed in Table 3.

Teratology Study

To determine the effects of 60-Hz magnetic fields on development, a teratology study was performed in Sprague-Dawley rats. Male and female rats used in the teratology study were obtained from Taconic Farms (Germantown, NY) and were 6 to 7 weeks old at receipt. All rats were quarantined for 10 days prior to mating. Male rats were used for breeding only.

Individual breeding pairs were cohoused overnight. The first day a sperm-positive vaginal smear was obtained was designated gestation day 0; thereafter, females were housed individually. On gestation day 5, pregnant females were weighed and randomized into exposure groups (55 per group). From gestation day 6 through 19, pregnant females were exposed to 0, 0.02, 2, or 10 gauss (10 G exposure was continuous or intermittent) for 18.5 hours per day. An additional 15 pregnant females maintained as positive controls received 85 mg ethylenethiourea/kg body weight in drinking water (concentration 11.5 mg/mL) on gestation days 11, 12, and 13. Water and feed (NIH-07 open formula ground pellets or meal; Zeigler Brothers, Gardners, PA) were available *ad libitum*. Feed consumption was recorded every 3 days. Dams were weighed on gestation days 0, 3, 5, and 6, every 3 days thereafter, and at the end of the study. Rats were observed twice daily. Further details of the study design and animal maintenance are given in Table 3.

Females were necropsied on gestation day 20. Fetuses, ovaries, and uterine horns were removed intact and weighed. The ovaries were removed and corpora lutea were counted. Each fetus was examined grossly and individually weighed. In addition, the heads of one-half of the fetuses from each litter were examined using a modified Wilson's razor blade sectioning technique. All fetuses (177 to 622 per group) were examined by a modified Staples wet visceral examination technique (Stuckhardt and Poppe, 1984) and processed according to a modified method of Marr for skeletal evaluations. Skeletal anomalies were recorded for each individual fetus.

Continuous Breeding Study

The effects of whole body exposure to 60-Hz magnetic fields on reproduction were assessed by the performance of a continuous breeding study in Sprague-Dawley rats. Reproductive assessment consists of four phases: dose finding, continuous breeding, identification of the affected sex, and offspring assessment. During the continuous breeding phase, the effects of the maximum tolerated exposure level estimated in the dose-finding phase and two lower exposure levels on fertility and reproduction are determined. If fertility is significantly affected during the continuous breeding phase, crossover mating trials are performed to determine if males, females, or both sexes are affected. Offspring assessment includes evaluation of reproductive performance of second-generation (F_1) animals from the final litters of the continuous breeding phase. The F_1 animals are raised to sexual maturity while receiving the same exposure levels as their parents, are mated, and are allowed to deliver the third-generation (F_2) offspring.

The magnetic field exposures in the continuous breeding study were the same as those in the 8-week toxicity study. Because overt toxicity was not expected, no short-term studies were conducted. Crossover mating trials were not conducted, as no exposure-related effects were found during the continuous breeding phase of the study.

The rats used in the continuous breeding study were obtained from Taconic Farms (Germantown, NY). Rats were 8 weeks old at receipt and were quarantined for 18 days prior to the beginning of the study. Blood samples were collected from male and female rats and analyzed for antibody titers to rodent viruses throughout the study; all serology results were negative.

For the continuous breeding phase, groups of 40 breeding pairs were exposed to 0, 0.02, 2, or 10 G (10 G exposure was intermittent or continuous). Rats were randomized into experimental groups and each sex was housed five per cage for 1 week; rats were then cohoused in pairs for 14 weeks during breeding. Dams were housed separately and males were housed in groups of five for a 3-week holding period to allow delivery of the final litters. During all phases of the study, rats were provided NIH-07 open formula diet (Zeigler Brothers, Gardeners, PA) in mash form and water *ad libitum*. Clinical findings, sire and dam body weights, fertility, number of litters per pair, number of live pups per litter, proportion of pups born alive, overall sex ratio of live pups, and pup body weight (total and per sex) within 24 hours of birth were recorded.

To assess the offspring of exposed animals, the final litter of rat pups produced by each breeding pair during the 3-week holding period was reared. Pup numbers and body weights and maternal body weights were measured during lactation. After weaning, two males and two females were removed from each litter and housed in pairs by sex under the same exposure conditions as their parents. At sexual maturity, 40 female rats from each group were cohoused in breeding pairs for 1 week with nonsibling males from the same exposure

group. After 7 days of cohousing, the pairs were separated and housed individually for at least 22 days. Clinical findings, sire and dam weights, pregnancy index, days to litter, number of live pups per litter (total and per sex), pup weights (total and per sex), and sex ratio were recorded. Further details of the study design and animal maintenance are given in Table 3.

At the end of each study phase, adult rats were necropsied and examined grossly. The adrenal glands, right cauda epididymis, right epididymis, kidneys, liver, ovaries, prostate gland, seminal vesicles, and right testis were weighed and then fixed in 10% neutral buffered formalin (ovaries and testes were fixed in Bouin's solution).

TABLE 3 Experimental Designs and Materials and Methods in the Studies of 60-Hz Magnetic Fields

Toxicity Study	Teratology Study	Continuous Breeding Study
EXPERIMENTAL DESIGN		
Study Laboratory IIT Research Institute (Chicago, IL)	IIT Research Institute (Chicago, IL)	IIT Research Institute (Chicago, IL)
Strain and Species F344/N rats B6C3F_1 mice	Sprague-Dawley rats	Sprague-Dawley rats
Animal Source Taconic Farms (Germantown, NY)	Taconic Farms (Germantown, NY)	F_0 – Taconic Farms (Germantown, NY) F_1 – bred at study laboratory
Route of Administration Whole body exposure to magnetic fields	Whole body exposure to magnetic fields	Whole body exposure to magnetic fields
Size of Study Groups 10 males and 10 females	55 pregnant females per exposure group 15 pregnant positive control females	F_0 and F_1 – 40 breeding pairs
Exposure Intensities Continuous exposure: 0, 0.02, 2, or 10 G, 18.5 hours per day, 7 days per week Intermittent exposure: 10 G (1 hour on and 1 hour off), 18.5 hours per day, 7 days per week	Same as in toxicity study	Same as in toxicity study
Duration of Exposure Rats: 58 or 59 days Mice: 56 or 57 days	Gestation days 6 through 19	F_0 – 18 weeks F_1 – perinatal exposure through weaning, then 12 to 14 weeks as adults
Date of First Exposure Rats: 1 September 1993 Mice: 2 September 1993	20-24 September 1993 and 18-22 October 1993	F_0 – 6-9 December 1993
Date of Last Exposure Rats: 28-29 October 1993 Mice: 27-28 October 1993	3-7 October 1993 1-4 November 1993	F_0 – April 1994 F_1 – August 1994
Date of Necropsy Rats: 28-29 October 1993 Mice: 27-28 October 1993	4-8 October 1993 and 1-5 November 1993	F_0 – April 1994 F_1 – August 1994
Type and Frequency of Observation Animals were observed twice daily and were weighed initially, weekly, and at the end of the study. Clinical observations were recorded weekly.	Animals were observed twice daily and were weighed on gestation days 0, 3, 5, 6, 9, 12, 15, 18, and 20. Clinical observations were recorded on gestation days 6 through 20 or on gestation days 11 through 20 (positive control).	Animals were observed twice daily. F_0 and F_1 rats were weighed on postpartum days 0, 4, 7, 14, and 21, and following the cohabitation period. F_0 rats were also weighed at the delivery of each litter, and F_1 rats were weighed prior to terminal sacrifice.

TABLE 3 Experimental Designs and Materials and Methods in the Studies of 60-Hz Magnetic Fields (continued)

Toxicity Study	Teratology Study	Continuous Breeding Study
Necropsy All core-study animals were necropsied. The following tissues were weighed: right adrenal gland, heart, right kidney, liver, lungs, right testis, and thymus.	Dams were necropsied on gestation day 20 and were subject to cesarean and gross necropsy to determine pregnancy status and the presence of lesions or abnormal conditions in the dams or fetuses. Fetuses, ovaries, and uterine horns were removed. Fetuses were examined for skeletal malformations.	At the end of each study phase, all adult animals were necropsied and the adrenal glands, right cauda epididymis, right epididymis, kidneys, liver, ovaries, prostate gland, seminal vesicles, and right testis were weighed.
Histopathology Histopathologic evaluations were performed on all core-study animals. The following tissues were evaluated microscopically: adrenal gland, brain, clitoral gland, esophagus, femur and marrow, gallbladder (mice), gross lesions and tissue masses, harderian gland, heart, large intestine (cecum, colon, rectum), small intestine (duodenum, jejunum, ileum), kidneys, liver, lungs, lymph nodes (mandibular and mesenteric), mammary gland, nasal cavity and turbinates, ovaries, pancreas, parathyroid glands, pituitary gland, preputial gland, prostate gland, salivary gland, seminal vesicle, spleen, stomach (forestomach and glandular stomach), testes (with epididymides), thymus, thyroid gland, trachea, urinary bladder, vagina, uterus, and Zymbal's gland.	None	None
Supplemental Evaluations ***Clinical Pathology*** After 7 weeks of exposure, blood was collected from the retroorbital sinus of rats under CO_2 anesthesia. *Hematology*: hematocrit; manual hematocrit; hemoglobin concentration; erythrocyte, reticulocyte, and nucleated erythrocyte counts; mean cell volume; mean cell hemoglobin; mean cell hemoglobin concentration; platelet count; and leukocyte count and differentials. *Clinical Chemistry*: urea nitrogen; creatinine; total protein; albumin; alanine aminotransferase; alkaline phosphatase; creatine kinase; sorbitol dehydrogenase; and bile acids.	None	None

TABLE 3 Experimental Designs and Materials and Methods in the Studies of 60-Hz Magnetic Fields (continued)

Toxicity Study	Teratology Study	Continuous Breeding Study
Supplemental Evaluations (continued) ***Pineal Gland Hormone Analyses*** Blood samples and pineal glands were collected after 10 weeks of exposure during the light cycle or the dark cycle (six male and six female rats and mice per group per cycle). Pineal gland hormone parameters included *N*-acetyl-transferase, 6-sulfatoxymelatonin (rats only), serum melatonin, and pineal gland melatonin.	None	None
ANIMAL MAINTENANCE		
Time Held Before Study 13 days	10 days	F_0 –18 days
Age When Study Began Rats: 6 weeks Mice: 6-7 weeks	8-9 weeks	11 weeks
Age When Killed 14-15 weeks (core study) 16-17 weeks (pineal gland hormone analyses)	11-12 weeks	F_0 – 29 weeks F_1 – 15-17 weeks
Method of Animal Distribution Animals were distributed randomly into groups of approximately equal body weights.	Same as toxicity study	Same as toxicity study
Diet NIH-07 Open Formula Diet (Zeigler Brothers, Inc., Gardeners, PA) in pellet form, and water (City of Chicago) were available *ad libitum*.	Same as toxicity study; feed in pellet or meal form.	Same as toxicity study; feed in pellet or meal form.
Animal Room Environment Male and female rats and female mice were housed five per cage and male mice were housed individually. The temperature was maintained at 71° ± 1.0° F and humidity was maintained at 47% ± 6.1%, with at least 10 air changes per hour. Fluorescent light was provided for 12 hours per day (5 a.m. to 5 p.m.).	During mating, males and females were housed in breeding pairs; mated females were housed individually for the remainder of the study. The temperature was maintained between 69° F and 73° F and the humidity was maintained between 46% and 50%, with at least 10 air changes per hour. Fluorescent light was provided for 12 hours per day.	Rats were housed as five per cage initially, as breeding pairs, and then as individual dams with litters, and males five per cage. The temperature was maintained between 69° F and 73° F and the humidity was maintained between 45% and 48%, with at least 10 air changes per hour. Fluorescent light was provided for 12 hours per day.

STATISTICAL METHODS

Two approaches were employed to assess the significance of pairwise comparisons between exposed and control groups in the analysis of continuous variables. Organ and body weight data, which are approximately normally distributed, were analyzed with the parametric multiple comparisons procedures of Williams (1971, 1972) or Dunnett (1955). Data that typically have skewed distributions (clinical chemistry, hematology, and pineal gland hormone data in the toxicity studies, and numbers of corpora lutea, implantations, resorptions, live and dead fetuses, and the sex ratios, in the teratology study) were analyzed with the nonparametric multiple comparisons methods of Shirley (1977) or Dunn (1964). In all studies, Jonckheere's test (Jonckheere, 1954) was used to assess the significance of dose-response trends and to determine whether a trend-sensitive test (Williams, Shirley) was more appropriate for comparisons than a test capable of detecting departures from monotonic dose response (Dunnett, Dunn). If the P value from Jonckheere's test was greater than or equal to 0.10, Dunn's or Dunnett's test was used rather than Shirley's or Williams' test.

The outlier test of Dixon and Massey (1951) was employed to detect extreme values. No value selected by the outlier test was eliminated unless it was at least twice the next largest value or at most half of the next smallest value. The extreme values chosen by the statistical test were subject to approval by the NTP personnel. In addition, values indicated by the laboratory report as being inadequate due to technical problems were eliminated from the analysis.

In the teratology study, the 0 G control and the positive control were compared with a *t*-test for all data but skeletal abnormalities. Skeletal abnormalities for exposed groups were analyzed by a chi-square test when the incidences were at least three greater than the 0 G control. Because 100% of the fetuses in the positive control group were malformed compared to 0% in the 0 G control and the significance was clear, no comparison was made between these two control groups.

In the continuous breeding study, the Cochran-Armitage test (Armitage, 1971) was used for proportional data (fertility and pregnancy indices) to analyze dose-related trends. Each exposure group was compared to the control group with a chi-square test (Conover, 1971). The number of litters and the number of live pups per litter were determined per fertile pair and then exposure group means were determined. The proportion of live pups was defined as the number of pups born alive divided by the total number of pups produced by each pair. The sex ratio was expressed as the number of male pups born alive divided by the total number of live pups born to each fertile pair. Least-square estimates of exposure group means adjusted for litter size were tested for pairwise equality by Dunnett's test (Dunnett, 1955); these tests were performed on males, females, and males and females combined to analyze potential sex differences.

QUALITY ASSURANCE

The animal studies of 60-Hz magnetic fields were performed in compliance with United States Food and Drug Administration Good Laboratory Practices regulations (21 CFR, Part 58). The Quality Assurance Unit of IIT Research Institute performed audits and inspections of protocols, procedures, data, and reports throughout the course of the studies.

RESULTS

8-WEEK STUDY IN F344/N RATS

One female rat exposed to 2 G died during the study (Table 4); though a complete necropsy and histopathologic examination failed to reveal a cause of death, this death was not considered to be related to exposure. Females exposed to 0.02 or 2 G had significantly lower final mean body weights and mean body weight gains than those of the control group (Table 4 and Figure 2); however, at necropsy body weights were similar (Table A1). There were no clinical findings of toxicity.

The absolute and relative liver weights of males exposed to 2 G and females exposed to 0.02, 2, or 10 G (intermittent or continuous) were significantly greater than those of the control groups (Table A1). The absolute right kidney weights of females exposed to 2 or 10 G (intermittent or continuous) were significantly greater than that of the control group.

There were no biologically significant effects of 60-Hz magnetic field exposure on hematology or clinical chemistry parameters (Tables B1 and B2). The daytime activity of *N*-acetyltransferase in supplemental male rats exposed to an intermittent 10 G field for 10 weeks was significantly higher than that in the control group; however, this result was not considered to be biologically significant.

No gross lesions or histopathologic findings were attributed to exposure to 60-Hz magnetic fields.

TABLE 4 Survival and Body Weights of F344/N Rats in the 8-Week Study of 60-Hz Magnetic Fields

Intensity (gauss)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
MALE					
0	10/10	121 ± 2	284 ± 4	163 ± 4	
0.02	10/10	120 ± 2	284 ± 3	163 ± 3	100
2	10/10	120 ± 3	283 ± 5	164 ± 4	100
10 intermittent	10/10	120 ± 2	290 ± 3	170 ± 3	102
10	10/10	121 ± 2	289 ± 5	168 ± 3	102
FEMALE					
0	10/10	103 ± 2	185 ± 2	82 ± 2	
0.02	10/10	102 ± 2	176 ± 3*	74 ± 2**	95
2	9/10[c]	104 ± 2	174 ± 3**	71 ± 1**	94
10 intermittent	10/10	104 ± 1	181 ± 1	77 ± 2	98
10	10/10	103 ± 2	183 ± 2	80 ± 1	99

* Significantly different ($P \leq 0.05$) from the control group by Dunnett's test
** $P \leq 0.01$
[a] Number of animals surviving at 8 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error.
[c] Week of death: 7

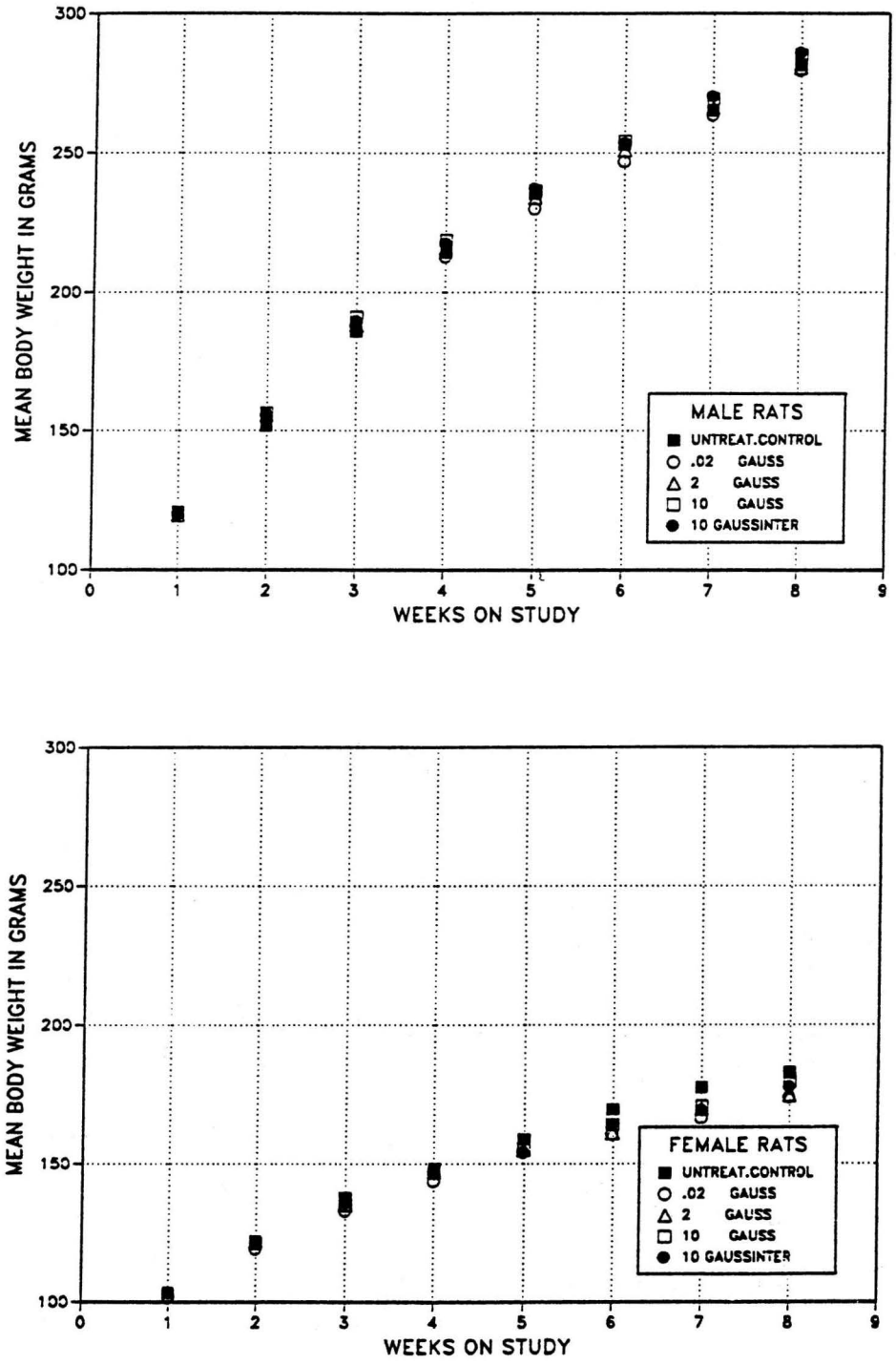

FIGURE 2 **Body Weights for Male and Female F344/N Rats Exposed to 60-Hz Magnetic Fields for 8 Weeks**

TERATOLOGY STUDY IN SPRAGUE-DAWLEY RATS

The gestational body weights and gravid uterine weights of exposed dams were similar to those of the control dams (Table 5). The numbers of pregnant females in exposed groups at the end of the study were lower than the number in the control group. Male and female fetuses exposed to 2 G had significantly lower mean body weights than those in the 0 G control group (Table 5). Male and female fetus weights in all exposed groups were significantly greater than those in the positive control group (Table 6). The incidence of variations in the thoracic/lumbar centrae in the 0.02 G exposure group was significantly less than that of the 0 G control group but was within normal limits (Table 7). None of these findings were considered biologically significant.

TABLE 5 Maternal Toxicity in Sprague-Dawley Rats Exposed to 60-Hz Magnetic Fields on Gestation Days 6 Through 19[a]

	0 G	Positive Control	0.02 G	2 G	10 G Intermittent	10 G
Number of sperm-positive females	55	15	55	55	55	55
Number pregnant at sacrifice	55 (100%)	15 (100%)	48 (87%)**	46 (84%)**	51 (93%)*	51 (93%)*
Number examined	55	15	48	46	51	51
Maternal body weight (g)						
Gestation day 0	204 ± 2	205 ± 4	204 ± 2	203 ± 2	205.4 ± 2.0	204 ± 2
Gestation day 3	222 ± 2	222 ± 5	222 ± 2	221 ± 2	223.1 ± 2.0	223 ± 2
Gestation day 5	233 ± 2	234 ± 4	233 ± 2	232 ± 2	233.2 ± 1.9	233 ± 2
Gestation day 6	238 ± 2	237 ± 4	236 ± 2	235 ± 2	235.7 ± 1.9	236 ± 2
Gestation day 9	253 ± 2	252 ± 4	251 ± 2	251 ± 2	251.7 ± 2.1	251 ± 2
Gestation day 12	272 ± 2	265 ± 5	269 ± 2	270 ± 2	269.4 ± 2.2	270 ± 2
Gestation day 15	295 ± 3	288 ± 5	290 ± 3	291 ± 3	290.4 ± 2.6	293 ± 3
Gestation day 18	335 ± 4	328 ± 7	328 ± 4	329 ± 4	328.6 ± 3.5	333 ± 3
Gestation day 20	366 ± 4	357 ± 8	360 ± 4	360 ± 5	358.9 ± 4.6	366 ± 4
Gravid uterine weight (g)	70.91 ± 3.05	68.08 ± 5.38	66.54 ± 3.36	70.57 ± 3.25	68.31 ± 3.32	73.25 ± 2.89
Extra-gestational weight gain (g)	295 ± 3	289 ± 5	293 ± 3	289 ± 3	291 ± 3	292 ± 3

* Significantly different from the 0 G control group (P 0.05) by a chi-square test
** Significantly different from the 0 G control group (P 0.01) by a chi-square test
[a] Mean ± standard error

TABLE 6 Developmental Toxicity in Sprague-Dawley Rats Following Maternal Exposure to 60-Hz Magnetic Fields on Gestation Days 6 Through 19[a]

	0 G	Positive Control	0.02 G	2 G	10 G Intermittent	10 G
Number of dams/litters examined	55	15	48	46	51	51
Corpora lutea left	7.02 ± 0.30	7.87 ± 0.48	6.66 ± 0.33[b]	7.20 ± 0.35[c]	6.80 ± 0.26[d]	7.28 ± 0.32[d]
Corpora lutea right	7.49 ± 0.30	6.60 ± 0.66	6.85 ± 0.39[b]	6.67 ± 0.33	7.00 ± 0.32[d]	6.64 ± 0.24[d]
Corpora lutea total	14.51 ± 0.37	14.47 ± 0.63	13.51 ± 0.51[b]	13.91 ± 0.48[c]	13.80 ± 0.40[d]	13.92 ± 0.33[d]
Implantations per dam	11.84 ± 0.51	12.40 ± 0.88	11.29 ± 0.55	12.35 ± 0.48	11.88 ± 0.52	12.22 ± 0.46
Preimplantation loss (%)	19.92 ± 2.82	15.06 ± 5.88	17.55 ± 3.28[b]	11.86 ± 2.25[c]	15.31 ± 3.15[d]	11.62 ± 2.10[d]
Resorptions per litter						
Early	0.509 ± 0.124	0.400 ± 0.131	0.625 ± 0.165	0.739 ± 0.180	0.667 ± 0.222	0.373 ± 0.148
Late	0.000 ± 0.000	0.067 ± 0.067	0.000 ± 0.000	0.022 ± 0.022	0.020 ± 0.020	0.000 ± 0.000
Dead fetuses per litter	0.000 ± 0.000	0.133 ± 0.133	0.000 ± 0.000	0.000 ± 0.000	0.020 ± 0.020	0.000 ± 0.000
Live fetuses per litter	11.33 ± 0.53	11.80 ± 0.95	10.67 ± 0.58	11.59 ± 0.54	11.18 ± 0.57	11.84 ± 0.51
Sex ratio (% males)	49.02 ± 2.02[e]	52.33 ± 6.12	45.67 ± 2.50	56.00 ± 2.12[f]	49.94 ± 2.90[d]	50.48 ± 2.45[d]
Male fetus weight (g)	4.32 ± 0.05	2.96 ± 0.08**	4.20 ± 0.05▲▲μ	4.14 ± 0.04*▲▲μ	4.20 ± 0.05▲▲μ	4.23 ± 0.04▲▲μ
Female fetus weight (g)	4.06 ± 0.05	2.79 ± 0.07**	4.00 ± 0.05▲▲μ	3.90 ± 0.04*▲▲μ	3.97 ± 0.03▲▲μ	4.02 ± 0.04▲▲μ
Combined fetus weight (g)	4.19 ± 0.05	2.90 ± 0.08**	4.09 ± 0.05▲▲μ	4.04 ± 0.03▲▲μ	4.10 ± 0.05▲▲μ	4.12 ± 0.04▲▲μ

* Significantly different (P 0.05) from the 0 G control by Dunnett's test
** Significantly different (P 0.01) from the 0 G control by a *t*-test
▲▲μSignificantly different (P 0.01) from the positive control by Williams' test (0.02 G, 2 G, 10 G intermittent, and 10 G)
[a] Mean ± the standard error
[b] n=47
[c] n=45
[d] n=50
[e] n=54
[f] n=44

TABLE 7 Skeletal Abnormalities Observed in Sprague-Dawley Rat Fetuses Following Maternal Exposure to 60-Hz Magnetic Fields on Gestation Days 6 Through 19[a]

	0 G	Positive Control	0.02 G	2 G	10 G Intermittent	10 G
Total live fetuses examined	622	177	511	533	569	604
Total litters examined	54	15	48	44	50	50
Skull[b]						
Fetuses affected	4	12	6	4	6	1
Litters affected	3	5	5	3	4	1
Affected fetuses (%)	1	14	2	1	2	0.3
Sternebrae						
Fetuses affected	28	80	25	39	40	31
Litters affected	16	14	18	19	25	19
Affected fetuses (%)	5	45	5	7	7	5
Thoracic/lumbar centrae						
Fetuses affected	82	121	104	79	98	88
Litters affected	37	15	34*	35	36	30
Affected fetuses (%)	13	68	20	15	17	15
Ribs						
Fetuses affected	88	11	53	44	49	51
Litters affected	31	6	21	21	19	26
Affected fetuses (%)	14	6	10	8	9	8
Pelvic girdle						
Fetuses affected	0	120	0	0	1	0
Litters affected	0	15	0	0	1	0
Affected fetuses (%)	0	68	0	0	0.2	0
Lumbar vertebrae						
Fetuses affected	0	0	6	0	0	0
Litters affected	0	0	2	0	0	0
Affected fetuses (%)	0	0	1	0	0	0
Sacral vertebrae						
Fetuses affected	0	168	0	1	0	0
Litters affected	0	15	0	1	0	0
Affected fetuses (%)	0	95	0	0.2	0	0
Total skeletal malformations						
Fetuses with malformations	0	177	0	0	0	0
Litters with malformations	0	15	0	0	0	0
Affected fetuses (%)	0	100	0	0	0	0

* Significantly different (P 0.05) from the 0 G control by a chi-square test

[a] Data are given as means

[b] All litters had fetuses with skulls examined; number of fetuses with skull examined: 0 G, 311; positive control, 87; 0.02 G, 247; 2 G, 267; 10 G intermittent, 284; 10 G , 308

CONTINUOUS BREEDING STUDY IN SPRAGUE-DAWLEY RATS

Continuous Breeding Phase

One dam in each of the 0.02 and 10 G continuous exposure groups died of parturition complications. In addition, one control male died during the holding period. Mean body weights of exposed rats were similar to those of the control groups (Table 8). Feed consumption by exposed rats was also similar to that by the control groups.

The fertility index, number of litters produced, average number of pups produced per pair, and number of days to litter were similar between exposed and control groups (Table 8). For the five successive litters, the number of pairs delivering and the number of live pups per litter in exposed groups were similar to those in the control group (Table 9). Male, female, and total live pup weights of exposed litters were similar to those of the controls. Survival and body weights of exposed F_1 pups were similar to those of control F_1 pups (Table 10). The relative liver weight of F_0 sires exposed to 10 G continuously was significantly greater than that of control sires (Table 11).

Offspring Assessment Phase

All F_1 rats survived to the end of the study. Mean body weights, pregnancy indexes, and days to litter of exposed groups were similar to those of the control group (Table 12). The number of pairs producing litters, number of pups per litter, number of live pups, and weight of pups produced in exposed groups were similar to those in the control group (Table 12). The absolute and relative adrenal gland weights of F_1 sires exposed to 10 G intermittently were significantly greater than those of the control group (Table 13).

TABLE 8 Fertility Data, Length of Gestation, and Body Weights for F_0 Sprague-Dawley Rats in the Continuous Breeding Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
Number of breeding pairs	40	40	40	40	40
Fertility index (litters produced/potential litters)	188/200	178/200	186/200	185/200	189/200
Average litters/pair	4.68 ± 0.47	4.45 ± 0.71	4.65 ± 0.77	4.63 ± 0.59	4.73 ± 0.55
Average number of pups/litter	11.3 ± 1.9	11.8 ± 2.1	11.5 ± 2.5	11.5 ± 2.3	11.4 ± 2.1
Cumulative days to litter					
Litter 1	35.8 ± 6.3	38.0 ± 9.7	35.6 ± 8.9	35.4 ± 7.5	34.7 ± 7.6
Litter 2	58.8 ± 6.5	61.5 ± 9.6	57.6 ± 6.2[b]	58.5 ± 7.6	57.7 ± 7.5
Litter 3	81.9 ± 6.5	84.4 ± 9.7[b]	81.8 ± 8.2[b]	81.5 ± 7.9	81.2 ± 7.9
Litter 4	106.4 ± 8.1	107.0 ± 7.5[c]	104.7 ± 7.4[d]	105.2 ± 7.2[d]	102.8 ± 3.9[d]
Litter 5	125.1 ± 1.9[e]	125.2 ± 1.7[f]	125.0 ± 1.5[g]	125.0 ± 1.8[h]	124.9 ± 1.5[i]
Sire weights (g)					
Pre-exposure body weight (g)	373 ± 3	375 ± 3	377 ± 3	371 ± 3	373 ± 4
Week 1 body weight (g)	388 ± 3	390 ± 4[b]	390 ± 4	394 ± 4	388 ± 4
Litter 1	463 ± 5	472 ± 5	470 ± 4	467 ± 6	466 ± 6
Litter 2	504 ± 6	514 ± 5	512 ± 5[b]	512 ± 6	505 ± 8
Litter 3	524 ± 7	539 ± 5[d]	540 ± 5[d]	537 ± 5[b]	528 ± 7[b]
Litter 4	558 ± 7[e]	556 ± 7[j]	564 ± 6[k]	555 ± 7[l]	543 ± 8[m]
Body weight at the end of cohousing (g)	560 ± 6	569 ± 6	576 ± 5	572 ± 6	558 ± 8
Terminal body weight	579 ± 7[b]	590 ± 6	593 ± 6	586 ± 7	580 ± 8
Dam weights (g)					
Pre-exposure body weight (g)	238 ± 2	235 ± 2	238 ± 2	235 ± 2	236 ± 2
Week 1 body weight (g)	245 ± 2	242 ± 2	247 ± 2	244 ± 2	244 ± 2
Litter 1	304 ± 3	307 ± 3	306 ± 3	307 ± 4	302 ± 3
Litter 2	334 ± 4	337 ± 4	338 ± 4[b]	336 ± 4	332 ± 3
Litter 3	361 ± 6	356 ± 4[d]	362 ± 5[d]	358 ± 4[b]	349 ± 3[b]
Litter 4	365 ± 8[e]	368 ± 6[j]	378 ± 6[k]	372 ± 6[l]	368 ± 3[m]
Litter 5	358 ± 5	356 ± 4[b]	367 ± 5	367 ± 5	361 ± 4[b]
Body weight at the end of cohousing (g)	374 ± 6	373 ± 6	375 ± 5	378 ± 6	372 ± 5
Terminal body weight	385 ± 6[b]	378 ± 5[n]	385 ± 7[c]	384 ± 5[c]	374 ± 4[n]

[a] Data for litters and pups per pair, cumulative days to litter, and sire and dam weights are given as mean ± standard error. Differences from the control group for fertility indexes are not significant by a chi-square test; differences from the control group for other parameters are not significant by Dunnett's (body weights only) or Dunn's test.

[b] n=39
[c] n=37
[d] n=38
[e] n=28
[f] n=22
[g] n=30
[h] n=27
[i] n=31
[j] n=24
[k] n=32
[l] n=29
[m] n=34
[n] n=36

TABLE 9 Litter Data and Body Weights of F_1 Sprague-Dawley Rat Pups in the Continuous Breeding Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
Litter 1					
Number of pairs delivering	40	40	40	40	40
Live pups/litter	12.8 ± 3.1	11.9 ± 3.3	11.8 ± 3.8	11.0 ± 4.1	12.4 ± 3.0
Live pups/litter (%)	99 ± 3	96 ± 10	96 ± 16	94 ± 20	98 ± 5
Male pup weight (g)	6.85 ± 0.09	6.99 ± 0.10	7.09 ± 0.09	7.00 ± 0.12	6.87 ± 0.09
Female pup weight (g)	6.52 ± 0.08	6.62 ± 0.09	6.70 ± 0.08	6.62 ± 0.09	6.47 ± 0.08
Total live pup weight (g)	6.66 ± 0.08	6.80 ± 0.10	6.91 ± 0.09	6.79 ± 0.09	6.67 ± 0.08
Litter 2					
Number of pairs delivering	40	40	39	40	40
Live pups/litter	11.6 ± 3.2	11.9 ± 3.4	12.4 ± 3.0	12.6 ± 3.4	12.6 ± 2.8
Live pups/litter (%)	98 ± 5	99 ± 3	97 ± 7	98 ± 6	99 ± 3
Male pup weight (g)	7.30 ± 0.09	7.21 ± 0.11	7.37 ± 0.09	7.14 ± 0.10	7.25 ± 0.11
Female pup weight (g)	6.93 ± 0.10	6.87 ± 0.11	7.01 ± 0.08	6.85 ± 0.07	6.88 ± 0.09
Total live pup weight (g)	7.12 ± 0.09	7.07 ± 0.11	7.18 ± 0.08	6.99 ± 0.08	7.06 ± 0.10
Litter 3					
Number of pairs delivering	40	38	38	39	39
Live pups/litter	11.5 ± 3.6	11.6 ± 3.0	12.1 ± 2.6	10.9 ± 2.8	10.6 ± 3.4
Live pups/litter (%)	95 ± 10	97 ± 5	97 ± 6	95 ± 9	97 ± 10
Male pup weight (g)	7.15 ± 0.11	7.30 ± 0.11	7.33 ± 0.08	7.09 ± 0.13	7.24 ± 0.09
Female pup weight (g)	6.76 ± 0.11	6.98 ± 0.10	6.92 ± 0.08	6.80 ± 0.11	6.80 ± 0.10
Total live pup weight (g)	6.96 ± 0.10	7.14 ± 0.10	7.11 ± 0.07	6.92 ± 0.11	7.01 ± 0.09
Litter 4					
Number of pairs delivering	28	24	32	29	34
Live pups/litter	9.6 ± 3.2	10.2 ± 3.2	11.1 ± 3.1	10.3 ± 4.0	9.8 ± 3.4
Live pups/litter (%)	95 ± 8	91 ± 19	96 ± 7	92 ± 19	96 ± 10
Male pup weight (g)	7.17 ± 0.12	7.19 ± 0.11	7.06 ± 0.12	6.95 ± 0.14	7.04 ± 0.11
Female pup weight (g)	6.88 ± 0.11	6.82 ± 0.13	6.72 ± 0.11	6.55 ± 0.13	6.73 ± 0.09
Total live pup weight (g)	7.04 ± 0.11	7.00 ± 0.11	6.91 ± 0.11	6.78 ± 0.13	6.86 ± 0.10
Litter 5					
Number of pairs delivering	39	36	37	37	36
Live pups/litter	8.9 ± 3.9	10.9 ± 2.8	8.8 ± 4.2	9.5 ± 4.0	9.9 ± 3.7
Live pups/litter (%)	96 ± 9	96 ± 10	93 ± 20	95 ± 12	92 ± 12
Male pup weight (g)	7.21 ± 0.09	7.24 ± 0.09	7.07 ± 0.09	6.97 ± 0.12	7.08 ± 0.09
Female pup weight (g)	6.78 ± 0.08	6.79 ± 0.09	6.77 ± 0.10	6.55 ± 0.11	6.70 ± 0.09
Total live pup weight (g)	7.00 ± 0.09	7.02 ± 0.08	6.93 ± 0.09	6.84 ± 0.11	6.85 ± 0.09
Litters 1 through 5					
Number of pairs delivering	40	40	40	40	40
Live pups/litter	11.0 ± 1.9	11.4 ± 2.2	11.1 ± 2.5	11.0 ± 2.4	11.1 ± 2.1
Live pups/litter (%)	97 ± 4	96 ± 6	96 ± 5	95 ± 8	97 ± 4
Sex ratio (%)	49.3 ± 1.1	48.0 ± 0.9	49.8 ± 1.1[b]	46.3 ± 1.3	48.9 ± 1.4
Male pup weight (g)	7.12 ± 0.44	7.15 ± 0.45	7.19 ± 0.39	7.03 ± 0.54	7.11 ± 0.46
Female pup weight (g)	6.77 ± 0.42	6.80 ± 0.44	6.82 ± 0.39[b]	6.69 ± 0.45	6.71 ± 0.40
Total live pup weight (g)	6.95 ± 0.41	6.98 ± 0.43	7.01 ± 0.38	6.86 ± 0.48	6.89 ± 0.42

[a] Mean ± standard error; differences from the control group are not significant by Dunn's test.
[b] n=39

TABLE 10 Survival and Body Weights of F_1 Sprague-Dawley Rat Pups (Final Litter) in the Continuous Breeding Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
Day 0					
Number of litters	39	36	37	37	36
Live pups/breeding pair (%)	96 ± 9	96 ± 10	93 ± 20	95 ± 12	92 ± 12
Male pup weight (g)	7.21 ± 0.09	7.24 ± 0.09	7.07 ± 0.09	6.97 ± 0.12	7.08 ± 0.09
Female pup weight (g)	6.78 ± 0.08	6.79 ± 0.09	6.77 ± 0.10	6.55 ± 0.11	6.70 ± 0.09
Day 4					
Total survival (%)	99.0 ± 0.5	99.3 ± 0.4	94.5 ± 2.9	95.1 ± 2.2	98.3 ± 0.8
Male pup weight (g)	12.8 ± 0.3	12.4 ± 0.3	12.3 ± 0.3	12.3 ± 0.3	12.1 ± 0.3
Female pup weight (g)	12.0 ± 0.3	11.6 ± 0.3	11.8 ± 0.3	11.6 ± 0.3	11.6 ± 0.3
Day 7					
Total survival (%)	97.7 ± 1.4	99.1 ± 0.4	93.3 ± 3.0	94.6 ± 2.2	97.9 ± 0.9
Male pup weight (g)	19.3 ± 0.6	17.8 ± 0.5	18.4 ± 0.5	18.1 ± 0.4	17.8 ± 0.5
Female pup weight (g)	18.1 ± 0.5	16.8 ± 0.5	17.9 ± 0.5	16.9 ± 0.5	17.3 ± 0.5
Day 14					
Total survival (%)	96.2 ± 2.6	99.1 ± 0.4	92.3 ± 3.1	93.9 ± 2.3	97.5 ± 0.9
Male pup weight (g)	35.1 ± 1.1	33.0 ± 0.8	34.6 ± 1.0	33.6 ± 0.8	32.5 ± 0.9
Female pup weight (g)	33.9 ± 0.9	31.7 ± 0.8	33.9 ± 1.0	32.6 ± 0.9	31.6 ± 0.8
Day 21					
Total survival (%)	96.2 ± 2.6	99.1 ± 0.4	91.3 ± 3.2	93.9 ± 2.3	97.5 ± 0.9
Male pup weight (g)	59.3 ± 1.8	57.2 ± 1.5	59.1 ± 1.8	58.0 ± 1.5	56.0 ± 1.7
Female pup weight (g)	57.1 ± 1.3	54.1 ± 1.3	57.8 ± 1.8	55.2 ± 1.6	53.8 ± 1.4

[a] Mean ± standard error; differences from the control group are not significantly different from the control group by Dunnett's test (pup weights) or Dunn's test (total survival).

TABLE 11 Organ Weights and Organ-Weight-to-Body-Weight Ratios for F_0 Sprague-Dawley Rats in the Continuous Breeding Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
SIRES					
n	39	40	40	40	40
Necropsy body wt	579 ± 7	590 ± 6	593 ± 6	586 ± 7	580 ± 8
Adrenal glands					
Absolute	0.049 ± 0.001	0.048 ± 0.001	0.049 ± 0.001	0.049 ± 0.001[b]	0.050 ± 0.001
Relative	0.08 ± 0.00	0.08 ± 0.00	0.08 ± 0.00	0.08 ± 0.00[b]	0.09 ± 0.00
Right cauda epididymis					
Absolute	0.283 ± 0.005	0.300 ± 0.006	0.292 ± 0.006	0.290 ± 0.006	0.288 ± 0.006
Relative	0.49 ± 0.01	0.51 ± 0.01	0.49 ± 0.01	0.50 ± 0.01	0.50 ± 0.01
Right epididymis					
Absolute	0.653 ± 0.009	0.648 ± 0.011	0.656 ± 0.010	0.642 ± 0.012	0.651 ± 0.012
Relative	1.13 ± 0.02	1.10 ± 0.02	1.11 ± 0.02	1.10 ± 0.02	1.13 ± 0.02
Kidneys					
Absolute	4.196 ± 0.085[c]	4.351 ± 0.084	4.345 ± 0.076	4.417 ± 0.078	4.365 ± 0.087
Relative	7.23 ± 0.11[c]	7.39 ± 0.14	7.33 ± 0.11	7.56 ± 0.13	7.55 ± 0.14
Liver					
Absolute	22.992 ± 0.467	24.518 ± 0.482	24.283 ± 0.422	24.068 ± 0.546	24.665 ± 0.515
Relative	39.67 ± 0.55	41.60 ± 0.71	40.97 ± 0.59	41.09 ± 0.82	42.51 ± 0.69*
Prostate gland					
Absolute	1.282 ± 0.039	1.330 ± 0.035	1.289 ± 0.039	1.304 ± 0.037	1.291 ± 0.047
Relative	2.22 ± 0.07	2.27 ± 0.07	2.18 ± 0.07	2.24 ± 0.07	2.23 ± 0.08
Seminal vesicles					
Absolute	2.225 ± 0.062[c]	2.259 ± 0.053	2.299 ± 0.054	2.254 ± 0.056	2.187 ± 0.074
Relative	3.85 ± 0.10[c]	3.85 ± 0.10	3.88 ± 0.08	3.88 ± 0.11	3.78 ± 0.13
Right testis					
Absolute	1.874 ± 0.024	1.894 ± 0.035	1.916 ± 0.040	1.888 ± 0.030	1.910 ± 0.033
Relative	3.25 ± 0.04	3.22 ± 0.06	3.25 ± 0.07	3.23 ± 0.05	3.31 ± 0.06
DAMS					
n	40	39	40	40	39
Necropsy body wt	358 ± 5	356 ± 4	367 ± 5	367 ± 5	361 ± 4
Adrenal glands					
Absolute	0.069 ± 0.002	0.073 ± 0.002	0.071 ± 0.002	0.069 ± 0.002	0.070 ± 0.002
Relative	0.19 ± 0.01	0.20 ± 0.00	0.19 ± 0.01	0.19 ± 0.01	0.19 ± 0.01
Kidneys					
Absolute	2.405 ± 0.035	2.437 ± 0.037	2.470 ± 0.035	2.473 ± 0.044	2.432 ± 0.035
Relative	6.73 ± 0.09	6.86 ± 0.09	6.75 ± 0.08	6.74 ± 0.11	6.74 ± 0.08
Liver					
Absolute	13.720 ± 0.195	13.861 ± 0.249	13.724 ± 0.276	14.157 ± 0.327	13.795 ± 0.252
Relative	38.43 ± 0.49	38.95 ± 0.54	37.44 ± 0.62	38.53 ± 0.75	38.29 ± 0.67
Ovaries					
Absolute	0.110 ± 0.002	0.116 ± 0.003	0.117 ± 0.003	0.113 ± 0.003	0.113 ± 0.003
Relative	0.31 ± 0.01	0.33 ± 0.01	0.32 ± 0.01	0.31 ± 0.01	0.31 ± 0.01

* Significantly different (P 0.05) from the control group by Dunnett's test

[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).

[b] n=39

[c] n=38

TABLE 12 Fertility, Reproductive Performance, and Body Weight Data for F_1 and F_2 Sprague-Dawley Rats in the Offspring Assessment Phase of the Continuous Breeding Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
F_1 ADULT DATA					
Number of breeding pairs	40	40	40	40	40
Sires					
Body weight at start of cohousing (g)	435 ± 6	434 ± 6	440 ± 8	440 ± 6	426 ± 6
Terminal body weight (g)	516 ± 6	514 ± 7	523 ± 8	519 ± 8	510 ± 8
Dams					
Body weight at start of cohousing (g)	281 ± 4	274 ± 4	280 ± 4	273 ± 5	268 ± 3
Pregnancy index[b]	35/40	33/40	35/40	34/40	33/40
Days to litter	25.2 ± 1.8[c]	24.8 ± 1.3[d]	24.7 ± 1.2[c]	24.9 ± 1.2[e]	25.0 ± 1.4[d]
Terminal body weight (g)	347 ± 4	336 ± 5	343 ± 5	337 ± 6	332 ± 5
F_2 PUP DATA					
Number of litters	35	33	35	34	33
Live male pups/litter	6.09 ± 2.38	6.52 ± 2.45	5.74 ± 1.98	6.62 ± 2.44	6.70 ± 2.24
Live female pups/litter	6.31 ± 2.46	6.21 ± 2.58	7.26 ± 2.35	5.79 ± 2.20	5.88 ± 2.13
Total live pups/litter	12.4 ± 3.7	12.7 ± 3.9	12.8 ± 2.8	12.2 ± 3.2	12.6 ± 2.9
Sex ratio (%)	49.1 ± 2.4	51.7 ± 2.3	44.8 ± 2.4[e]	53.6 ± 2.6[d]	53.2 ± 2.2
Live pups/litter (%)	95.1 ± 12.8	98.5 ± 3.5	99.0 ± 2.6	96.5 ± 9.6	98.8 ± 3.3
Male pup weight (g)	6.90 ± 0.52	6.92 ± 0.58	7.14 ± 0.60	6.98 ± 0.65	7.02 ± 0.61
Female pup weight (g)	6.51 ± 0.59	6.65 ± 0.63	6.80 ± 0.56[e]	6.70 ± 0.53[d]	6.66 ± 0.55
Total live pup weight (g)	6.70 ± 0.53	6.77 ± 0.56	6.95 ± 0.56	6.85 ± 0.56	6.85 ± 0.57

[a] Body weight data, days to litter, and live pups/litter are given as mean ± standard error. Differences from the control group for pregnancy indexes are not significant by a chi-square test. Differences from the control group for other parameters are not significant by Dunnett's test (F_1 rat body weights only) or Dunn's test.

[b] Litters produced/cohoused pairs

[c] n=35

[d] n=33

[e] n=34

TABLE 13 Organ Weights and Organ-Weight-to-Body-Weight Ratios for F_1 Sprague-Dawley Rats in the Continuous Breeding Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
SIRES					
n	40	40	40	40	40
Necropsy body wt	516 ± 6	514 ± 7	523 ± 8	519 ± 8	510 ± 8
Adrenal glands					
Absolute	0.045 ± 0.001[b]	0.049 ± 0.002[b]	0.049 ± 0.002[b]	0.052 ± 0.001**	0.048 ± 0.001
Relative	0.09 ± 0.00[b]	0.10 ± 0.00[b]	0.09 ± 0.00[b]	0.10 ± 0.00**	0.09 ± 0.00
Right cauda epididymis					
Absolute	0.264 ± 0.004	0.278 ± 0.005	0.275 ± 0.005	0.269 ± 0.005	0.272 ± 0.005
Relative	0.51 ± 0.01	0.54 ± 0.01	0.53 ± 0.01	0.52 ± 0.01	0.54 ± 0.01
Right epididymis					
Absolute	0.613 ± 0.009	0.626 ± 0.009	0.636 ± 0.009	0.617 ± 0.009	0.631 ± 0.011
Relative	1.19 ± 0.02	1.22 ± 0.02	1.22 ± 0.02	1.19 ± 0.02	1.24 ± 0.02
Kidneys					
Absolute	3.599 ± 0.049	3.552 ± 0.049	3.634 ± 0.063	3.616 ± 0.061	3.600 ± 0.066
Relative	6.98 ± 0.08	6.92 ± 0.08	6.96 ± 0.10	6.99 ± 0.10	7.05 ± 0.07
Liver					
Absolute	20.702 ± 0.376	20.365 ± 0.362	21.395 ± 0.367	20.673 ± 0.390	20.781 ± 0.405
Relative	40.09 ± 0.53	39.58 ± 0.44	40.94 ± 0.46	39.87 ± 0.51	40.68 ± 0.43
Prostate					
Absolute	1.017 ± 0.029	0.976 ± 0.033	1.010 ± 0.029	1.055 ± 0.036	1.066 ± 0.029
Relative	1.98 ± 0.06	1.91 ± 0.07	1.94 ± 0.05	2.05 ± 0.07	2.11 ± 0.06
Seminal vesicles					
Absolute	1.374 ± 0.061	1.383 ± 0.053	1.401 ± 0.050	1.365 ± 0.049	1.456 ± 0.046
Relative	2.66 ± 0.12	2.71 ± 0.11	2.69 ± 0.10	2.65 ± 0.10	2.87 ± 0.09
Right Testis					
Absolute	1.816 ± 0.028	1.887 ± 0.027	1.900 ± 0.031	1.893 ± 0.031	1.885 ± 0.028
Relative	3.54 ± 0.07	3.68 ± 0.05	3.65 ± 0.07	3.66 ± 0.06	3.71 ± 0.06
DAMS					
n	40	40	40	40	40
Necropsy body wt	347 ± 4	336 ± 5	343 ± 5	337 ± 6	332 ± 5
Adrenal glands					
Absolute	0.075 ± 0.002[c]	0.075 ± 0.002	0.078 ± 0.002	0.078 ± 0.002	0.077 ± 0.002
Relative	0.22 ± 0.01[c]	0.22 ± 0.01	0.23 ± 0.01	0.23 ± 0.01	0.23 ± 0.01
Kidneys					
Absolute	2.345 ± 0.034	2.334 ± 0.039	2.422 ± 0.037	2.347 ± 0.045	2.322 ± 0.035
Relative	6.77 ± 0.07	6.96 ± 0.10	7.07 ± 0.08	6.98 ± 0.09	7.01 ± 0.10
Liver					
Absolute	13.219 ± 0.249	13.149 ± 0.293	13.526 ± 0.211	12.741 ± 0.274	12.861 ± 0.242
Relative	38.12 ± 0.48	39.11 ± 0.66	39.46 ± 0.36	37.79 ± 0.44	38.72 ± 0.54
Ovaries					
Absolute	0.127 ± 0.003	0.128 ± 0.003	0.131 ± 0.004	0.130 ± 0.003	0.130 ± 0.004
Relative	0.37 ± 0.01	0.38 ± 0.01	0.38 ± 0.01	0.39 ± 0.01	0.39 ± 0.01

** Significantly different (P 0.01) from the control group by Dunnett's test

[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).

[b] n=39

[c] n=38

8-WEEK STUDY IN B6C3F$_1$ MICE

All mice exposed to 60-Hz magnetic fields survived until the end of the study (Table 14). The mean body weight gain of males exposed to 2 G was significantly less than that of the control group (Table 14 and Figure 3). The final mean body weight of females exposed to 10 G continuously was significantly greater than that of the control group. There were no clinical findings of toxicity or organ weight changes considered related to exposure to magnetic fields.

Pineal gland hormone activities of mice exposed to 60-Hz magnetic fields for 10 weeks were similar to those in the control groups (Table B4). No gross lesions or histopathologic findings were attributed to exposure to 60-Hz magnetic fields.

TABLE 14 Survival and Body Weights of B6C3F$_1$ Mice in the 8-Week Study of 60-Hz Magnetic Fields

Intensity (gauss)	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
MALE					
0	10/10	23.4 ± 0.3	33.4 ± 0.9	10.0 ± 0.7	
0.02	10/10	24.1 ± 0.3	32.9 ± 1.0	8.8 ± 0.8	98
2	10/10	23.9 ± 0.3	31.2 ± 0.6	7.3 ± 0.6*	93
10 intermittent	10/10	24.1 ± 0.2	31.7 ± 0.6	7.6 ± 0.7	95
10	10/10	24.0 ± 0.2	32.0 ± 0.7	8.0 ± 0.7	96
FEMALE					
0	10/10	19.6 ± 0.2	26.7 ± 0.8	7.2 ± 0.7	
0.02	10/10	19.5 ± 0.2	26.5 ± 0.6	7.0 ± 0.5	99
2	10/10	19.9 ± 0.4	27.9 ± 0.7	8.0 ± 0.5	104
10 intermittent	10/10	19.7 ± 0.2	26.5 ± 0.5	6.8 ± 0.4	99
10	10/10	20.3 ± 0.2	29.1 ± 0.4*	8.8 ± 0.5	109

* Significantly different (P 0.05) from the control group by Williams' or Dunnett's test
[a] Number of animals surviving at 8 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error.

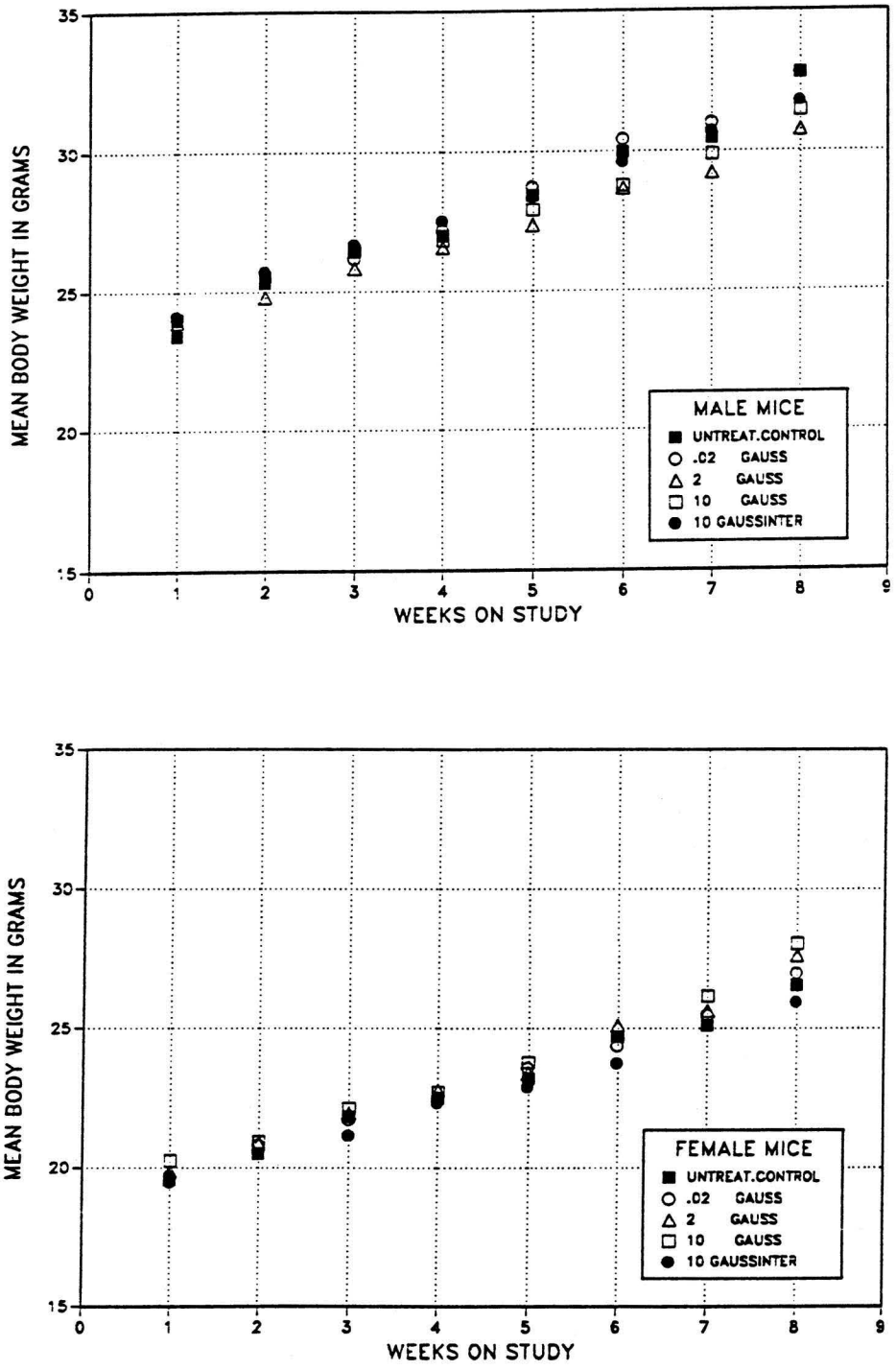

FIGURE 3 **Body Weights for Male and Female B6C3F$_1$ Mice Exposed to 60-Hz Magnetic Fields for 8 Weeks**

DISCUSSION

The generation, distribution, and use of electricity creates weak 60-Hz electric and magnetic fields that are ubiquitous. Potential exposures to electric and magnetic fields exist near power lines, near appliances and power tools in residential settings, in public transport systems, and in the workplace. The potential risk to humans from exposure to these fields is uncertain, in part because potential human exposure is so widespread. It is difficult to reconstruct human exposures during the 5 to 10 years that precede the development of cancer, and it is almost impossible to control for all the variables concerning human exposure (Savitz *et al.*, 1988, 1990; Bates, 1991; Savitz, 1993a,b; Savitz and Kaune, 1993; Savitz and Ananth, 1994).

Animal studies offer the possibility to carefully control many variables, and thus the Department of Energy and the Electric Power Research Institute requested that the NIEHS begin a series of animal studies to explore the possible toxic and carcinogenic effects of exposure to these fields. Because magnetic fields are complex and interactive, the studies used 60-Hz sine-wave magnetic fields, the major component of many human exposures.

The goal of the present studies was to evaluate the toxicity of the predominant field associated with the generation, transmission, and use of electricity (60 Hz) and when possible, to avoid the confounding factors of transients and harmonics. The magnetic field studies reported here include exposure of F344/N and Sprague-Dawley rats and B6C3F$_1$ mice to 60-Hz magnetic fields composed of nearly pure, linearly polarized sine waves with less than 3% harmonics. In addition, field production was begun at zero amplitude. To avoid transient effects, fields were turned on by gradually increasing the amplitude over 9 cycles (0.15 seconds), and similarly, when fields were shut off they were gradually decreased. Analyses of the fields indicate that the field parameters were within acceptable ranges throughout the study. The exposures were to field intensities that were as high as practicable (10,000 milligauss, 10 G) and for periods that were as long as practically consistent with good laboratory animal management (18.5 hours on; 5.5 hours off for animal maintenance). Since it is possible that changes in field intensity are important determinants of biological activity, one 10 G group included intermittent (1 hour on, 1 hour off) exposures. In this group, transient effects were avoided by gradually increasing or decreasing field intensity when the field was turned on or off.

Eight weeks was selected as a short-term exposure duration for general toxicology studies because this length of exposure would be adequate to produce alterations in physiological parameters, such as hematology or melatonin concentrations, and to produce signs of toxicity. Additional data concerning the potential toxicity of 60-Hz magnetic field exposure will be obtained through clinical observations, body weight measurements, and mortality rates during a 2-year study being conducted by the NTP.

In the eight-week toxicity study, exposure of male rats to 60-Hz magnetic fields had no effect on clinical signs, body weight, or survival. Female rats exposed to 0.02 or 2 G had lower final mean body weights than that of the control group. In the 0.02 G group this was due to the low body weight of one female. In the 2 G group, there was a decrease in mean body weight from week 7 to week 8. This did not occur in any other group and is consistent with a temporary interruption of the water supply to the cage rack. This is supported by the fact that body weights were similar for all groups at necropsy later in the same week. Further, there were no body weight changes in the male F344/N rats or in Sprague-Dawley rats in the teratology or continuous breeding study. At week 7, the 2 G group mean body weight was similar to that of the control group, further evidence that this decreased weight was a spurious result. Final mean body weights of male and female mice were similar to those of the control groups. These results suggest that 60-Hz magnetic field exposure has no effect on body weights of rats or mice at these field intensities.

In rats, the absolute and relative liver weights of males exposed to 2 G and of all groups of exposed females were significantly greater than those of the control groups. An organ weight difference restricted to a mid-exposure group, as with the increased liver weight in 2 G males, is usually of little toxicologic significance. It is possible that the average liver weight of the control females was low, because the liver weights of all exposed groups of females were similar. It should be noted that there were no histologic changes in the livers of these rats. In the Sprague-Dawley rats exposed during the continuous breeding study, there were no alterations in the liver weights (Table 11). No liver weight data from other studies using female F344/N rats exposed to magnetic fields for 8 weeks are available. In an initiation/promotion study in Sprague-Dawley rats, the body weight gains and relative liver weights of 50-Hz magnetic field-exposed rats were similar to those of control rats (Rannug *et al.*, 1993b). The magnetic field exposure either resulted in a slight reduction in size and number of focal lesions in the liver of Sprague-Dawley rats (Rannug *et al.*, 1993c) or had no effect (Rannug *et al.*, 1993b). Thus, the literature does not suggest an effect on liver weights with magnetic field exposure. In the present study, liver weights of exposed male and female mice were similar to those of the control groups.

In general, the hematology and clinical chemistry parameters of exposed rats were similar to those of their respective controls. Several reports that magnetic fields alter melatonin levels led to the analysis of daytime and nighttime blood and pineal gland melatonin concentrations. Some of these studies relied on perturbation of the earth's static field, while other studies used extremely low frequency alternating magnetic fields. For example, both hooded rats and albino rats show inhibition of nocturnal pineal melatonin synthesis with a 50-degree rotation of the earth's magnetic field horizontal component (Olcese and Reuss, 1986). Experimental inversion of the horizontal component of the natural magnetic field, performed at night, led to a significant decrease of pineal *N*-acetyltransferase activity (the rate-limiting enzyme in pineal gland melatonin biosynthesis) and pineal gland melatonin content in male Sprague-Dawley rats (Welker *et al.*, 1983). Results of other studies failed to demonstrate a decrease in pineal and serum melatonin concentrations with exposure to static magnetic

fields but have demonstrated decreased activity of *N*-acetyltransferase in the pineal gland (Lerchl *et al.*, 1990). Most of the reports of alterations in melatonin concentrations have involved exposure to static magnetic fields, circularly polarized magnetic fields, or rapid perturbation of the earth's magnetic field. There is very little evidence that pineal function in rats, mice, or humans is altered by exposure to linearly polarized 50- or 60-Hz magnetic fields; positive findings that have been reported have generally been observed in Siberian hamsters.

Exposure to 60-Hz electric fields caused decreased serum melatonin concentrations in adult rats (Wilson *et al.*, 1986; Grota *et al.*, 1994), and in rat pups exposed from conception to 23 days of age (Reiter *et al.*, 1988). Increased daytime melatonin concentrations occurred with 10-Hz magnetic field exposure (Jentsch *et al.*, 1993). Other studies reported decreased pineal and serum melatonin concentrations in rats exposed to circular, but not linear, polarized magnetic fields (Kato *et al.*, 1993, 1994a,b). The mechanisms whereby non-visible electromagnetic fields influence the melatonin-forming ability of the pineal gland are unknown; however, the cells of the retina may serve as magnetoreceptors (Martinez *et al.*, 1992; Reiter, 1993b). Pigmentation may play a role, as pigmented gerbils have no significant changes in pineal melatonin synthesis, while albino gerbils and Sprague-Dawley rats show decreases in pineal *N*-acetyltransferase activity and melatonin content following magnetic-field exposure (Stehle *et al.*, 1988). In another study, both albino rats (Sprague-Dawley) and pigmented rats (Long-Evans) exhibit melatonin suppression when exposed to alternating magnetic fields (Kato *et al.*, 1994b).

No biologically significant alterations in serum and pineal gland melatonin concentrations were observed in the current studies. Why these data differ from the literature findings is uncertain. The published literature for melatonin alterations appears most convincing for studies involving a rapid shift in the earth's magnetic field and less convincing for exposures involving alternating fields. There were also no alterations in serum and pineal gland melatonin concentrations or pineal gland *N*-acetyltransferase levels in the present studies. Our results include a single evaluation during daylight and a single nocturnal sample collected at the peak serum melatonin level for each sex and species; circadian rhythms for pineal function were established in F344/N rats and B6C3F$_1$ mice during a preliminary study. Thus, our results only suggest no alteration in peak melatonin levels. An alteration in the duration of the nocturnal melatonin secretion is possible; however, similar results were obtained for both male and female rats and mice in the present studies. Additional melatonin studies are underway in mice to determine whether there is an alteration in the duration of the nocturnal melatonin secretion.

No adverse effects of magnetic field exposure were observed in the teratology study in Sprague-Dawley rats; no gross, visceral, or skeletal abnormalities were found. In contrast, 100% of the fetuses were malformed in the positive control group exposed *in utero* to ethylenethiourea. This study, with over 3,000 fetuses examined,

suggests that exposure of Sprague-Dawley rats to 60-Hz magnetic fields of up to 10 G intensity does not cause birth defects.

Similarly, there were no observable effects of magnetic-field exposure in the continuous breeding study in Sprague-Dawley rats. The continuous breeding protocol is one of the more sensitive assays for detecting chemical toxicity in the male and female rat reproductive systems. After four consecutive matings and removal of the resulting pups, the pups from the fifth mating remained in the fields during lactation and growth; these F_1 offspring were mated to produce the F_2 generation. In this study, the number of breeding pairs, approximately 40 per field intensity, was large enough to detect minimal effects. Examination of over 10,000 pups in this study increased sensitivity. The results of this study suggest that exposure to 60-Hz magnetic fields of up to 10 G intensity does not cause reproductive effects in Sprague-Dawley rats.

In conclusion, exposure of male and female F344/N rats and B6C3F_1 mice to 60-Hz magnetic fields up to 10 G intensity for 8 weeks appeared to cause little or no toxicity. No developmental effects were observed in Sprague-Dawley rats exposed from days 6 to 19 of gestation, and reproductive effects were not observed in a 6-month continuous breeding study in Sprague-Dawley rats. The present studies only evaluated 60-Hz magnetic fields composed of pure sine waves and lacking transients or significant harmonics. Human residential and occupational exposure to electric and magnetic fields is very complex, and the lack of adverse effects in the present studies is insufficient, by itself, to determine the potential human health hazard of exposure to magnetic fields. These studies do, however, begin to limit the uncertainty associated with the generation, distribution, and use of electricity. A series of epidemiology, animal, and mechanistic studies is needed to answer this complicated biophysical issue.

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APPENDIX A
ORGAN WEIGHTS AND
ORGAN WEIGHT-TO-BODY-WEIGHT RATIOS

TABLE A1 Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 8-Week Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
MALE					
n	10	10	9[b]	10	10
Necropsy body wt	289 ± 4	289 ± 3	288 ± 6	293 ± 4	293 ± 5
Right adrenal gland					
Absolute	0.038 ± 0.001	0.039 ± 0.001	0.039 ± 0.001	0.038 ± 0.002	0.038 ± 0.002
Relative	0.13 ± 0.01	0.13 ± 0.00	0.13 ± 0.00	0.13 ± 0.01	0.13 ± 0.01
Heart					
Absolute	0.909 ± 0.014	0.915 ± 0.016	0.913 ± 0.013	0.912 ± 0.015	0.925 ± 0.020
Relative	3.15 ± 0.03	3.17 ± 0.04	3.18 ± 0.08	3.11 ± 0.03	3.16 ± 0.04
Right kidney					
Absolute	1.108 ± 0.026	1.116 ± 0.009	1.170 ± 0.032	1.128 ± 0.025	1.155 ± 0.025
Relative	3.84 ± 0.08	3.86 ± 0.03	4.05 ± 0.08	3.85 ± 0.05	3.94 ± 0.07
Liver					
Absolute	12.486 ± 0.247	13.368 ± 0.288	13.707 ± 0.453*	13.486 ± 0.335	13.274 ± 0.306
Relative	43.28 ± 0.64	46.26 ± 0.95	47.04 ± 1.31*	45.99 ± 0.64	45.31 ± 0.81
Lung					
Absolute	1.408 ± 0.040	1.421 ± 0.047	1.380 ± 0.062	1.468 ± 0.050	1.391 ± 0.044
Relative	4.90 ± 0.19	4.92 ± 0.15	4.71 ± 0.19	5.01 ± 0.15	4.75 ± 0.15
Right testis					
Absolute	1.334 ± 0.010	1.323 ± 0.017	1.324 ± 0.030	1.349 ± 0.019	1.326 ± 0.020
Relative	4.63 ± 0.06	4.58 ± 0.04	4.57 ± 0.07	4.60 ± 0.03	4.53 ± 0.04
Thymus					
Absolute	0.288 ± 0.011	0.293 ± 0.008	0.271 ± 0.009	0.278 ± 0.006	0.267 ± 0.009
Relative	1.00 ± 0.04	1.01 ± 0.02	0.94 ± 0.05	0.95 ± 0.02	0.91 ± 0.02

TABLE A1 Organ Weights and Organ-Weight-to-Body-Weight Ratios for F344/N Rats in the 8-Week Study of 60-Hz Magnetic Fields (continued)

	0 G	0.02 G	2 G	10 G Intermittent	10 G
FEMALE					
n	10	10	9[b]	9[b]	10
Necropsy body wt	176 ± 4	180 ± 4	181 ± 3	182 ± 2	183 ± 2
Right adrenal gland					
Absolute	0.045 ± 0.002	0.046 ± 0.002	0.046 ± 0.002	0.046 ± 0.002	0.047 ± 0.002
Relative	0.26 ± 0.01	0.25 ± 0.01	0.26 ± 0.01	0.25 ± 0.01	0.26 ± 0.01
Heart					
Absolute	0.616 ± 0.009	0.607 ± 0.011	0.609 ± 0.012	0.623 ± 0.008	0.622 ± 0.008
Relative	3.52 ± 0.08	3.38 ± 0.07	3.37 ± 0.04	3.42 ± 0.04	3.40 ± 0.04
Right kidney					
Absolute	0.654 ± 0.012	0.699 ± 0.022	0.703 ± 0.019*	0.712 ± 0.017*	0.713 ± 0.010*
Relative	3.74 ± 0.11	3.87 ± 0.06	3.89 ± 0.09	3.91 ± 0.08	3.90 ± 0.04
Liver					
Absolute	6.165 ± 0.283	6.947 ± 0.144**	7.152 ± 0.100**	7.134 ± 0.157**	7.220 ± 0.089**
Relative	34.93 ± 0.91	38.62 ± 0.64**	39.63 ± 0.51**	39.12 ± 0.53**	39.49 ± 0.42**
Lung					
Absolute	1.077 ± 0.054	1.065 ± 0.037	1.102 ± 0.093	1.023 ± 0.047	1.022 ± 0.015
Relative	6.16 ± 0.36	5.93 ± 0.22	6.13 ± 0.53	5.61 ± 0.22	5.59 ± 0.10
Thymus					
Absolute	0.256 ± 0.012	0.260 ± 0.008	0.256 ± 0.008	0.267 ± 0.009	0.271 ± 0.010
Relative	1.46 ± 0.05	1.45 ± 0.05	1.42 ± 0.04	1.47 ± 0.05	1.48 ± 0.05

* Significantly different (P 0.05) from the control group by Williams' or Dunnett's test
** P 0.01
[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).
[b] Histopathology performed on 10 animals

TABLE A2 Organ Weights and Organ-Weight-to-Body-Weight Ratios for B6C3F$_1$ Mice in the 8-Week Study of 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
MALE					
n	10	10	10	10	10
Necropsy body wt	32.7 ± 0.9	33.4 ± 0.9	30.5 ± 0.5	31.9 ± 0.8	31.5 ± 0.5
Right adrenal gland					
Absolute	0.007 ± 0.001	0.006 ± 0.001	0.008 ± 0.001	0.007 ± 0.001	0.009 ± 0.001
Relative	0.21 ± 0.03	0.19 ± 0.02	0.27 ± 0.03	0.21 ± 0.03	0.29 ± 0.03
Heart					
Absolute	0.151 ± 0.004	0.159 ± 0.006	0.144 ± 0.005	0.149 ± 0.003	0.147 ± 0.003
Relative	4.63 ± 0.11	4.77 ± 0.14	4.71 ± 0.13	4.71 ± 0.20	4.68 ± 0.08
Right kidney					
Absolute	0.291 ± 0.007	0.300 ± 0.008	0.284 ± 0.008	0.284 ± 0.009	0.299 ± 0.006
Relative	8.94 ± 0.22	9.00 ± 0.12	9.30 ± 0.26	8.91 ± 0.25	9.51 ± 0.16
Liver					
Absolute	1.551 ± 0.054	1.693 ± 0.055	1.508 ± 0.041	1.563 ± 0.053	1.531 ± 0.057
Relative	47.48 ± 1.09	50.72 ± 0.81	49.37 ± 1.06	49.01 ± 1.28	48.61 ± 1.48
Lung					
Absolute	0.194 ± 0.014	0.247 ± 0.021	0.219 ± 0.016	0.248 ± 0.015	0.225 ± 0.014
Relative	5.94 ± 0.39	7.34 ± 0.50	7.15 ± 0.47	7.82 ± 0.51*	7.19 ± 0.50
Right testis					
Absolute	0.117 ± 0.001	0.121 ± 0.004	0.118 ± 0.002	0.117 ± 0.004	0.119 ± 0.003
Relative	3.59 ± 0.09	3.63 ± 0.11	3.88 ± 0.07	3.67 ± 0.11	3.79 ± 0.08
Thymus					
Absolute	0.042 ± 0.004	0.049 ± 0.004	0.041 ± 0.004	0.045 ± 0.005	0.042 ± 0.005
Relative	1.28 ± 0.12	1.45 ± 0.11	1.33 ± 0.13	1.41 ± 0.15	1.32 ± 0.14

TABLE A2 Organ Weights and Organ-Weight-to-Body-Weight Ratios for B6C3F$_1$ Mice in the 8-Week Study of 60-Hz Magnetic Fields (continued)

	0 G	0.02 G	2 G	10 G Intermittent	10 G
FEMALE					
n	10	10	10	10	10
Necropsy body wt	26.6 ± 0.9	26.4 ± 0.5	27.0 ± 0.8	26.2 ± 0.6	28.5 ± 0.5
Right adrenal gland					
Absolute	0.010 ± 0.001	0.012 ± 0.001	0.011 ± 0.001	0.010 ± 0.001	0.011 ± 0.001
Relative	0.37 ± 0.05	0.45 ± 0.04	0.41 ± 0.03	0.39 ± 0.04	0.39 ± 0.02
Heart					
Absolute	0.125 ± 0.003	0.128 ± 0.003	0.129 ± 0.003	0.124 ± 0.002	0.129 ± 0.003
Relative	4.71 ± 0.09	4.86 ± 0.06	4.81 ± 0.15	4.76 ± 0.11	4.55 ± 0.13
Right kidney					
Absolute	0.187 ± 0.008	0.200 ± 0.005	0.199 ± 0.004	0.198 ± 0.002	0.204 ± 0.004
Relative	7.03 ± 0.16	7.59 ± 0.10	7.41 ± 0.20	7.60 ± 0.16*	7.18 ± 0.16
Liver					
Absolute	1.314 ± 0.069	1.244 ± 0.031	1.306 ± 0.031	1.309 ± 0.022	1.437 ± 0.043
Relative	49.24 ± 1.36	47.24 ± 1.00	48.54 ± 1.07	50.15 ± 0.73	50.46 ± 1.03
Lung					
Absolute	0.208 ± 0.013	0.174 ± 0.003	0.197 ± 0.009	0.180 ± 0.005	0.232 ± 0.016
Relative	7.80 ± 0.34	6.61 ± 0.09	7.34 ± 0.35	6.91 ± 0.23	8.15 ± 0.56
Thymus					
Absolute	0.045 ± 0.003	0.051 ± 0.002	0.053 ± 0.004	0.051 ± 0.003	0.051 ± 0.002
Relative	1.69 ± 0.10	1.93 ± 0.09	1.95 ± 0.13	1.96 ± 0.15	1.80 ± 0.06

* Significantly different (P 0.05) from the control group by Dunnett's test

[a] Organ weights and body weights are given in grams; organ-weight-to-body-weight ratios are given as mg organ weight/g body weight (mean ± standard error).

APPENDIX B
HEMATOLOGY, CLINICAL CHEMISTRY, AND PINEAL GLAND HORMONE RESULTS

TABLE B1 Hematology Data for F344/N Rats After 7 Weeks of Exposure to 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
MALE					
n	10	9	10	10	10
Hematocrit (%)	47.9 ± 1.0	47.9 ± 0.5	48.5 ± 0.5	48.1 ± 0.4	47.3 ± 0.6
Manual hematocrit (%)	49.0 ± 0.7	49.1 ± 0.6[b]	49.9 ± 0.4	47.3 ± 0.7	48.5 ± 0.4
Hemoglobin (g/dL)	16.6 ± 0.3	16.9 ± 0.1	16.8 ± 0.2	16.7 ± 0.1	16.5 ± 0.2
Erythrocytes ($10^6/\mu L$)	9.02 ± 0.18	9.05 ± 0.10	9.15 ± 0.10	9.06 ± 0.11	8.97 ± 0.11
Reticulocytes ($10^6/\mu L$)	0.15 ± 0.02	0.16 ± 0.02	0.21 ± 0.02	0.25 ± 0.02**	0.19 ± 0.02
Nucleated erythrocytes ($10^3/\mu L$)	0.09 ± 0.04	0.03 ± 0.02	0.05 ± 0.03	0.04 ± 0.02	0.06 ± 0.03
Mean cell volume (fL)	53.1 ± 0.2	53.0 ± 0.2	53.1 ± 0.3	53.1 ± 0.2	52.8 ± 0.2
Mean cell hemoglobin (pg)	18.4 ± 0.1	18.7 ± 0.1	18.4 ± 0.1	18.4 ± 0.1	18.4 ± 0.2
Mean cell hemoglobin concentration (g/dL)	34.8 ± 0.2	35.2 ± 0.2	34.6 ± 0.1	34.6 ± 0.2	34.9 ± 0.2
Platelets ($10^3/\mu L$)	816.1 ± 18.3	873.2 ± 16.2	815.5 ± 13.1	813.3 ± 17.0	822.1 ± 11.8
Leukocytes ($10^3/\mu L$)	12.24 ± 0.97	11.71 ± 0.82	12.67 ± 1.10	12.85 ± 0.65	11.68 ± 0.68
Segmented neutrophils ($10^3/\mu L$)	0.99 ± 0.16	1.29 ± 0.13	1.47 ± 0.18	1.30 ± 0.16	1.18 ± 0.13
Lymphocytes ($10^3/\mu L$)	10.77 ± 0.85	9.99 ± 0.71	10.65 ± 1.01	10.97 ± 0.49	10.03 ± 0.58
Monocytes ($10^3/\mu L$)	0.39 ± 0.08	0.37 ± 0.12	0.43 ± 0.09	0.48 ± 0.13	0.37 ± 0.07
Eosinophils ($10^3/\mu L$)	0.09 ± 0.03	0.04 ± 0.02	0.12 ± 0.03	0.09 ± 0.03	0.09 ± 0.04
FEMALE					
n	10	10	10	10	10
Hematocrit (%)	47.7 ± 0.3	47.1 ± 0.6	47.5 ± 0.3	48.4 ± 0.3	47.8 ± 0.6
Manual hematocrit (%)	47.1 ± 0.2	46.6 ± 0.3	47.5 ± 0.2	47.5 ± 0.6	47.5 ± 0.4
Hemoglobin (g/dL)	16.0 ± 0.1	15.7 ± 0.2	16.0 ± 0.1	16.0 ± 0.1	16.0 ± 0.2
Erythrocytes ($10^6/\mu L$)	8.32 ± 0.07	8.22 ± 0.10	8.33 ± 0.05	8.42 ± 0.08	8.36 ± 0.10
Reticulocytes ($10^6/\mu L$)	0.23 ± 0.03	0.20 ± 0.02	0.22 ± 0.02	0.20 ± 0.01	0.20 ± 0.05
Nucleated erythrocytes ($10^3/\mu L$)	0.08 ± 0.03	0.10 ± 0.03	0.07 ± 0.02	0.18 ± 0.05	0.15 ± 0.04
Mean cell volume (fL)	57.3 ± 0.2	57.3 ± 0.3	57.0 ± 0.2	57.6 ± 0.3	57.2 ± 0.4
Mean cell hemoglobin (pg)	19.3 ± 0.1	19.1 ± 0.1	19.2 ± 0.1	19.0 ± 0.1	19.1 ± 0.1
Mean cell hemoglobin concentration (g/dL)	33.6 ± 0.2	33.5 ± 0.3	33.7 ± 0.2	33.0 ± 0.2	33.5 ± 0.3
Platelets ($10^3/\mu L$)	830.2 ± 16.0	846.8 ± 17.9	844.1 ± 15.5	857.3 ± 17.4	862.7 ± 11.7
Leukocytes ($10^3/\mu L$)	10.79 ± 0.83	11.26 ± 0.33	11.18 ± 0.46	10.74 ± 0.77	11.20 ± 0.41
Segmented neutrophils ($10^3/\mu L$)	1.06 ± 0.12	1.23 ± 0.14	1.10 ± 0.11	0.89 ± 0.10	1.23 ± 0.14
Lymphocytes ($10^3/\mu L$)	9.50 ± 0.76	9.82 ± 0.27	9.84 ± 0.44	9.53 ± 0.68	9.69 ± 0.46
Monocytes ($10^3/\mu L$)	0.15 ± 0.04	0.14 ± 0.05	0.14 ± 0.05	0.23 ± 0.04	0.16 ± 0.06
Eosinophils ($10^3/\mu L$)	0.04 ± 0.02	0.06 ± 0.03	0.10 ± 0.04	0.08 ± 0.03	0.09 ± 0.03

** Significantly different (P 0.01) from the control group by Dunn's test
[a] Mean ± standard error; statistical tests were performed on unrounded data.
[b] n=10

TABLE B2 Clinical Chemistry Data for F344/N Rats After 7 Weeks of Exposure to 60-Hz Magnetic Fields[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
n	10	10	10	10	10
MALE					
Urea nitrogen (mg/dL)	23.1 ± 0.5	24.8 ± 0.4	24.2 ± 0.7	23.2 ± 0.3	22.3 ± 0.4
Creatinine (mg/dL)	0.59 ± 0.02	0.61 ± 0.04	0.66 ± 0.04	0.63 ± 0.03	0.59 ± 0.02
Total protein (g/dL)	6.9 ± 0.1	6.9 ± 0.1	6.7 ± 0.1	6.8 ± 0.1	6.8 ± 0.1
Albumin (g/dL)	4.9 ± 0.1	4.9 ± 0.1	4.8 ± 0.1	4.9 ± 0.1	4.9 ± 0.1
Alanine aminotransferase (IU/L)	64 ± 7	62 ± 9	58 ± 6	59 ± 7	53 ± 3
Alkaline phosphatase (IU/L)	356 ± 8	358 ± 12	348 ± 7	357 ± 6	356 ± 7
Creatine kinase (IU/L)	300 ± 32	333 ± 67	246 ± 20	359 ± 90	327 ± 70
Sorbitol dehydroginase (IU/L)	36 ± 6	32 ± 7	32 ± 5	30 ± 5	27 ± 2
Bile acids (μmol/L)	26.5 ± 3.6	23.1 ± 3.0	22.0 ± 1.7	27.6 ± 2.8	22.1 ± 1.7
FEMALE					
Urea nitrogen (mg/dL)	20.8 ± 0.5	20.4 ± 0.6	21.6 ± 0.6	20.5 ± 0.7	21.4 ± 0.6
Creatinine (mg/dL)	0.63 ± 0.02	0.59 ± 0.02	0.60 ± 0.03	0.60 ± 0.01	0.62 ± 0.02
Total protein (g/dL)	6.6 ± 0.1	6.6 ± 0.1	6.7 ± 0.1	6.7 ± 0.1	6.9 ± 0.1
Albumin (g/dL)	4.9 ± 0.1	4.9 ± 0.1	5.0 ± 0.1	5.0 ± 0.1	5.1 ± 0.1*
Alanine aminotransferase (IU/L)	37 ± 1	41 ± 3	40 ± 1	37 ± 1	41 ± 2
Alkaline phosphatase (IU/L)	293 ± 5	304 ± 11	303 ± 11	288 ± 8	277 ± 7
Creatine kinase (IU/L)	258 ± 58	223 ± 27	370 ± 117	202 ± 18	254 ± 22
Sorbitol dehydrogenase (IU/L)	24 ± 1	25 ± 1	24 ± 1	23 ± 1	28 ± 3
Bile acids (μmol/L)	26.0 ± 2.9	25.6 ± 2.8	26.0 ± 2.8	26.1 ± 2.5	33.4 ± 6.1

* Significantly different (P 0.05) from the control group by Shirley's test
[a] Mean ± standard error; statistical tests were performed on unrounded data.

TABLE B3 Pineal Gland Hormone Data for F344/N Rats Exposed to 60-Hz Magnetic Fields for 10 Weeks[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
n	6	6	6	6	6
MALE					
Daytime					
N-acetyltransferase (pg/pineal gland)	6.35 ± 2.20	19.42 ± 5.47	11.98 ± 4.08	24.59 ± 5.41*	13.26 ± 4.65
6-Sulfatoxymelatonin (pg/mL serum)	29.20 ± 2.01	29.75 ± 1.91	28.29 ± 0.45	32.26 ± 1.57	30.29 ± 2.80
Melatonin (pg/mL serum)	15.49 ± 4.43	14.67 ± 2.96	15.98 ± 1.01	12.08 ± 2.05	15.43 ± 2.01
Melatonin (pg/pineal gland)	169.2 ± 35.3	175.1 ± 21.7	153.8 ± 23.0	172.1 ± 24.1	175.2 ± 16.4
Nighttime					
N-acetyltransferase (pg/pineal gland)	837.5 ± 115	647.3 ± 160	892.1 ± 152	597.7 ± 127	700.6 ± 230
6-Sulfatoxymelatonin (pg/mL serum)	82.17 ± 4.08	87.59 ± 5.89	87.71 ± 5.83	78.66 ± 1.82	78.70 ± 2.68
Melatonin (pg/mL serum)	50.83 ± 3.40	49.16 ± 6.36	64.58 ± 9.22	52.71 ± 2.80	49.90 ± 4.64
Melatonin (pg/pineal gland)	9,236 ± 474	7,707 ± 1,793	9,254 ± 1,011	6,953 ± 1,311	6,142 ± 1,485
FEMALE					
Daytime					
N-acetyltransferase (pg/pineal gland)	26.40 ± 6.46	21.40 ± 9.33	10.33 ± 4.17	18.84 ± 5.12	49.26 ± 20.06
6-Sulfatoxymelatonin (pg/mL serum)	24.24 ± 1.16	24.83 ± 0.76	25.40 ± 1.38	25.18 ± 0.76	24.24 ± 1.11
Melatonin (pg/mL serum)	16.75 ± 2.42	17.89 ± 1.03	16.49 ± 0.80	16.72 ± 1.41	16.69 ± 0.44
Melatonin (pg/pineal gland)	73.53 ± 10.33	124.77 ± 29.11	94.20 ± 19.64	79.23 ± 18.40	107.03 ± 12.80
Nighttime					
N-acetyltransferase (pg/pineal gland)	673.0 ± 128	1,017.2 ± 66	740.0 ± 211	619.6 ± 115	1,098.7 ± 209
6-Sulfatoxymelatonin (pg/mL serum)	59.07 ± 4.65	60.67 ± 2.55	62.04 ± 3.13	62.11 ± 2.01	60.66 ± 2.37
Melatonin (pg/mL serum)	86.64 ± 5.29	83.84 ± 10.96	92.86 ± 9.49	76.61 ± 11.22	85.18 ± 9.52
Melatonin (pg/pineal gland)	8,123 ± 708	9,995 ± 541	8,483 ± 1,601	6,987 ± 1,243	7,599 ± 1,479

* Significantly different (P 0.05) from the control group by Dunn's test
[a] Mean ± standard error; statistical tests were performed on unrounded data.

TABLE B4 Pineal Gland Hormone Data for B6C3F$_1$ Mice Exposed to 60-Hz Magnetic Fields for 10 Weeks[a]

	0 G	0.02 G	2 G	10 G Intermittent	10 G
n	6	6	6	6	6
MALE					
Daytime					
N-acetyltransferase (pg/pineal gland)	10.03 ± 3.20[b]	11.20 ± 2.17	3.75 ± 0.90[b]	5.85 ± 1.61	11.39 ± 3.00
Melatonin (pg/mL serum)	67.52 ± 6.76	58.22 ± 3.69	50.17 ± 6.37	56.63 ± 8.39	65.43 ± 3.51
Melatonin (pg/pineal gland)	59.35 ± 18.17[b]	58.63 ± 9.57	76.70 ± 11.58[c]	32.26 ± 6.58	62.35 ± 9.32
Nighttime					
N-acetyltransferase (pg/pineal gland)	19.80 ± 1.45	22.89 ± 3.66	20.66 ± 2.99	21.69 ± 2.24	18.52 ± 1.62
Melatonin (pg/mL serum)	104.6 ± 6.2	108.5 ± 7.1	132.1 ± 27.1	110.8 ± 5.7	119.3 ± 5.8
Melatonin (pg/pineal gland)	197.9 ± 11.4	194.4 ± 26.4	175.4 ± 24.1	189.7 ± 24.3	146.0 ± 26.9
FEMALE					
Daytime					
N-acetyltransferase (pg/pineal gland)	15.51 ± 10.38[b]	5.03 ± 1.87[c]	4.69 ± 2.12[c]	9.37 ± 3.57[b]	9.35 ± 2.89[c]
Melatonin (pg/mL serum)	79.54 ± 3.20	65.19 ± 4.49	84.45 ± 8.12	65.82 ± 7.82	63.77 ± 6.03
Melatonin (pg/pineal gland)	72.98 ± 7.76	61.76 ± 14.41	53.07 ± 11.16	61.88 ± 13.55	57.13 ± 15.52
Nighttime					
N-acetyltransferase (pg/pineal gland)	15.44 ± 1.87	16.29 ± 1.93	20.68 ± 2.10	15.51 ± 3.81	15.55 ± 1.59
Melatonin (pg/mL serum)	118.3 ± 13.0	127.4 ± 7.5	175.5 ± 22.0	155.0 ± 18.9	136.4 ± 4.6
Melatonin (pg/pineal gland)	179.6 ± 24.6	214.9 ± 9.7	204.9 ± 34.3	194.0 ± 27.0	214.1 ± 41.2

[a] Mean ± standard error; statistical tests were performed on unrounded data. Differences from the control group were not significant by Dunn's test.
[b] n=5
[c] n=4